Horizon 2020

Call: H2020-MSCA-ITN-2016

(Marie Skłodowska-Curie Innovative Training Networks)

Topic: MSCA-ITN-2016

Type of action: MSCA-ITN-ETN

(European Training Networks)

Proposal number: 721906

Proposal acronym: TRACT

Deadline Id: H2020-MSCA-ITN-2016

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How to fill in the forms?

The administrative forms must be filled in for each proposal using the templates available in the submission system. Some data fields in the administrative forms are pre-filled based on the previous steps in the submission wizard.

This proposal version was submitted by **Daniela ZISTERER** on **11/01/2016 17:32:48** Brussels Local Time. Issued by the Participant Portal Submission Service.

Proposal ID **721906** *Acronym* **TRACT**

1 - General information

Topic	MSCA-ITN-2016
Call Identifier	H2020-MSCA-ITN-2016
Type of Action	MSCA-ITN-ETN
Deadline Id	H2020-MSCA-ITN-2016

Acronym	TRACT
Proposal title	Training in Cancer Mechanisms and Therapeutics

Note that for technical reasons, the following characters are not accepted in the Proposal Title and will be removed: < > " &

Duration in months	*48*
Panel	LIF

Please select up to 5 descriptors (and at least 1) that best characterise the subject of your proposal, in descending order of relevance. Note that descriptors will be used to support REA services in identifying the best qualified evaluators for your proposal.

Descriptor 1	*Cancer and its biological basis*	Add	
Descriptor 2	*Metabolism, biological basis of metabolism related disord*	Add	Remove
Descriptor 3	*Pharmacology, pharmacogenomics, drug discovery and d*	Add	Remove

Free keywords	*Oral cancer, metabolism, biomakers, drug discovery*

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Proposal ID **721906** *Acronym* **TRACT**

Abstract

The European community requires early stage researchers (ESRs) trained in next-generation technologies for improved detection and treatment of oral and oesophageal cancers. The number of oral cancers diagnosed in the EU has increased by over 75% in the last 30 years, with long-term survival rates of only 50%. This is typically due to the late diagnosis of the disease and resistance to current therapies. Through the collaborative expertise of clinicians, biochemists, immunologists, and chemists TRACT will enable ESRs to discover novel insights into the molecular and cellular basis of these cancers and generate new diagnostic tools and therapeutics that improve patient response and survival. Each Institution brings unique but complementary expertise in cancer metabolism, metabolomics, high-resolution imaging, biomarker identification, computational modelling, medicinal chemistry, target validation, drug development and translational medicine. Industrial placements in five European countries will ensure ESRs receive specialised training in the development of next-generation technologies in such areas as whole genome sequencing, CRISPR technology, drug screening, exosome isolation and analysis, cancer imaging, metabolism and metabolite analysis in addition to the unique employment experience of working in the private sector. Courses in commercialisation, project management and presentation skills will ensure ESRs will have the ability to present their results to the entire cross-section of the European community, through public engagement. TRACT will deliver a cohort of internationally mobile cancer researchers with interdisciplinary skills who will have enhanced career prospects and be in a position to have an impact on the European and global research stage by providing new technologies that can drive entrepreneurship into the European economy and improved diagnostics and treatment options for cancer patients in Europe and beyond.

Remaining characters 38

Has this proposal (or a very similar one) been submitted in the past 2 years in response to a call for proposals under the 7th Framework Programme, Horizon 2020 or any other EU programme(s)? (•) Yes ( ) No

Please give the proposal reference or contract number.	
674880	

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Declarations

1) The coordinator declares to have the explicit consent of all applicants on their participation and on the content of this proposal.	☒
2) The information contained in this proposal is correct and complete.	☒
3) This proposal complies with ethical principles (including the highest standards of research integrity — as set out, for instance, in the European Code of Conduct for Research Integrity — and including, in particular, avoiding fabrication, falsification, plagiarism or other research misconduct).	☒

4) The coordinator confirms:

- to have carried out the self-check of the financial capacity of the organisation on http://ec.europa.eu/research/participants/portal/desktop/en/organisations/lfv.html or to be covered by a financial viability check in an EU project for the last closed financial year. Where the result was "weak" or "insufficient", the coordinator confirms being aware of the measures that may be imposed in accordance with the H2020 Grants Manual (Chapter on Financial capacity check); or	○
- is exempt from the financial capacity check being a public body including international organisations, higher or secondary education establishment or a legal entity, whose viability is guaranteed by a Member State or associated country, as defined in the H2020 Grants Manual (Chapter on Financial capacity check); or	◉
- as sole participant in the proposal is exempt from the financial capacity check.	○

5) The coordinator hereby declares that each applicant has confirmed:

- they are fully eligible in accordance with the criteria set out in the specific call for proposals; and	☒
- they have the financial and operational capacity to carry out the proposed action.	☒

The coordinator is only responsible for the correctness of the information relating to his/her own organisation. Each applicant remains responsible for the correctness of the information related to him/her and declared above. Where the proposal to be retained for EU funding, the coordinator and each beneficiary applicant will be required to present a formal declaration in this respect.

According to Article 131 of the Financial Regulation of 25 October 2012 on the financial rules applicable to the general budget of the Union (Official Journal L 298 of 26.10.2012, p. 1) and Article 145 of its Rules of Application (Official Journal L 362, 31.12.2012, p.1) applicants found guilty of misrepresentation may be subject to administrative and financial penalties under certain conditions.

Personal data protection

Your reply to the grant application will involve the recording and processing of personal data (such as your name, address and CV), which will be processed pursuant to Regulation (EC) No 45/2001 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data. Unless indicated otherwise, your replies to the questions in this form and any personal data requested are required to assess your grant application in accordance with the specifications of the call for proposals and will be processed solely for that purpose. Details concerning the processing of your personal data are available on the privacy statement. Applicants may lodge a complaint about the processing of their personal data with the European Data Protection Supervisor at any time.

Your personal data may be registered in the Early Warning System (EWS) only or both in the EWS and Central Exclusion Database (CED) by the Accounting Officer of the Commission, should you be in one of the situations mentioned in:
-the Commission Decision 2008/969 of 16.12.2008 on the Early Warning System (for more information see the Privacy Statement), or
-the Commission Regulation 2008/1302 of 17.12.2008 on the Central Exclusion Database (for more information see the Privacy Statement) .

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Proposal ID **721906** *Acronym* **TRACT**

List of participants

#	Participant Legal Name	Country
1	THE PROVOST, FELLOWS, FOUNDATION SCHOLARS & THE OTHER MEMBERS OF BOARD OF THE COLLEGE OF THE HOLY & UNDIVIDED TRINITY OF QUEEN ELIZABETH NEAR DUBLIN	Ireland
2	OROBOROS INSTRUMENTS GmbH	Austria
3	UNIVERSITAT DE VALENCIA	Spain
4	UNIVERSITA' DEGLI STUDI DI SIENA	Italy
5	THE QUEEN'S UNIVERSITY OF BELFAST	United Kingdom

Information on partner organisations

Partner Organisation number	PIC Search PIC	Organisation legal name	Country	Academic Sector	Role of associated: Provide training	Role of associated: Host secondmends	
1		Seahorse	United Kingdom	No	Yes	No	
2		National Institute for Bioprocessing Re	Ireland	No	Yes	Yes	
3		Fraunhofer Society	Germany	No	Yes	Yes	
4		Andor Technology PLC	United Kingdom	No	Yes	Yes	
5		Almac Diagnostics	United Kingdom	No	Yes	Yes	
6		Opsona Therapeutics	Ireland	No	Yes	Yes	
7		Exosomics Siena S.p.A.	Italy	No	Yes	Yes	

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Proposal ID **721906** *Acronym* **TRACT** *Short name* **TRINITY COLLEGE DUBLIN**

2 - Administrative data of participating organisations

Coordinator

PIC	***Legal name***
999845446	*THE PROVOST, FELLOWS, FOUNDATION SCHOLARS & THE OTHER MEMBERS OF BOARD OF*

Short name: TRINITY COLLEGE DUBLIN

Address of the organisation

Street College Green

Town DUBLIN

Postcode 2

Country Ireland

Webpage www.tcd.ie

Legal Status of your organisation

Research and Innovation legal statuses

Public body ..... yes
Non-profit ..... yes
International organisation ..... no
International organisation of European interest ..... no
Secondary or Higher education establishment ..... yes
Research organisation ..... no

Legal person ..... yes
Academic Sector ..... yes

Enterprise Data

SME self-declared status ..... 2007 - no
SME self-assessment ..... unknown
SME validation sme ..... 2007 - no

Based on the above details of the Beneficiary Registry the organisation is not an SME (small- and medium-sized enterprise) for the call.

Nace code 853 -

This proposal version was submitted by **Daniela ZISTERER** on **11/01/2016 17:32:48** Brussels Local Time. Issued by the Participant Portal Submission Service.

Proposal ID **721906** *Acronym* **TRACT** *Short name* **TRINITY COLLEGE DUBLIN**

Department(s) carrying out the proposed work

Department 1

Department name: Biochemistry & Immunology ☐ not applicable

☐ Same as organisation address

Street: Trinity College Dublin, Pearse Street

Town: Dublin 2

Postcode: Dublin 2

Country: Ireland

Dependencies with other proposal participants

Character of dependence	***Participant***	

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Proposal ID **721906** *Acronym* **TRACT** *Short name* **TRINITY COLLEGE DUBLIN**

Person in charge of the proposal

Title: Prof.

Sex: ○ Male ◉ Female

First name: **Daniela** Last name: **ZISTERER**

E-Mail: **dzistrer@tcd.ie**

Position in org.: Lecturer & Director of Research

Department: Biochemistry & Immunology, Trinity Biomedical Sciences Institute ☐ Same as organisation

☐ Same as organisation address

Street: Trinity College Dublin, Pearse St

Town: Dublin Post code: Dublin 2

Country: Ireland

Website: http://www.tcd.ie/Biochemistry

Phone: 353-1-8961628 Phone 2: +xxx xxxxxxxxx Fax: 353-1-6772400

This proposal version was submitted by **Daniela ZISTERER** on **11/01/2016 17:32:48** Brussels Local Time. Issued by the Participant Portal Submission Service.

Proposal ID **721906** *Acronym* **TRACT** *Short name* **OROBOROS INSTRUMENTS GmbH**

Participant

PIC	***Legal name***
969066473	*OROBOROS INSTRUMENTS GmbH*

Short name: OROBOROS INSTRUMENTS GmbH

Address of the organisation

Street SCHOPFSTRASSE 18

Town INNSBRUCK

Postcode 6020

Country Austria

Webpage www.oroboros.at

Legal Status of your organisation

Research and Innovation legal statuses

Public body ..... no

Non-profit ..... no

International organisation ..... no

International organisation of European interest ..... no

Secondary or Higher education establishment ..... no

Research organisation ..... no

Legal person ..... yes

Academic Sector ..... no

Enterprise Data

SME self-declared status ..... 2012 - yes

SME self-assessment ..... 2012 - yes

SME validation sme ..... 2010 - yes

Based on the above details of the Beneficiary Registry the organisation is an SME (small- and medium-sized enterprise) for the call.

Nace code G - Wholesale & retail trade

This proposal version was submitted by **Daniela ZISTERER** on **11/01/2016 17:32:48** Brussels Local Time. Issued by the Participant Portal Submission Service.

Department(s) carrying out the proposed work

Department 1

Department name: Oroboros Instruments GmbH ☐ not applicable

☒ Same as organisation address

Street: SCHOPFSTRASSE 18

Town: INNSBRUCK

Postcode: 6020

Country: Austria

Dependencies with other proposal participants

Character of dependence	***Participant***	

This proposal version was submitted by **Daniela ZISTERER** on **11/01/2016 17:32:48** Brussels Local Time. Issued by the Participant Portal Submission Service.

Proposal ID **721906** *Acronym* **TRACT** *Short name* **OROBOROS INSTRUMENTS GmbH**

Person in charge of the proposal

Title: Dr.

Sex: (•) Male ( ) Female

First name: **Erich** Last name: **Gnaiger**

E-Mail: **erich.gnaiger@oroboros.at**

Position in org.: CEO

Department: OROBOROS INSTRUMENTS GmbH ☒ Same as organisation

☒ Same as organisation address

Street: SCHOPFSTRASSE 18

Town: INNSBRUCK Post code: 6020

Country: Austria

Website: www.oroboros.at

Phone: +43512566796 Phone 2: *+xxx xxxxxxxxx* Fax: *+xxx xxxxxxxxx*

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Participant

PIC	***Legal name***
999953019	*UNIVERSITAT DE VALENCIA*

Short name: UVEG

Address of the organisation

Street AVENIDA BLASCO IBANEZ 13

Town VALENCIA

Postcode 46010

Country Spain

Webpage www.uv.es

Legal Status of your organisation

Research and Innovation legal statuses

Public body ..... yes

Non-profit ..... yes

International organisation ..... no

International organisation of European interest ..... no

Secondary or Higher education establishment ..... yes

Research organisation ..... yes

Legal person ..... yes

Academic Sector ..... yes

Enterprise Data

SME self-declared status ..... 2014 - no

SME self-assessment ..... unknown

SME validation sme ..... unknown

Based on the above details of the Beneficiary Registry the organisation is not an SME (small- and medium-sized enterprise) for the call.

Nace code 853 -

This proposal version was submitted by **Daniela ZISTERER** on **11/01/2016 17:32:48** Brussels Local Time. Issued by the Participant Portal Submission Service.

Department(s) carrying out the proposed work

Department 1

Department name: Stromatology & Maxillofacial Surgery, University General Hospital ☐ not applicable

☐ Same as organisation address

Street: Avda de tres Cruces s/n 46014

Town: Valencia

Postcode: 46014

Country: Spain

Dependencies with other proposal participants

Character of dependence	***Participant***	

This proposal version was submitted by **Daniela ZISTERER** on **11/01/2016 17:32:48** Brussels Local Time. Issued by the Participant Portal Submission Service.

Proposal ID **721906** *Acronym* **TRACT** *Short name* **UVEG**

Person in charge of the proposal

Title: Prof. Sex: (•) Male ( ) Female

First name: **Jose** Last name: **Bagan**

E-Mail: **bagan@uv.es**

Position in org.: Professor of Oral Medicine

Department: Stromatology & Maxillofacial Surgery, University General Hospital ☐ Same as organisation

☐ Same as organisation address

Street: Avda de tres Cruces s/n 46014

Town: Valencia Post code: 46014

Country: Spain

Website: www.uv.es/bagan

Phone: 34961972127 Phone 2: +xxx xxxxxxxxx Fax: 34963941854

This proposal version was submitted by **Daniela ZISTERER** on **11/01/2016 17:32:48** Brussels Local Time. Issued by the Participant Portal Submission Service.

Participant

PIC	***Legal name***
999898020	*UNIVERSITA' DEGLI STUDI DI SIENA*

Short name: UNISI

Address of the organisation

Street VIA BANCHI DI SOTTO 55

Town SIENA

Postcode 53100

Country Italy

Webpage www.unisi.it

Legal Status of your organisation

Research and Innovation legal statuses

Public body ..... yes

Non-profit ..... yes

International organisation ..... no

International organisation of European interest ..... no

Secondary or Higher education establishment ..... yes

Research organisation ..... yes

Legal person ..... yes

Academic Sector ..... yes

Enterprise Data

SME self-declared status ..... 2007 - no

SME self-assessment ..... unknown

SME validation sme ..... 2007 - no

Based on the above details of the Beneficiary Registry the organisation is not an SME (small- and medium-sized enterprise) for the call.

Nace code 853 -

This proposal version was submitted by **Daniela ZISTERER** on **11/01/2016 17:32:48** Brussels Local Time. Issued by the Participant Portal Submission Service.

Department(s) carrying out the proposed work

Department 1

Department name: European Research Centre for Drug Discovery & Development ☐ not applicable

☐ Same as organisation address

Street: Via Aldo Moro 2

Town: Siena

Postcode: 53100

Country: Italy

Dependencies with other proposal participants

Character of dependence	***Participant***	

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Proposal ID **721906** *Acronym* **TRACT** *Short name* **UNISI**

Person in charge of the proposal

Title: Prof.

Sex: (•) Male ( ) Female

First name: **Giuseppe** Last name: **Campiani**

E-Mail: **campiani@unisi.it**

Position in org.: Professor of Medicinal Chemistry

Department: European Research Centre for Drug Discovery & Development ☐ Same as organisation

☐ Same as organisation address

Street: Via Aldo Moro 2

Town: Siena Post code: 53100

Country: Italy

Website: www.natsyndrugs.org

Phone: 390577234172 Phone 2: +xxx xxxxxxxxx Fax: 390577234333

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Participant

PIC	***Legal name***
999992013	*THE QUEEN'S UNIVERSITY OF BELFAST*

Short name: THE QUEEN'S UNIVERSITY OF BELFAST

Address of the organisation

Street UNIVERSITY ROAD LANYON BUILDING

Town BELFAST

Postcode BT7 1NN

Country United Kingdom

Webpage www.qub.ac.uk

Legal Status of your organisation

Research and Innovation legal statuses

Public body ..... yes
Non-profit ..... yes
International organisation ..... no
International organisation of European interest ..... no
Secondary or Higher education establishment ..... yes
Research organisation ..... yes
Legal person ..... yes
Academic Sector ..... yes

Enterprise Data

SME self-declared status ..... 2013 - no
SME self-assessment ..... unknown
SME validation sme ..... unknown

Based on the above details of the Beneficiary Registry the organisation is not an SME (small- and medium-sized enterprise) for the call.

Nace code 853 -

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Department(s) carrying out the proposed work

Department 1

Department name: Centre for Cancer Research & Cell Biology ☐ not applicable

☐ Same as organisation address

Street: 97 Lisburn Road

Town: Belfast

Postcode: BT 7AE

Country: United Kingdom

Dependencies with other proposal participants

Character of dependence	***Participant***	

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Proposal ID **721906** *Acronym* **TRACT** *Short name* **THE QUEEN'S UNIVERSITY OF BELFAST**

Person in charge of the proposal

Title: Dr. Sex: (•) Male ( ) Female

First name: **Richard** Last name: **Turkington**

E-Mail: **rturkington01@qub.ac.uk**

Position in org.: Clinical Senior Lecturer (Medical Oncology)

Department: Centre for Cancer Research and Cell Biology ☐ Same as organisation

☐ Same as organisation address

Street: 97 Lisburn Road

Town: Belfast Post code: BT9 7BL

Country: United Kingdom

Website: www.qub.ac.uk/research-centres/CentreforCancerResearchCell

Phone: +44 (0) 28 9097 2756 Phone 2: *+xxx xxxxxxxxx* Fax: +44 (0) 28 9097 2776

Other contact persons

First Name	*Last Name*	*E-mail*	*Phone*
Richard	Kennedy	r.kennedy@qub.ac.uk	+44 (0) 28 9097 2776
Patricia	McCrory	p.mccrory@qub.ac.uk	
Colleen	Spence	colleen.spence@qub.ac.uk	
Siobhan	McGlinchey	s.mcglinchey@qub.ac.uk	

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Proposal ID **721906** *Acronym* **TRACT**

3 - Budget

Researcher Number	Recruiting Participant (short name)	Planned start month	Duration (months)
1	UVEG	6	36
2	THE QUEEN'S UNIVERSITY OF BELFAST	6	36
3	UVEG	6	36
4	THE QUEEN'S UNIVERSITY OF BELFAST	6	36
5	TRINITY COLLEGE DUBLIN	6	36
6	UNISI	6	36
7	TRINITY COLLEGE DUBLIN	6	36
8	UNISI	6	36
9	TRINITY COLLEGE DUBLIN	6	36
10	OROBOROS INSTRUMENTS GmbH	6	36
11	TRINITY COLLEGE DUBLIN	6	36
Total			396

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Proposal ID **721906** *Acronym* **TRACT**

Participant Number	Organisation Short Name	Country	IOEI	No of researchers	Number of person.months	Researcher Unit Cost			Institutional Unit Cost		TOTAL
						Living allowance	Mobility Allowance	Family Allowance	Research, training and networking costs	Management and overheads	
1	TRINITY COLLEGE DUBLIN	IE	no	4	144	508298,40	86400,00	36000,00	259200,00	172800,00	1062698,40
2	OROBOROS INSTRUMENT	AT	no	1	36	117334,08	21600,00	9000,00	64800,00	43200,00	255934,08
3	UVEG	ES	no	2	72	218545,92	43200,00	18000,00	129600,00	86400,00	495745,92
4	UNISI	IT	no	2	72	238922,64	43200,00	18000,00	129600,00	86400,00	516122,64
5	THE QUEEN'S UNIVERSIT	UK	no	2	72	269375,76	43200,00	18000,00	129600,00	86400,00	546575,76
Total				11	396	1352476,80	237600,00	99000,00	712800,00	475200,00	2877076,80

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4 - Ethics issues table

1. HUMAN EMBRYOS/FOETUSES		Page
Does your research involve Human Embryonic Stem Cells (hESCs)?	○ Yes ◉ No	
Does your research involve the use of human embryos?	○ Yes ◉ No	
Does your research involve the use of human foetal tissues / cells?	○ Yes ◉ No	
2. HUMANS		**Page**
Does your research involve human participants?	○ Yes ◉ No	
Does your research involve physical interventions on the study participants?	○ Yes ◉ No	
3. HUMAN CELLS / TISSUES		**Page**
Does your research involve human cells or tissues (other than from Human Embryos/ Foetuses, i.e. section 1)?	○ Yes ◉ No	
4. PERSONAL DATA		**Page**
Does your research involve personal data collection and/or processing?	○ Yes ◉ No	
Does your research involve further processing of previously collected personal data (secondary use)?	○ Yes ◉ No	
5. ANIMALS		**Page**
Does your research involve animals?	◉ Yes ○ No	46
Are they vertebrates?	◉ Yes ○ No	46
Are they non-human primates?	○ Yes ◉ No	
Are they genetically modified?	○ Yes ◉ No	
Are they cloned farm animals?	○ Yes ◉ No	
Are they endangered species?	○ Yes ◉ No	

Please indicate the species involved(Maximum number of characters allowed: 1000)

6. THIRD COUNTRIES		Page

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In case non-EU countries are involved, do the research related activities undertaken in these countries raise potential ethics issues?	◯ Yes ◉ No	
Do you plan to use local resources (e.g. animal and/or human tissue samples, genetic material, live animals, human remains, materials of historical value, endangered fauna or flora samples, etc.)?	◯ Yes ◉ No	
Do you plan to import any material - including personal data - from non-EU countries into the EU? *For data imports, please fill in also section 4.* *For imports concerning human cells or tissues, fill in also section 3.*	◯ Yes ◉ No	
Do you plan to export any material - including personal data - from the EU to non-EU countries? *For data exports, please fill in also section 4.* *For exports concerning human cells or tissues, fill in also section 3.*	◯ Yes ◉ No	
If your research involves low and/or lower middle income countries, are benefits-sharing actions planned?	◯ Yes ◉ No	
Could the situation in the country put the individuals taking part in the research at risk?	◯ Yes ◉ No	
7. ENVIRONMENT & HEALTH and SAFETY		Page
Does your research involve the use of elements that may cause harm to the environment, to animals or plants? *For research involving animal experiments, please fill in also section 5.*	◯ Yes ◉ No	
Does your research deal with endangered fauna and/or flora and/or protected areas?	◯ Yes ◉ No	
Does your research involve the use of elements that may cause harm to humans, including research staff? *For research involving human participants, please fill in also section 2.*	◯ Yes ◉ No	
8. DUAL USE		Page
Does your research have the potential for military applications?	◯ Yes ◉ No	
9. MISUSE		Page
Does your research have the potential for malevolent/criminal/terrorist abuse?	◯ Yes ◉ No	
10. OTHER ETHICS ISSUES		Page
Are there any other ethics issues that should be taken into consideration? Please specify	◯ Yes ◉ No	

I confirm that I have taken into account all ethics issues described above and that, if any ethics issues apply, I will complete the ethics self-assessment and attach the required documents. ☒

How to Complete your Ethics Self-Assessment

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5 - Call Specific Questions

Open Research Data Pilot in Horizon 2020

If selected, all applicants have the possibility to participate in the Pilot on Open Research Data in Horizon 2020[1], which aims to improve and maximise access to and re-use of research data generated by actions. Participating in the Pilot does not necessarily mean opening up all research data. Actions participating in the Pilot will be invited to formulate a Data Management Plan in which they will determine and explain which of the research data they generate will be made open.

We wish to participate in the Pilot on Open Research Data in Horizon 2020 on a voluntary basis	○ Yes	◉ No

Participation in this Pilot does not constitute part of the evaluation process. Proposals will not be evaluated favourably because they are part of the Pilot and will not be penalised for not participating.

[1] *According to article 43.2 of Regulation (EU) No 1290/2013 of the European Parliament and of the Council, of 11 December 2013, laying down the rules for participation and dissemination in "Horizon 2020 - the Framework Programme for Research and Innovation (2014-2020)" and repealing Regulation (EC) No 1906/2006.*

Data management activities

The use of a Data Management Plan (DMP) is required for projects participating in the Open Research Data Pilot in Horizon 2020, in the form of a deliverable in the first 6 months of the project.

All other projects may deliver a DMP on a voluntary basis, if relevant for their research.

Are data management activities relevant for your proposed project?	○ Yes	◉ No

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START PAGE

MARIE SKŁODOWSKA-CURIE ACTIONS

Innovative Training Networks (ITN)
Call: H2020-MSCA-ITN-2016

PART B

"TRACT"
TRAining in **C**ancer Mechanisms & **T**herapeutics

This proposal is to be evaluated as: ETN

This proposal version was submitted by **Daniela ZISTERER** on **11/01/2016 17:32:48** Brussels Local Time. Issued by the Participant Portal Submission Service.

LIST OF PARTICIPANTS

Consortium Member	Legal Entity Short Name	Academic	Non-academic	Awards Doctoral Degrees	Country	Dept./ Division / Laboratory	Scientist-in-Charge	Role of Partner Organisation
Beneficiaries								
Trinity College Dublin	TCD	√		√	IRL	Biochemistry & Immunology /Cancer	Daniela Zisterer	
University of Valencia	UVEG	√		√	ES	Faculty of Medicine and Odontology	Jose Bagan	
University of Siena	UNISI	√		√	IT	Medicinal Chemistry	Giuseppe Campiani	
The Queen's University of Belfast	QUB	√		√	UK	Centre for Cancer Research and Cell Biology	Richard Turkington	
Oroboros Instruments	OROBOROS		√		AT	Bioenergetics	Erich Gnaiger	
Partner Organisation								
Seahorse Bioscience	Seahorse		√		UK	Metabolism & Bioenergetics	Alex Liversage	Deliver training course
National Institute for Bioprocessing Training Research	NIBRT		√		IE	Glycan Biomarkers	Pauline Rudd	Deliver training courses & host secondment
Exosomics Siena S. p. A.	Exosomics		√		IT	Exosomes	Antonio Chiesi	Host secondments
Fraunhofer Society	IME-SP		√		DE	High-Throughput Screening	Björn Windshügel	Host secondments
Andor Technology	ANDOR		√		UK	Microscopy	Orla Hanrahan	Deliver training courses & host secondments
Almac Diagnostics	ALMAC		√		UK	Bioinformatics	Timothy Davison	Host secondments
Opsona Therapeutics	OPSONA		√		IE	Cancer Immunology	Luke O'Neill	Host secondment

Data for non-academic beneficiaries:

Name	Location of research premises (city / country)	Type of R&D activities	No. of full - time employees	No. of employees in R&D	Web site	Annual turnover (approx, in Euro)	Enterprise status (Yes/No)	SME status (Yes/No)
OROBOROS	Innsbruck Austria	High-resolution respirometry	8	3.5	www.oroboros.at	3,139,000	Yes	Yes

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Declarations

Name (institution / individual)	Nature of inter-relationship
Richard Kennedy (Queen's University Belfast/Almac Diagnostics)	McClay Professor in Medical Oncology, Queen's University Belfast, Vice President and Medical Director, Almac Diagnostics

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1 Excellence

1.1 Quality, innovative aspects & credibility of research programme

1.1.1 Introduction

In 2012, 8.2 million people worldwide died of cancer, of which 5.3% or **over half a million deaths were accounted for by oral and oesophageal cancer (OOC)**[1]. Oral cancer includes carcinoma of the mouth (oral cavity) and the back of the mouth (oropharynx) and oesophageal cancer includes carcinoma of the oesophagus and the gastro-oesophageal junction. The predominant cause of OOC is exposure to topical carcinogens, in particular alcohol and tobacco, giving rise to squamous cell carcinomas[2] (OSCC). Adenocarcinoma, another sub-type of OOC, may also be related to smoking and alcohol abuse, but to a lesser extent than squamous cell carcinoma. Oesophageal adenocarcinomas (OAC) are mostly found to occur at the junction of the oesophagus and stomach and are associated with a history of inflammation - gastroesophageal reflux and Barrett's oesophagus (where the normal tissue lining the oesophagus changes to resemble the lining of the intestine)[3].

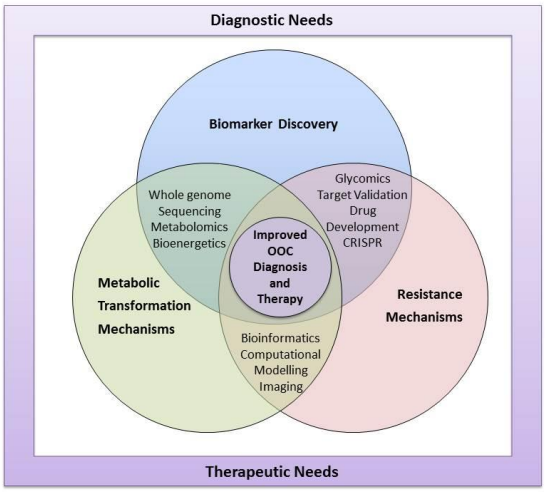
Despite efforts to screen for the pre-malignant condition Barrett's oesophagus and pre-operatively select OAC patients for potentially curative surgery, the **five-year survival rate in early stage disease is only 25-35%.** The incidence of OAC in men has also risen 50% in the last 25 years[4]. This is **due to late diagnosis of disease and resistance to chemotherapy**. In order to improve outcomes for OOC patients, there is an urgent need to discover biomarkers for early detection of the disease and patient monitoring/stratification, and to better understand the molecular basis of metabolic transformation and drug resistance in OOC in order to develop novel therapies.

The TRACT research training programme will carry out high-quality research in three interconnected thematic areas (Biomarker Discovery, Molecular Resistance Mechanisms and Metabolic Transformation Mechanisms) in order to **address current diagnostic, prognostic and therapeutic clinical needs in OOC**. Early stage researchers (ESRs) recruited to the project will undertake a broad-based training and research programme encompassing both basic research and clinical translation to develop methods for early diagnosis and novel treatment strategies. ESRs will particularly concentrate their research efforts on the two most common sub-types of OOC, oral squamous cell carcinoma (OSCC) and oesophageal adenocarcinoma (OAC).

TRACT will provide ESRs with exposure to a collaborative network of European academic and industrial experts working in the complementary domains of cancer metabolism, metabolomics, high-resolution imaging, bioinformatics, biomarker identification, computational modelling, medicinal chemistry, target validation, drug development, nanotechnology and translational medicine**. Although there are many researchers working on OOC in the relevant domains listed above, there is a lack of integration between domains** - through a programme of **integrative training and research,** TRACT will bring together relevant domains to **deliver better diagnostics and therapeutics for OOC** with the overall aim of **improving patient response and survival**.

1.1.2 Research Objectives

The **overall aim of the research programme** is to integrate basic and applied research in three related themes in order to deliver new diagnostic & prognostic tools and therapeutic approaches for patients with OOC.



During the project, TRACT ESRs will undertake novel research to:

1) Determine novel biomarkers at the protein, glycan and molecular level to enable early detection of OOC and to predict patient response to therapy (WP1).

2) Uncover the molecular basis of drug resistance in OOC leading to the identification of new drug targets and the development of novel cancer therapeutics (WP2).

3) Enhance knowledge of metabolic transformation in OOC leading to the identification of novel targets for therapeutic intervention (WP3).

1 http://www.wcrf.org/int/cancer-facts-figures/worldwide-data
2 Vokes EE, et al., N Engl J Med. 1993 Jan 21;328(3):184-94.
3 Lepage C1,et al., . Dig Liver Dis. 2013 Aug;45(8):625-9.
4 http://www.cancerresearchuk.org/cancer-info/cancerstats/types/oesophagus/mortality/#source1

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1.1.3 Overview of the research programme

During the project, 11 ESRs will be recruited to complete research projects in: Biomarker Discovery (WP1), Molecular Resistance Mechanisms (WP2) and Metabolic Transformation Mechanisms (WP3) (see Table 1.1a below). Outputs from WP1 will address current diagnostic clinical needs and also provide prognostic means for predicting therapeutic responses in patients, while outputs from WPs 2 and 3 will address current therapeutic unmet needs. The individual ESR projects will **integrate research across biochemistry, immunology, dental science and medicinal chemistry academic disciplines to deliver diagnostic, prognostic and therapeutic options with clinical relevance**. Through our SME/industrial partners, ESRs will be exposed to **next-generation technologies in cancer diagnosis, metabolism (including glycomics, metabolomics), genome scale CRISPR knockout and next generation sequencing, imaging, biomarker identification, exosome isolation/analysis, medicinal chemistry, target identification/validation, bioinformatics, protein structure, computational modelling and drug development.**

TRACT will implement a multi-faceted approach to discover novel diagnostic and prognostic biomarkers to enable more focused administration of current chemotherapeutics. In parallel with and complementing these studies, novel protein targets will be determined and initial PoC small molecule modulators will be discovered to serve as a starting point towards the ultimate target validation in future clinical trials. The **successful completion** of the project goals is bolstered by the fact that: (1) The ESR projects will **not be interdependent** which is a key strength of the programme; (2) each ESR will be co-supervised by an academic and industrial **world-leader** in their area of expertise thereby significantly enhancing the likelihood of success of the individual projects and of the research programme as a whole.

1.1.4 Research Methodology and approach

Table 1.1a: Work Package List

WP No	Work Package Title	Lead Beneficiary No.	Start Month	End Month	Activity Type	Lead Beneficiary Short Name	ESRs involve-ment
WP1	Biomarker Discovery	3	6	42	Research/Training	UVEG	ESR1 -3
WP2	Resistance Mechanisms	4	6	42	Research/Training	UNISI	ESR4 - 9
WP3	Metabolic Transformation	2	6	42	Research/Training	OROBOROS	ESR10 - 11
WP4	Training	3	1	42	Training	UNISI	ESR1 - 11
WP5	Dissemination	5	1	45	Dissemination	QUB	ESR1 - 11
WP6	Project Management	1	1	45	Management	TCD	ESR on SB

Biomarker discovery (WP1)

TRACT will carry out discovery research into biomarkers associated with OOC to develop state-of-the-art diagnostic assays for 1) earlier, more reliable detection, and 2) therapeutic response prediction. Overall, research carried out under WP1 will improve OOC survival rates by developing biomarker-based assays for **earlier, more reliable disease diagnosis** and **stratification of individual patients to more effective chemotherapeutic regimes**. This comprehensive patient profiling provides essential information to the clinician, enabling earlier and more **accurate diagnosis** and the potential to administer more **appropriate treatment**. This approach will not only benefit the patient, with the potential for improved **quality of life, disease control** and **minimise side-effects** by administering more targeted treatment, but will also potentially lead to **reduced costs** for healthcare providers.

The most effective approach to reducing OOC morbidity is early detection, yet **no effective diagnostic procedures for OOC currently exist**. At present, definitive diagnosis of OOC relies upon tissue biopsy, a procedure that often yields false-negative diagnoses and results in the recovery of non-diagnostic tissue[5]. ESR 1 (UVEG recruit; NIBRT secondment) will explore the development of a biomarker-based diagnostic approach as an alternative to tissue biopsy. To date, the search for biomarkers associated with the early onset of oral squamous cell carcinoma (OSCC) has focused on a single proteomic approach and has met with only limited success[6]. ESR 1 will adopt an alternative approach using state-of-the-art multidisciplinary techniques to **determine novel salivary biomarkers at protein, glycan and molecular levels**. Saliva collection has distinct advantages over tissue and blood collection as the collection procedure is non-invasive and does not require specialised resources, and the resulting samples are safer to handle and easier to store[7]. Saliva is currently being used in many diagnostic procedures, including

5 Scully C, Bagan JV, et al.. Am J Dent. 2008 Aug;21(4):199-209.
6 Tung CL,et al., (2013). J Pharm Biomed Anal. J Pharm Biomed Anal. 2013 Mar 5;75:7-17.
7 Yoshizawa JM et al (2013) Clin. Microbiol. Rev. Oct;26 (4):781-791
8 Feller L et al., (2013) Oral Oncol. 2013 Sep; 49(9):887-892.

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screening for HIV, hepatitis and ebola.[7] Currently the O'Sullivan lab in TCD has built up a biobank of saliva samples from patients exhibiting a fixed stage of oral pre-cancer/cancer along with positive pilot studies demonstrating the use of saliva as an oral cancer diagnostic tool. As inflammation has previously been linked to the pathogenesis of OSCC[8], saliva from OSCC patients will be analysed to determine the relationship between pro-inflammatory cytokine markers (TNF-α, IL-1β, IL-6, and IL-8), salivary glycan profiles and early disease progression. Results from this profiling will ultimately lead to the development of a clinical test for early diagnosis of OSCC.

The application of pre-operative, neo-adjuvant chemotherapy or chemoradiotherapy has delivered significant improvements in disease free and overall survival in oesophageal cancer[7]. However, **not all patients respond equally well to all treatments**. ESR 2 (QUB recruit; TCD, ALMAC secondments) will undertake whole genome sequencing and microarray-based gene expression profiling of biopsies from early stage OAC to identify molecular signatures predictive of response to chemotherapy. Results from this profiling will ultimately lead to the **development of a clinical diagnostic test to predict responders and non-responders**.

The typically late diagnosis of oral cancer patients usually necessitates radiotherapy and surgical intervention. Lower inflammatory responses post-intervention are associated with successful recovery from cancer treatment. Monitoring the healing rate and control of inflammation is essential to aid in successful recovery. However, researchers and clinicians are currently unable to determine the effect of inflammation on wound healing, as the associated inflammatory profile is unknown. Thus, inflammatory profiles have the potential to be utilised as a measure of patient recovery, but there are **currently no clinical assays for monitoring inflammation during treatment**. ESR 3 (UVEG recruit; IME-SP secondment) will evaluate the levels of local inflammatory markers as an indicator of positive response to treatment in order to **determine specific inflammatory profiles linked to wound healing and develop assays to monitor toxicity, tumour control and patient recovery**. This project builds on the use of diagnostic tools developed in the Bagan lab which identified EGF as a discriminating factor in oral cancer[8]

Resistance mechanisms (WP2)

TRACT will uncover the molecular basis of drug resistance mechanisms in OOC with the aim of 1) improving the efficacy of existing therapies, 2) identifying new drug targets, and 3) developing novel therapies. Initial pre-clinical testing will be carried out to support future translation to clinical studies.

Current treatment strategies for OOC include a combination of surgery, radiotherapy and chemotherapy. **Chemotherapeutic treatment is currently impeded by drug resistance and a lack of selectivity**. A greater understanding of the cellular mechanisms that contribute to chemotherapeutic resistance in OOC will enable the **development of combination therapies with greater efficacy** than current chemotherapeutic regimes. Targeted combination therapies hold the promise of **improved response rates, decreased chemotherapeutic toxicity and enhanced survival rates**.

ESR 4 (QUB recruit; ALMAC, IME-SP, TCD secondments) will perform RNA-seq and microarray-based gene expression profiling on matched pre-chemotherapy endoscopic biopsies of early stage oesophageal adenocarcinomas and normal tissue resections. The resulting profiles will allow the **identification of differentially expressed/frequently mutated genes and associated molecular pathways in pathological responders and non-responders**, informing the design of **new therapies for OAC**. Preliminary data analysis has identified the MAPK and glycolytic pathways as potential targetable pathways. Determinants of drug resistance may also lead to the development of a **potential diagnostic test** to classify non-responders versus responders.

Recent research by Creagh in TCD has implicated inflammatory caspases as key mediators of intestinal inflammation and as biomarkers for colon cancer[9]. As OAC is an inflammation-associated cancer, ESR 5 (TCD recruit; QUB, OPSONA secondments) will conduct a study to establish whether inflammatory caspases may also represent biomarkers for early stage OAC. The involvement of inflammatory caspases in OAC development and resistance will also be examined using siRNA and inflammation/caspase inhibitors in OAC cell lines & *in vivo* models, ultimately leading to the **development of novel diagnostics for OAC, and assays for enhanced patient stratification, enabling more effective therapeutic choices**.

Drug resistance and a lack of selectivity impede current chemotherapeutics for OOC. Thus, **new therapeutic options for the treatment of recurrent OOCs are urgently needed**[10]. Cancer biology research has led to the selective inhibition of rate-limiting targets in the progression of many chemotherapy resistant cancers (e.g. Cetuximab (anti-EGFR) - colorectal cancer[11]; Bortezomib (Proteasome inhibitor) - multiple myeloma)[12]. Resistance

7 Sjoquist KM, et al., . Lancet Oncol. 2011 Jul;12(7):681-92.

8 Bagan et al., (2012) J Oral Pathol Med. 2012 Oct;41(9):662-6.

9 Flood, B. et al. (2015) Clin. Exp. Immunol.181, 39-50.

10 Da Silva, S.D. et al., (2012) Front Pharmacol. 3: 149.

11 Debucquoy A. et al., (2010) Clin. Cancer Res.16, 2709–2714

12 Mahindra A., et al., (2012). Nat. Rev. Clin. Oncol.9, 135–143.

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to cell death is a common hallmark of cancer and is often mediated by the Bcl-2 family of proteins. Among all anti-apoptotic Bcl-2 members, Mcl-1 functions as a major survival factor, particularly in solid cancers. In the last year Mcl-1 has been identified as an important therapeutic target for OOC[13]. However, no specific Mcl-1 inhibitors exist. ESR 6 (UNISI recruit; Exosomics, TCD secondments) will **computationally design and synthesise Mcl-1 inhibitors** with the ability to sensitise OOC cells to apoptosis with appropriate pharmacokinetic properties. The agents will be tested in models of OSCC and efficacy of the novel compounds will also be determined by means of exosome content evaluation.

Pre-operative reduction of OOC tumour masses greatly improves patient survival post surgery. However, **current chemo- and radio-therapeutic strategies have undesirable long-term effects**. Full length and peptide fragments of the natural human milk protein α-lactalbumin non-covalently bound to oleic acid (a.k.a HAMLET) have proven effective in treating bladder and intestinal tumors with no observable side effects[14],[15]. The tumoricidal mechanism is multi-faceted (work by Mok in TCD and others[16],[17]), providing further opportunities to design targeted therapeutics. ESR 7 (TCD recruit; Oroboros & UNISI secondments) **will generate neo-adjuvant HAMLET therapy of enhanced efficacy** by chemically coupling oleic acid to a variety of α-lactalbumin peptides (UNISI). **Hamlet derivatives will be tested on OAC cell** lines, and the **mode of action studied by genome-scale CRISPR knockout[18] and next generation sequencing (TCD).** Metabolic changes will also be analysed by respirometry (OROBOROS).

Genetic and pharmacological screens have identified autophagic mediators as effective adjuvant and neoadjuvant targets. However, results from a recent phase 1 trial of the autophagy inhibitor hydroxychloroquine to treat newly diagnosed glioma patients demonstrated dose limiting toxicity[19]. Therefore, in order to exploit autophagic mediators as therapeutic targets, lower toxicity compounds are required. ESR 8 (UNISI recruit; Exosomics, TCD secondments) will carry out **bioinformatic screening to identify and develop new targets**. Novel compounds against promising targets will be rationally designed and synthesised, and **efficacy screening will be carried out in OSCC models**. **Efficacy of the novel compounds will also be evaluated by means of exosome content evaluation.**

Tumour resistance to therapy is related to the cell survival properties of autophagy and this pathway is frequently activated by chemotherapies in patients with various types of cancer. However, the **role of autophagy in OSCC remains unclear**, although preliminary studies in TCD have demonstrated that OSCC cell lines undergo autophagy in response to chemotherapy treatment. ESR 9 (TCD recruit; UVEG and Andor secondments) will investigate the expression of key autophagic regulatory proteins in OSCC patient samples and **correlate expression with clinicopathologic factors and overall patient survival**. ESR 9 will also **determine whether combining existing OSCC chemotherapy strategies with autophagy inhibition represents a better treatment strategy** for the benefit of OSCC patients.

Metabolic transformation (WP3)

TRACT will examine metabolic transformation mechanisms in OOC with the aim of identifying new drug targets for future therapeutic development. Metabolic transformation is a universal property of tumour formation and is a rich source of targets for development of therapeutic interventions[20]. Pilot studies performed in QUB using a pathways based approach to identify determinants of drug resistance in OOC have identified the glycolytic pathway as a potential targetable pathway. ESR 10 (Oroboros recruit; TCD secondment) will further **characterise the bioenergetic and metabolic differences in normal, dysplastic and cancerous oral cancer cells** using the Oroboros Respirometer Multisensor system and state-of-the-art Seahorse analysis. This approach will **identify differential novel drug targets** and means to **enhance the chemotherapeutic sensitivity of cancer cells**.

Factors that control mitochondrial dynamics in cancer cells have also emerged as possible therapeutic targets. The dynamic structure of the mitochondria in mammalian cells is defined by the opposing forces of fission and fusion, but the **regulation of these mitochondrial processes is poorly understood**[21]. This is an emerging area in cancer research where cutting-edge imaging technologies are merging with molecular and cellular biology techniques. Pilot studies performed by Porter in TCD have identified a key molecule involved in controlling mitochondrial abundance (namely SIRT3) as a determinant of drug resistance in some solid cancers (manuscript in

[13] Maji et al., (2015) Oncotarget, 6, 16623-16636.
[14] Payton S. (2013) Nat Rev Urol. 10(3):126.
[15] Puthia M, et al., (2014) Gut. 2014 Jan;63(1):131-42.
[16] Storm P, et al., (2013) PLoS One. 2013;8(3):e58578.
[17] Nadeem A, (2015) Sci Rep. 5:16432
[18] Shalem O, (2014) Science. 343(6166):84-7.
19 www.uphs.upenn.edu/news/News_Releases/2014/05/hcq/
20 Smolková K, et al., (2011) Int J Biochem Cell Biol. 43:950-68.
21 Chan D.C. (2012) Annual Review of Genetics 46: 265-287

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preparation). ESR 11 (TCD recruit; Oroboros secondment) will establish the **relationship between mitochondrial abundance, morphology, functional proteins involved in mitochondrial dynamics and metabolic differences in normal, dysplastic and oral cancer cells**. This new knowledge will lead to the **identification of novel therapeutic targets**.

Table 1.1b Delivering novel OOC diagnostics and therapeutics through integrated ESR research programme

ESR	Project Title	Research Objectives/Clinical Need
1	Inflammatory response elements and glycan profiles as salivary biomarkers for the early diagnosis of OSCC	Biomarker Discovery/Diagnostic
2	Identification of novel molecular biomarkers predictive of benefit to neo-adjuvant chemotherapy in OAC	Biomarker Discovery/Diagnostic & Therapeutic
3	Modulation of salivary inflammatory markers in patients undergoing radiotherapy for OSCC	Biomarker Discovery/Diagnostic & Therapeutic
4	A pathways-based approach to identify determinants of drug resistance in OAC	Resistance Mechanisms/Diagnostic & Therapeutic
5	Inflammatory caspases as biomarkers for OAC? Determining the role of inflammatory caspases in OAC development and resistance	Resistance Mechanisms/Diagnostic & Therapeutic
6	Mcl-1 inhibitors for the treatment of OSCC	Resistance Mechanisms /Therapeutic
7	HAMLET derivatives as a pre-operative therapy in OAC	Resistance Mechanisms / Therapeutic
8	Development of novel autophagy modulators to improve sensitivity of OSCC to chemotherapy	Resistance Mechanisms / Therapeutic
9	Pre-clinical evaluation of targeting autophagy for the treatment of OSCC	Resistance Mechanisms / Therapeutic
10	Metabolic profiles in normal, dysplastic and cancerous oral cells	Metabolic Transformation/ Diagnostic & Therapeutic
11	Mitochondrial function linked to metabolic differences in normal, dysplastic and cancerous oral cells	Metabolic Transformation/ Therapeutic

1.1.5 Originality & innovative aspects of the research programme

The past decade has witnessed a renewed appreciation of the complexity of cancer cell metabolism, survival and therapeutic resistance. These characteristics are especially important in the context of OOC, which is difficult to detect, is frequently diagnosed late, has few therapeutic options and has poor survival rates. Current state of the art in clinical diagnosis is limited to visual/endoscopic examination of the oral/oesophageal region and histological analysis of tumour biopsies. In addition, the predominant treatment approach is neo-adjuvant chemotherapy/radiotherapy followed by surgery. The TRACT project will focus on developing **original and innovative solutions to key challenges in OOC diagnosis and treatment** through the development of methods for early and accurate diagnosis, methods for monitoring patients during therapy, approaches for prognostic stratification of patients, novel therapeutics to overcome resistance and novel target pathways, including metabolic transformation pathways. The consortium will also look to build on the advances of other funded European projects, such as GlycoHIT. This FP7-funded project, of which NIBRT was a partner, developed technologies that enable fast and accurate analysis of glycosylation in blood samples from cancer patients. TRACT will build on the findings and expertise developed by NIBRT during the project. Currently, scientists working in the area of oral cancer research, diagnosis and therapeutic development receive **restricted training in specific disciplines**. This narrow approach limits the innovation potential of OOC basic and applied research in both academic and non-academic settings. There are currently no multidisciplinary doctoral training programmes focussed on OOC. There is an oesophageal cancer network, the OCCAMS network based out of Cambridge[22], but it is primarily a sequencing project for the International Cancer Genome Consortium and is not involved in doctoral training. The TRACT approach is unique in that it is focused on biomarker and novel therapeutic, prognostic and diagnostic development and their translation into clinical practice which is something the OCCAMS group have not done to date. TRACT will advance the state-of-the-art by integrating multidisciplinary, intersectoral research with outputs from cutting-edge technologies including next-generation whole genome sequencing, RNA-seq analysis, CRISPR technology, 2-D NMR metabolomics, exosome analysis, Seahorse bioenergetic analysis, in vivo imaging, and in-silico drug screening. **Therapeutic benefits from the research programme are promising since potential molecular drug targets and biomarkers have already been identified by pilot studies.**

[22] http://www.mrc-cu.cam.ac.uk/research/rebecca-fitzgerald/clinical-studies/occams

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1.1.6 Gender aspects of the research programme

Oral cancer historically has a high male to female ratio in terms of incidence. In a case study of 1564 diagnoses, the gender difference was calculated as 2.8:1 males to females[23]. Explanations include a greater propensity for men to engage in high-risk habits, as noted in a study carried out on people < 45 years of age, which showed large gender differences in common oral cancer risk factors, such as cigarettes and alcohol use[24]. However, more recent data and reports show a convergence of decreasing male and increasing female incidence rates of major tobacco related cancers including OSCC[25]. In particular, eastern and central European regions show increased female incidence rates of oral cancer mostly due to increased alcohol and tobacco consumption by females whilst rates in males remained static[26,27]. Thus, TRACT research is vital for the future health of both young European women and men. Consideration of sex/gender differences in differential responses within clinical patient samples will be integrated into the research. For example, gender differences will be examined in studies to identify responder/non-responder groups.

1.2 Quality and innovative aspects of the training programme

1.2.1 Overview and content structure of the training

TRACT proposes a high-level, joint research-training programme that focuses on exploiting the research expertise and infrastructure of all the beneficiaries and associated partners, availing of complementarity with programmes offered locally at participating institutions and promoting scientific excellence and innovation. Specifically, the TRACT training programme includes mechanisms to:

- **Develop research-related competencies** in the area of cancer research in a cohort of ESRs under three research themes (Biomarker Discovery, Resistance Mechanisms and Metabolic Transformation) through carefully supervised individual research projects,
- **Extend the traditional academic research training environment** to include exposure to private sector research and development activities through secondments and intersectoral training events,
- **Equip a cohort of ESRs with the skills needed to translate basic research findings** into future products and services, with a particular focus on clinical translation for patient benefit,
- **Foster a multidisciplinary mindset to enable more effective innovation** through a programme of structured knowledge exchange (conferences, workshops) and networking,
- **Widen the perspectives of the participating ESRs on future careers** in both academic and non-academic sectors through secondments and intersectoral training events,
- **Provide a career development plan for participating ESRs** (see section 1.3.2 for more details),
- **Promote international, interdisciplinary and intersectoral mobility** through exposure to a range of working environments, and
- **Exploit complementarity with programmes offered locally** at participating institutions ("Innovation Academy at TCD, 'Computational Biology' and 'Generic Skills in Communicating Science' workshops at QUB, etc.).

The TRACT **training objectives** are to:

1) Train ESRs in techniques relevant to cancer biomarker discovery, drug discovery and validation, and assessment of cellular metabolic changes, including whole genome sequencing, RNA-seq analysis, high-throughput glycoarrays, metabolomics, real-time Seahorse respiration technologies, advanced imaging, CRISPR generated cancer models, exosome analysis, medicinal chemistry, bioinformatics and systems biology techniques.

2) Provide ESRs with a solid foundation in commercialisation to improve links between industry and research organisations in order to drive more rapid and effective translation of research findings into products that will enhance cancer diagnosis and management for the benefit of patients and the European life sciences industry.

3) Train ESRs in transferable skills relevant for future academic and non-academic careers, including entrepreneurship, project management, communication, management of Intellectual Property, ethics, scientific writing and personal development planning.

The training objectives will be achieved through individual, project-specific training undertaken by each ESR at their recruiting institution (Table 1.2a) and through participation in two parallel, project-wide training streams devoted to scientific and

Table 1.2a Recruitment Deliverables per Beneficiary

Researcher No.	Recruiting Participant (short name)	Planned Start Month (0-45)	Duration (months, 3-36)
ESR 1	UVEG	6	36
ESR 2	QUB	6	36

23 Marocchio, L.S., et al., J Oral Sci, 2010. 52(2): p. 267-73.
24 Llewellyn, C.D., et al., Oral Oncol, 2004. 40(3): p. 304-13.
25 Lortet-Tieulent et al. Eur J Cancer. 2013 Nov 20. pii: S0959-8049(13)00952-0.
26 La Vecchia et al., Oral Oncol. 2004 Apr;40(4):433-9.
27 Garavello et al., 2010 Jul 1;127(1):160-71.

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complementary skills (Table 1.2b). In this way, all ESRs will benefit from the expertise and experience of their recruiting and secondment institutions, as well as from that of the consortium as a whole. All ESRs will be registered to a PhD programme. ESR 10 (based at the SME Oroboros) will be registered for a PhD at the Medical University of Innsbruck, where the Oroboros CEO (Erich Gnaiger) is also a lecturer. Supervision arrangements are detailed in section 1.3.2.

ESR 3	UVEG	6	36
ESR 4	QUB	6	36
ESR 5	TCD	6	36
ESR 6	UNISI	6	36
ESR 7	TCD	6	36
ESR 8	UNISI	6	36
ESR 9	TCD	6	36
ESR 10	OROBOROS	6	36
ESR 11	TCD	6	36
Total: 11			

Table 1.2b Main Network-Wide Training Events, Conferences and Contribution of Beneficiaries

([C] Compulsory Attendance; [E] Elective)

	Main Training Events & Conferences	ECTS	Lead Institution	Project Month
1	Kick-off Meeting (includes Introduction to OOC, Research Integrity, Gender/Sex in Research/ Open Science)[C]		TCD	6
2	Tumor histology[E]		TCD	6
3	Antibody technology in cancer research and therapy[E]		TCD	6
4	Animal models in cancer research and drug discovery[E]		TCD	6
5	Whole body imaging in xenograft cancer models[E]		TCD	6
6	Drug discovery & medicinal chemistry[E]		UNISI	6
7	Biomarker discovery[E]		UVEG	6
8	Cancer cell metabolism[E]		Seahorse	12
9	Training in mitochondrial and cellular respiratory physiology[E]		Oroboros	12
10	Generic skills in communicating science[C]		QUB	18
11	Fluorescence and electron microscopy imaging of cells[E]		Andor	18
12	Computational Biology[E]		QUB	18
13	Year 1 Meeting[C]		QUB	18
14	Outreach event for OOC patient/advocacy groups[C]		QUB	18
15	NMR Mini Boot Camp of BioBank Analyses and Metabolomic Transformation in Cancer[E]		TCD	24
16	Analytical techniques in glycobiology[E]		NIBRT	24
17	Project management targeted to industrial needs[C]		NIBRT	24
18	Innovation Academy & Career Development Workshop (includes Gender Issues, WiseR)[C]	30	TCD/QUB	24, 30, 36
19	Year 2 Meeting		TCD	30
20	TRACT Marie Sklodowska-Curie ITN Open Day/Exploitation Workshop[C]		TCD	36
21	Closing Symposium[C]		UNISI	45

1.2.1.1 Scientific Training

Scientific Methods: Training in general scientific methods will be carried out locally, through both hands-on and classroom-based training, delivered by the primary supervisor and the recruiting institution. Training will be tailored to the previous experience of each ESR, and will be carried out on an on-going basis. Key topics include:

- **Laboratory safety training** - site-specific procedures (evacuation, waste disposal, etc.), risk assessments, etc.
- **Research planning** - performing literature searches, critically reviewing publications, etc.
- **Experimental design** - planning research experiments through development of clear objectives and experimental design (design of appropriate controls, etc.).
- **Data collection** - how to record data in a notebook, how to manage electronic data, etc.
- **Data analysis** - critical evaluation of scientific data, statistical analysis, etc.

Technical Methods: TRACT ESRs will also receive technical training in a) methods specific to the individual ESR research projects, and b) methods common across the three TRACT research themes. Training in project-specific methods will be delivered locally under the direction of the Primary Supervisor and Secondary Supervisor. Training in project-wide methods will be delivered through a series of workshops held throughout the project (see workshops described below and Table 1.2b). ESRs will be required to attend four elective training events, which they will select with their Support Team and specify in their **Personal Development Plan** (section 1.3.2). At M6, all ESRs will receive initial training in TCD over a two-week period coinciding with the Kick-off Meeting:

'Tumour Histology' (Organiser: TCD; **Duration:** 2 days**):** This course will familiarise students with histology and its use in tumour grading and tissue of origin determination. Hands-on-experience in tissue sectioning, tissue embedding,

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immunohistochemical (IHC) staining and H&E staining will be provided using tumour samples recovered from the xenograft workshop. This course will also be open to wider research community.
'Antibody Technology in Cancer Research and Therapy' (Organiser: TCD; **Duration:** 2 days**):** A local specialist training course in antibody technologies will be delivered at TBSI where ESRs will attend lectures on the theory of antibody technologies and therapeutics widely used in cancer research and in the clinic. A series of practicals will also be given as part of the workshop, where ESRs will perform experiments using each of these technologies.
'Animal Models in Cancer Research and Drug Discovery' (Organiser: TCD; **Duration:** 2 days**):** This event will include four lectures on the use of animals in cancer research: xenograft, transgenic, gene-targeted and CRISPR generated cancer models and the technologies that have been developed to evaluate and analyse tumour status. Students will gain hands-on-experience, of benefit for subsequent training events (see below). TBSI is equipped with a state-of-the-art transgenic facility, *in vivo* animal imaging capabilities (with multiphoton intravital microscope), histology suite, MoFlo 4-Color High Performance Cell Sorter and an 800 MHz NMR spectrometer.
'Whole Body Imaging in Xenograft Cancer Models' (Organiser: TCD; **Duration:** 2 days**):** *In vivo* live imaging of tumour xenografts has become a key technology to understanding cancer development and metastasis and in the evaluation of cancer therapeutic drugs. Students will have the opportunity to carry out imaging of xenograft animals, and evaluate and quantitate the growth over time. This course will also be open to wider research community.
'Drug Discovery and Medicinal Chemistry' (Organiser: UNISI; **Duration: 2 days):** This workshop will cover the principal discovery and development phases of small drug molecules. Topics covered will include: target selection; biochemical and computational strategies of molecular design; optimisation and selection processes; pharmacokinetic and toxicological assays used to inform transition to phase I trials. This course will also be open to wider research community.
'Biomarker Discovery' (Organiser: UVEG**; Duration 2 days):** This course will examine the need and potential for novel biomarker discovery in a clinical setting. ESRs will receive structured training in current genomic, proteomic and glycomic biomarker discovery theory and techniques. The workshop will also provide grounding in the use of bioinformatics and analytical tools in biomarker validation. This course will also be open to wider research community.

At M12, 18 and 24, relevant ESRs will be able to attend project-wide workshops hosted locally as detailed below:

M12
'Cancer Cell Metabolism' (Organiser: Seahorse; **Duration:** 2 days**):** Metabolic transformation is a universal property of tumour formation and a promising mode of treatment. Through state-of-the-art Seahorse analysis ESRs will learn about the alterations in metabolism that sustain cancer cell growth and resistance to therapy.
'Training in Mitochondrial and Cellular Respiratory Physiology' (Organiser: Oroboros; **Duration:** 3 days**):** Oroboros will provide O2k- Workshops to TRACT ESRs on use of the Oxygraph-2k respirometer to measure oxygen consumption rates, transmembrane potential differences using TPP-electrodes and fluorescence sensitive electrodes to determine hydrogen peroxide production (Amplex red), membrane potential (Safranin), ATP production (Mg green) or Ca2+ (Ca green).
M18
'Fluorescence and Electron Microscopy Imaging of Cells' (Organiser: Andor/TCD; **Duration:** 4 days**):** This training course will consist of a placement on the Andor Academy level three training programme at the Andor facility in Belfast. This element will cover topics in advanced light microscopy and will take two days. The CMA/TBSI in TCD will run a two-day workshop on the use and application of electron microscopy for biological imaging.
'Computational Biology' (Organiser: QUB; **Duration:** 3 days**):** In this training course ESRs will be given a systematic introduction to quantitative analysis methods for high-throughput data which is needed to analyse genomics data from biology and cancer biology. This course will also be open to wider research community.
M24
'NMR Mini Boot Camp of BioBank Analyses and Metabolomic Transformation in Cancer' (Organiser: TCD; **Duration:** 2 days**):** TCD's TBSI are developing 2D NMR metabolomics methodologies. This training course will be targeted to provide the ESRs (as well as to others in the medical, pharma, and bio research sectors): (1) lectures introducing the underlying principles and practices of modern NMR spectroscopy, with (2) hands-on experience to be able to run and analyse biomolecular samples.
'Analytical Techniques in Glycobiology: Applications to biomarker discovery' (Organiser: NIBRT; **Duration:** 3 days**):** This course will be run by NIBRT in their research facilities in Dublin and specifically trains researchers in biomarker discovery and validation. The focus will be on glycan biomarkers and blood samples from cancer patients will be analysed during the 3-day course. Complex HPLC and MS techniques will be presented to TRACT researchers who will carry out sample clean-up experiments, derivatization procedures, HPLC analysis and interpretation of results using established in-house database systems (GlycoBase).

Research Ethics & Integrity: As part of their local induction training, all ESRs will be trained on recognised ethical practices and fundamental ethical principles relevant to their discipline(s), as well as to ethical standards as documented in the different institutional Codes of Ethics. In addition, at the first project meeting (M6), TRACT researchers will receive instruction from Prof Orla Sheils, Chair of TCD Research Ethics Committee, on matters

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such as informed consent, social/cultural impact of research and research integrity. Training in research integrity will ensure research is performed according to the highest standards of professionalism and rigour, and ensure the accuracy and integrity of the research record in publications and elsewhere.[28]

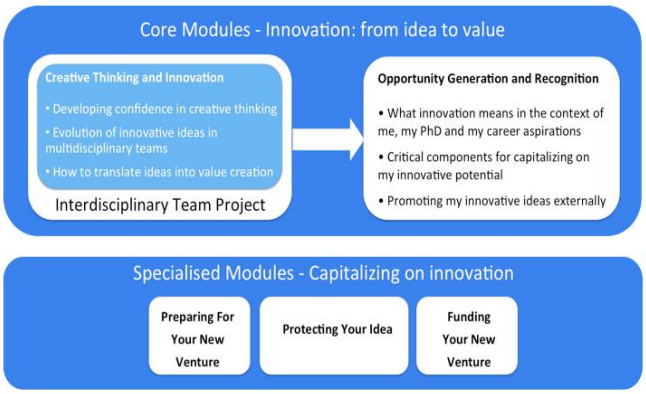
Gender/Sex in Research: Sex/gender differences may impact on the research planned in TRACT. Training by Yellow Window, an FP7-funded initiative, will be compulsory for all TRACT ESRs and will be delivered at the 'kick off' meeting. This training includes a practical toolkit on how to consider gender in all aspects of research. ESRs will also learn about the role of gender/sex in research through their individual projects. For example, gender differences will be examined when analysing responses to chemotherapy or assessing drug resistance.

Open Science: Niamh Brennan from TCD is a consortium member of OpenAIRE, a H2020 funded project on open science and will deliver a session at the introductory meeting.

1.2.1.2 Complementary Skills Training

Innovation: TRACT ESRs will receive training from the Innovation Academy (www.innovationacademy.ie) at M24, 30 and 36. The Innovation Academy was established in 2010 by TRACT Coordinator TCD, in collaboration with University College Dublin and TRACT partner QUB, with a mission to transform PhD graduates into energetic and resourceful entrepreneurs with the requisite skills to pursue fresh ideas and new ventures. Innovation Academy modules completed by the TRACT ESRs can be applied towards a **Postgraduate Certificate in Innovation & Entrepreneurship**, giving them formal recognition of their transferable skills training. Modules include:

- Module 1 (2 weeks) - *Creative Thinking and Innovation* (10ECTS) aims to ignite creative thinking in early stage researchers, with an emphasis on building foundations of non-discipline specific innovation as part of multi-disciplinary teams.
- Module 2 (1 week) - *Opportunity Generation and Recognition* (5ECTS) aims to aid in the ESRs' identification and assessment skill-sets required to develop ideas related to their individual projects. Upon completion, ESRs should be able to develop and assess the most innovative aspects of their PhD thesis research, as well as identify potential pitfalls to further development and implementation and develop a strategy to navigate these pitfalls. A key outcome of the module is a 'researcher pitch' video.



Structure of the Postgraduate Certificate in Innovation & Entrepreneurship

- Module 3 (1 week) - *Protecting Your Idea, Novelty, Copyright and Intellectual Property* (5ECTS) introduces ESRs to quality, early identification and protection of IP, including an exploration of copyright, patenting, trademarks, industrial design and know-how as well as ways of deriving value from the 'unprotectable'.
- Module 4 (1 week) - *Planning Your New Venture* (5ECTS) This module will provide an understanding of the components of a comprehensive business plan for a new venture and the ESRs will examine the potential problems that may be encountered in developing a business plan.
- Module 5 (1 week) - *Creative Capital: Financing Your New Venture* (5ECTS) ESRs will learn how to evaluate the financial performance, financial position and cash flow of an enterprise and be able to identify target areas to consider whilst seeking finance for a new venture.

Project Management: All ESRs will complete a formal, two-day workshop **'Project Management Targeted to Industrial Needs'** run by industrial partner NIBRT. The formal training will consist of a two-day training course with a focus on project management in industrial settings. Topics covered will include writing project proposals/business plans, recruitment, outsourcing, safety and regulatory issues, costing, project management tools, meeting deadlines and setting up contingency plans.

In addition, all ESRs will receive hands-on training for managing their individual research project. Hands-on project management training will focus on management of academic research projects, and will be delivered by the Primary Supervisor of each ESR on an on-going basis over the project. The training will include regular planning and progress meetings, with ESR reports at M18, 30 and 42 as formal outputs.

Finally, all ESRs will collaborate to organise a **'TRACT Marie Sklodowska-Curie ITN Open Day and Exploitation Workshop'** at M36 to help them develop project management and event organisation skills (see section 2.4).

[28] http://www.iua.ie/research-innovation/research-integrity/.

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Communication/Outreach: All ESRs will be involved in, at minimum, two outreach activities per year over their three year appointments and the activities chosen will be included in each ESRs' PDP.
At M18, all ESRs will attend a two-day workshop in **'Generic Skills in Communicating Science'**, including modules entitled 'Writing a PhD Thesis', 'Writing a Good Scientific Paper', 'Critiquing a Research Paper' and 'Giving a Research Talk'. This workshop has been developed by the Centre for Cancer Research and Cell Biology (CCRCB) in QUB and is currently delivered to all QUB postgraduate students. ESRs will be given multiple opportunities to apply the workshop learnings though presentations at TRACT project meetings, involvement in public engagement outreach activities with a focus on communicating science to the general public and attendance at external academic conferences. In addition, in conjunction with the M18 project meeting, all ESRs will present their research to a lay audience at an **outreach event for OOC patient/advocacy groups,** organised by QUB and chaired by Dr. Richard Turkington (QUB) (see section 2.4 for further details).

At M45, the project will host a two-day **'Closing Symposium'** at UNISI. Attendees will include all ESRs and supervisory personnel involved in the project, as well as interested researchers and industry representatives from a variety of related fields, such as drug discovery and diagnostics. The symposium will include oral presentations by all ESRs. In addition, the Principal Investigators (PIs) will lead discussion sessions on exploitation of project findings, including the presentation of market research and business plans by the ESRs. The discussion sessions will promote the future commercial development of novel biomarkers and chemical/biological therapeutics arising from the project through our industrial partners.

Teaching/Training: ESRs will be involved in teaching and training activities through their recruiting institutions, including laboratory demonstrating, tutorials/seminars, undergraduate project supervision and supervision of technical staff. These activities will be overseen by the Primary Supervisors and will be detailed in each ESRs' PDP.

Gender Issues: All ESRs will receive training by Prof Eileen Drew of Women in Science & Engineering Research (WiseR) as part of the Career Development Workshops at M24. WiseR is an initiative, partly funded by FP7, which works to 'recruit, retain, return and advance' women in academic science, engineering & technology (SET). Training will include networking/building a research profile and maintaining work/life balance. WiseR will also advise researchers on how to influence policy in their own institution in a range of areas, such as representation of women in senior positions and flexible working arrangements. In addition, a speaker from the Research Centre for European Integration, a Jean Monnet Centre of Excellence hosted by UNISI, will deliver a session on gender quality in the public sector to all ESRs at the project meeting at M45.

1.2.1.3 Career Planning

Upon completion of the project, ESRs will have developed skills that will enable them to pursue **careers in academia, industry or as entrepreneurs.** TRACT will include career planning activities, including:

- **Career development workshops** - will be held in conjunction with the Innovation Academy modules and will focus on CV preparation and interview skills, effective networking, job-seeking strategies and proposal writing/securing funding,
- **Supervisory Board member presentations** - academic and non-academic representatives will share their career paths and tips for success,
- **External keynote speakers** - successful researchers, including successful life science entrepreneurs, will be invited to present at project-wide meetings.

1.2.1.4 Multidisciplinary and Intersectoral Exposure

One of the intents of TRACT is to expose ESRs to a wide range of disciplines and sectors involved in cancer research and development. This will be achieved through the multidisciplinary nature of the individual research projects and the intersectoral secondments, but a wider exposure will also be achieved through annual project-wide meetings, held at M6, 18 and 30, and the **'Closing Symposium'** held at M45. The '**Kick-off Meeting'** at M6 will include presentations from all PIs on the state-of-the art of their subject area. A workshop entitled 'An Introduction to Oral and Oesophageal Cancer' will be given by PIs from UVEG and QUB and will provide ESRs with an up-to-date review of the current practises in the diagnosis and treatment of OOC and problems associated with current treatments. In order to minimise travel expenses, various partners will deliver elective workshops in TCD over a two-week period directly following the Kick-off meeting (section 1.2.1.1). At the **"Year 1 Meeting'** in M18 and the **'Year 2 Meeting'** in M30, all ESRs will present oral presentations on their research. In addition to formal presentations, time will be devoted to workshops and discussion sessions where the impact of individual projects on the direction of the research programme as a whole can be explored. Presentations from Supervisory Board members and external keynote speakers will also be included to support career planning.

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1.2.2 Role of non-academic sector in the training programme

The non-academic sector has a key role in TRACT in delivery of both the research/training elements of the programme and overall project oversight. Non-academic **research involvement** includes hosting secondments and ESR recruitment (OROBOROS), on-going review of emerging research results to identify new opportunities for innovation and involvement in IP identification and management through initial submission of invention disclosure forms. **Training involvement** includes delivery of formal training workshops as presented above (Cancer Cell Metabolism (Seahorse), Training in Mitochondrial and Cellular Respiratory Physiology (OROBOROS), Exosome-based Drug Discovery (Exosomics), Fluorescence and Electron Microscopy Imaging of Cells (Andor), Project Management Targeted to Industrial Needs (NIBRT)). Through participation in the Career Development Workshops held in conjunction with the Innovation Academy at M24, 30 and 36, industrial representatives will identify career opportunities for qualified researchers in their respective industries. Non-academic participants will also contribute to **project oversight** through representation on the Supervisory Board and regular consultations with the management of all our industry partners.

1.3 Quality of the supervision

1.3.1 Qualifications and supervision experience of supervisors

The combined supervisory experience in TRACT is excellent. Academic Primary and Secondary Supervisors have supervised a total of 165 PhD students to completion, and are leading experts in their respective fields:

PI	Expertise & Publications	Supervision Experience & Leadership Roles	ESR
Prof. Jose Bagan, MD, DDS, PhD (UVEG)	Oral medicine and pathology, discovery of novel biomarkers for treatment of OSCC; 326 publications	43 PhDs completed; 3 PhDs in progress; Head of Stomatology and Maxillofacial Surgery; Coordinator of Doctoral Programme in Clinical Dentistry; Director of research and teaching at University General Hospital in Valencia; Director of the School of Doctoral Programmes for UVEG	1, 3
Prof. Richard Kennedy, MB, BAO, Bch, BSc, PhD, FRCP (QUB)	Medical oncology and drug discovery, 90 publications	10 PhDs completed; 6 PhDs and 4 clinical fellows in progress; Director for undergraduate academic training in medicine	2, 4
Dr Richard Turkington, MB BCh BAO, BSc, PhD, MRCP	Medical Oncology and Upper-gastrointestinal cancer, 13 publications	1 PhD and 1 Clinical Fellow in progress. Director of the Academic Foundation Program	2,4 (Co-Supervisor: Kennedy)
Prof. Emma Creagh, B.A Mod, PhD (TCD)	Cancer inflammation; 24 publications	3 PhD/2 MSc completed; 1 PhD in progress; Co-ordinator of Freshman Biochemistry teaching	5, (Co-Supervisor: Murray)
Prof. James Murray, BSc, PhD (TCD)	Enzymology and metabolism; 30 publications	5 PhD/2 MSc completed; 2 PhDs in progress; Coordinator of Undergraduate Erasmus Exchange programme	5,
Prof. Giuseppe Campiani, MSc, PhD (UNISI)	Medicinal chemistry; 154 publications	28 PhDs completed; 4 PhDs in progress; Director of European Research Centre for Drug Discovery and Development; Rector's Delegate for International Cooperation & Development.	6, 8
Prof. Vincent Kelly, B.A. Mod, PhD (TCD)	Cancer biology; 23 publications	6 PhDs/1 MSc completed; 2 PhDs in progress; Coordinator of Molecular Medicine Undergraduate Degree; Director of the Transgenic Unit in TCD	7, (Co-Supervisor: Mok)
Prof. Mok, PhD (TCD)	Structural biology and NMR metabolomics; 47 publications	3 PhDs completed; 2 PhDs in progress; Director of TBSI NMR Facility	7
Prof. Daniela Zisterer, PhD (Coordinator, TCD)	Cell death mechanisms, development of anti-cancer therapeutics; 70 publications	15 PhDs completed; 2 PhDs in progress; Director of Research for School of B & I; Biochemistry Undergraduate Degree Coordinator; Coordinator of cancer stream of PRTLI funded structured PhD training programme (2011-2015)	9 (Co-supervisor O'Sullivan)
Prof. Jeffrey O'Sullivan, BSc,	Oral cancer;	8 PhDs (Clinical Dentistry)/3 PhDs completed; 5 PhDs in progress; Coordinator of Biochemistry Teaching to	9

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PhD (TCD)	19 publications	Undergraduate Dental Science Students	
Prof. Erich Gnaiger, PhD (OROBOROS)	Mitochondrial physiology & pathology; 82 publications	10 PhDs completed; 3 PhDs in progress; Organiser of > 90 international workshops on high-resolution respirometry	10
Prof. Richard Porter B.A. Mod, PhD (TCD)	Metabolism and bioenergetics; 45 publications	7 PhDs/2 MSc completed; 3 PhDs in progress; Head of Biochemistry in Trinity Biomedical Sciences Institute; Coordinator of Biochemistry Teaching to Undergraduate Medical Students	11

Non-academic supervisors also have significant experience in leading large teams of PhD level scientists. For example, Dr. Tim Davison from Almac Diagnostics has led teams of 17 PhD/11 MSc level scientists over the last 9 years. Many partners from the non-academic sector also have current and/or previous involvement in doctoral programmes. Notably, Andor and NIBRT are currently supervising ESR secondments from the FP7-funded ITN TINTIN (see Capacities Tables in section 5 for more detail).

1.3.2 Joint Supervision Arrangements - Academic/Non-Academic Collaboration

Each ESR will be supervised by an ESR Support Team, consisting of the Primary Supervisor from the recruiting, institution, a Secondary Supervisor(s) from each secondment-hosting institution and a Mentor (independent PI in the recruiting institution). The **Support Team will include both academic and non-academic representation**. As recommended by the European Charter for Researchers, the Mentor will provide support and guidance for personal and professional development, with a particular focus on transferable skills and career planning.

All ESRs will meet with their Support Team when they join the project at M6 to devise a Personal Development Plan (PDP). The PDP will detail the training they will receive throughout the programme and mechanisms for on-going assessment of progress. Each ESR will meet weekly with their Primary Supervisor when at the recruiting institution and the relevant Secondary Supervisor while on secondment. Monthly meetings will take place between ESR and their full Support Team (virtually or face-to-face). The Primary and Secondary Supervisors will have overall responsibility for introducing the ESR to their institute and the goals of the training programme, maintaining open lines of communication, co-developing an effective PDP with the ESR and providing timely feedback and support. A copy of the PDP will be sent to the project Supervisory Board for approval along with regular (six monthly) updates so that the Supervisory Board can monitor progress and provide constructive feedback. ESRs will receive informal feedback following each monthly meeting with their Support Team. Formal feedback will be provided to ESRs following their presentation at the annual meeting.

1.4 Quality of the proposed interaction between the participating organisations

1.4.1 Contribution of all participants to the research and training programme

The aim of TRACT is to **train a cohort of ESRs** to use the expertise and state-of-the-art technology contributed by all participants **to research cancer cell mechanisms** and to **discover new methods for OOC detection and treatment.** The programme has been designed so that all participants contribute to both research and formal/informal training activities (Table 1.4a). In addition to specific interactions with ESRs working within their institutions, TRACT participants will **contribute multidisciplinary and intersectoral knowledge** in bioenergetics (Seahorse, Oroboros), exosomes (Exosomics), cell imaging (Andor), bioinformatics (Almac Diagnostics, UNISI), biomarkers (UVEG, QUB, Almac Diagnostics, NIBRT), immunotherapeutics (TCD, Opsona) and drug discovery (UNISI, IME-SP, Exosomics) to all ESRs through project-wide meetings. Participants will also provide **access to a broad range of technologies** such as through project-wide meetings. Participants will also provide access to state-of-the-art technologies such as genome scale CRISPR knockout and next generation sequencing, metabolomics, Seahorse bioenergetic analysis, *in vivo* imaging and *in-silico* drug screening.

Table 1.4a Contribution of all participants to TRACT

Participant	Recruitment & Hosting of ESR	Hosting ESR Secondment	Provision of training workshop
TCD	√ (ESR 5,7,9,11)	√(ESR 2,4,6,8,10	√
QUB	√ (ESR 2,4)	√ (ESR 5, 7)	√
UNISI	√ (ESR 6,8)	√ (ESR 7)	√
UVEG	√ (ESR 1,3)	√ (ESR 9)	√
OROBOROS	√ (ESR 10)	√ (ESR 7, 11)	√
Almac Diagnostics		√ (ESR 2,4)	
Andor		√ (ESR 9)	√
Exosomics		√ (ESR 6,8)	
IME-SP		√ (ESR 3,4)	
NIBRT		√ (ESR 1,3)	√
Seahorse			√
Opsona		√ (ESR 5)	

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1.4.2 Synergies between participants

Partnerships between industry and academia enhance the strengths of both partners and provides access to resources and expertise neither party could achieve alone. Key to the success of the partnerships in TRACT is the principle of knowledge transfer, whereby ESRs are able to draw experience from both high quality environments.

TRACT builds on previous and on-going collaborations between a number of consortium partners, which leverage complementary expertise. For example, Almac Diagnostics was originally formed as a spin-out company from the Centre Cancer Research and Cell Biology (CCRCB) at QUB. As a leader in biomarker development, Almac Diagnostics have developed a rigorous approach to the analysis of genomic data for the identification of novel diagnostics. This involves expertise in project management, quality assurance and design control, with a focus on advancing biomarkers to meet current regulatory standards. A long standing collaboration (21 years) has also existed between Zisterer in TCD and Campiani in UNISI. Principally, UNISI, experts in medicinal chemistry, have provided novel drugs to TCD for biological evaluation. UNISI and TCD hold a joint patent as a result of this collaboration and have jointly published 35 research articles.

1.4.3 Exposure of recruited researchers to different research environments

All ESRs will be recruited or seconded to both academic and non-academic environments. Furthermore, secondments for each ESR have been specifically designed to avail of industry expertise, facilitating complementary advanced training in specialised technologies, exchange of knowledge and ideas and meaningful exposure to different research environments.

Table 1.4b Secondments of ESRs to academic and non-academic partners

ESR No	Host Beneficiary (Academic/SME)	Secondment(s) (non-academic)	Secondment (academic)
1	UVEG (academic)	NIBRT	
2	QUB (academic)	Almac Diagnostic	TCD
3	UVEG (academic)	IME-SP	
4	QUB (academic)	IME-SP & Almac Diagnostic	TCD
5	TCD (academic)	Opsona	QUB
6	UNISI (academic)	Exosomics	TCD
7	TCD (academic)	OROBOROS	UNISI
8	UNISI (academic)	Exosomics	TCD
9	TCD (academic)	Andor	UVEG
10	OROBOROS (SME)		TCD
11	TCD (academic)	OROBOROS	TCD

2 Impact

2.1 Enhancing the career perspectives and employability of researchers and contribution to their skills development

Research excellence is the fundamental principle on which TRACT is built. Eleven novel research projects are proposed, which will challenge ESRs to push the boundaries of the research field under the guidance and supervision of experienced clinicians and leading researchers from multiple disciplines. Interactions with the non-academic sector is also embedded in both research and training aspects of the programme, enabling ESRs to receive intensive training in advanced technologies. TRACT research and training activities will benefit the careers of the participating fellows in a number of ways.

Intersectoral and multidisciplinary skills and perspectives: The doctoral training achieved through TRACT will exceed traditional PhD training. TRACT ESRs will benefit from exposure to an array of disciplines and sectors, regardless of their intended, future career paths. The research training will allow ESRs to develop discipline-specific skills through hands-on research and training courses. Secondments, training events and project-wide meetings will expose them to real-world applications of basic research and how research is brought to the clinic and market. Fellows trained through the TRACT network will be **uniquely positioned for careers in academia, industry or as entrepreneurs**. The interdisciplinary nature of the project will give them access to the collaborative expertise of clinicians, biochemists, immunologists and chemists, so that the TRACT cohort of researchers will be able to communicate across scientific disciplines. Involvement of the non-academic sector in governance, supervision of projects, training and hosting of secondments will ensure network ESRs will be able to work across the public-private divide, for example through research collaborations between universities and industry.

Impact on academic career prospects: Oral and oesophageal cancer are one of the few cancers which are increasing in incidence, particularly among women (see Section 2.2.2). This, together with the multidisciplinary approach and the highly innovative techniques such as CRISPR technology that the ESRs will be exposed to, will position graduates of this programme to become research leaders and also to potentially inform the development of academic curricula. They will be equipped with skills to develop their own ideas and will have a broader

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perspective, making them more competitive for academic positions. It is expected that the ambitious research programme will produce several high-quality publications which will benefit the academic career prospects of ESRs. As recommended by the LERU Good Practice Elements in Doctoral Training[29], TRACT ESRs will establish research networks beyond their own discipline, essential for a future research career which is unlikely to remain limited to one narrow domain. They will benefit from the opportunity to develop an international profile at an early stage in their career through secondments, attendance at conferences, and network-wide training and meetings. The extensive training programme described in Section 1.2 includes training in proposal writing, teaching experience, and access to leading academic researchers, all of which will benefit their academic career prospects.

Exposure to leading research and technologies: ESRs recruited to the programme will work in a stimulating research and training environment with access to state-of-the-art infrastructure and facilities under the guidance of highly-experienced supervisors. Through secondments and participation in project-wide meetings and training events, TRACT ESRs will gain a wider exposure than researchers involved in traditional PhD programmes. This exposure will open new career perspectives beyond those related to their specific discipline, and equip them with the skills to enter careers that span sectors and disciplines. This will positively impact their career prospects in industry (SME/BIOTECH/PHARMA).

Innovation training: The Europe 2020 Flagship Initiative – 'Agenda for new skills and jobs'[30] emphasises the importance of promoting entrepreneurship, self-employment and innovation. ESRs trained through the TRACT programme will be introduced at an early stage to the concepts of creativity and entrepreneurship and how their discoveries can be translated to the commercial setting. A unique aspect of the TRACT programme is inclusion of training dedicated to innovation and entrepreneurship through the 'Innovation Academy'. This training will enable TRACT ESRs to pursue innovation through their research during the project but will also equip them with the requisite skills to pursue fresh ideas and new ventures in future positions. The formal nature of this training will enhance the attractiveness of TRACT graduates to future employers.

Career planning: ESRs in TRACT will have the opportunity to explore academic and non-academic careers, in line with the LERU Good Practice Elements in Doctoral Training. The TRACT programme includes both informal and formal supports for career planning. Unlike researchers engaged in more traditional PhD programmes, TRACT ESRs will receive support and input from both academics and non-academics through interactions with their own Support Team and with others across the consortium at project meetings. Participation in dedicated career workshops will also be required, with opportunities to develop essential complementary skills, such as networking, CV preparation and interview skills.

Mobility: Mobility is recognised as a key factor in research career progression. According to the EU Commission's Researchers' Report 2014[31] only 15% of researchers who currently work in the EU are 'mobile', with men significantly more likely to be internationally mobile than women. In line with the programme requirements, all ESRs will be required to undertake transnational mobility at recruitment. All ESRs will also participate in secondments in different countries from their host institution. Thus, TRACT ESRs will be exposed to new and different research and industrial cultures, so that they can experience firsthand the potential benefits of mobility and learn valuable skills for adapting to new working environments. They will also gain experience in managing the practical aspects of mobility, such as dealing with immigration requirements and moving country, in a supported environment. In these ways, TRACT will prepare ESRs to pursue a wider range of future career opportunities across Europe.

2.2 Contribution to structuring doctoral / early-stage research training at the European level and to strengthening European innovation capacity

2.2.1 Structuring training across Europe

The TRACT programme has been designed with close reference to the EU Principles for Innovative Doctoral Training[32] and it is expected that the programme will contribute to the mainstreaming of a multidisciplinary, intersectoral, structured approach to doctoral training in the TRACT host institutions and beyond. TRACT will provide evidence of the benefit of a multidisciplinary, intersectoral approach to PhD training to support changes in curriculum in the participating beneficiaries. TRACT will also demonstrate that formal links between academic

29 (http://www.leru.org/files/publications/LERU_AP_15_Good_practice_elements_in_doctoral_training_2014.pdf)

30 http://ec.europa.eu/social/main.jsp?catId=738&langId=en&pubId=626&type=2&furtherPubs=yes

31 http://ec.europa.eu/euraxess/index/cfm/services/researchPolicies

32 http://ec.europa.eu/euraxess/pdf/research_policies/Principles_for_Innovative_Doctoral_Training.pdf

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and industry partners in the design of multidisciplinary structured doctoral programmes at a European level are an invaluable resource in the training of future ESRs. A number of PIs in the academic beneficiaries are already responsible for doctoral curriculum design. For example, Prof Zisterer was the Co-ordinator of the cancer stream of the very successful PRTLI structured PhD programme 'Molecular and Cellular Mechanisms underlying inflammatory processes' in TCD (2011-2015). Prof. Bagan (UVEG) is Co-ordinator of the structured doctoral programme in Dentistry and is Director of the School of Doctoral Programmes for the entire University.
The consortium also plans to interact with current and future related ITNs and research actions funded by the Commission, as described below (section 2.3.2).

2.2.2 Strengthening European innovation capacity

TRACT will strengthen European innovation capacity specifically in terms of contributions to European capabilities for cancer diagnostics and therapeutics for OOC. **Patentable and commercially exploitable discoveries relevant to OOC are expected to arise from the project**, including new diagnostic kits (swab-based genotyping) for diagnosis and therapy monitoring, and novel therapeutics. Despite efforts to screen for and pre-operatively select OAC patients for potentially curative surgery, the five-year survival rate in early stage disease is only 25-35%. The incidence of OAC in men has also risen 50% in the last 25 years[33]. This is due to late diagnosis of disease and resistance to chemotherapy. In order to identify novel therapeutic agents and improve outcomes for OOC patients, there is an urgent need to discover biomarkers for early detection of the disease and to better understand the molecular basis of metabolic transformation and drug resistance in OOC. The ambitious goal set by the 'Commission Communication on Action Against Cancer: European Partnership' is to reduce cancer incidence by 15% by 2020[34]. TRACT will contribute to this goal by early diagnosis and improved therapy of OOC. **Therapeutic benefits from the research programme are promising since a number of molecular drug targets and potential biomarkers have already been identified by pilot experiments** (see section 1.1.4).
There will also be more general impacts in terms of training researchers to deliver innovation in basic and applied research and bringing together European academics and industrialists. TRACT will contribute to delivering on the commitments of the Europe 2020 Flagship Initiative - Innovation Union,[35] in particular by **promoting excellence in education and skills development** through the proposed doctoral training programme. It will contribute to establishing Europe as a world-class science performer by generating a talent pool of internationally mobile researchers in the field of cancer research, an area of enormous significance to Europe, both societally and economically. The highly-talented cohort of researchers with international and intersectoral experience will greatly enhance the capacity of Europe to address the enormous challenge of cancer diagnosis and therapy. TRACT will also contribute to **removing the obstacles to innovation by addressing the skills shortage and the "knowledge gap" between academic researchers and the commercial world.** The project will contribute to a framework to deliver on the commitment to revolutionise how the public and private sectors work together by promoting the flow of researchers and expertise between the sectors.
Through the project, existing links between academia and industry will be strengthened and new links forged. This will not only open up broader career paths for the ESRs, but will also **drive more rapid, more effective translation of research findings into products** that will enhance cancer diagnosis and management, and will **deliver growth in revenue and employment** for European SMEs in the life sciences.
TRACT has the capacity to progress innovative multiplex companion diagnostics, with the inclusion of OOC genetic signatures, to the market. For example, partner organisation Almac has developed a microarray-based gene signature test for stage II colon cancer recurrence which was launched on the US market by Helomics Therapeutics Inc.® as GeneFX colon and a number of additional tests for breast, ovarian and prostate cancer are in Almac's development pipeline.

2.2.3 Contribution of the non-academic sector to the doctoral/research training

Non-academic partners will provide **state of the art training in drug design, biomarker discovery, exosome analysis, metabolism and therapeutics**. To achieve the ambitious objectives, all the ESRs will be seconded to SME/industry companies relevant to their chosen project across Europe for minimum periods of 3 months for intensive training in advanced technologies and research areas central to the TRACT theme. The TRACT SME/industry partners have been specifically identified as leaders in their field in terms of both technology and its application to cancer research and their involvement is essential for a full and integrated training program for the ESRs. TRACT will also **provide very useful networks of contacts to the researchers employed on the network**

33 http://www.cancerresearchuk.org/cancer-info/cancerstats/types/oesophagus/mortality/#source1
34 http://ec.europa.eu/health/major_chronic_diseases/diseases/cancer/index_en.htm
35 http://ec.europa.eu/research/innovation-union/index_en.cfm?pg=action-points

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grant for their future careers. The specific capabilities of each SME/industry partner are incorporated into the programme overview. A potential impact of the close collaboration between the academic and non-academic partners may be the development of joint PhD programmes in future and also the exchange of other researchers between the sectors.

2.3 Quality of the proposed measures to exploit and disseminate the project results

2.3.1 Dissemination of the research results

Dissemination of research results from the project will take place via a number of channels.

Publications/presentations: Project results will be published in relevant peer-reviewed journals, such as Cancer Research and the British Journal of Cancer, and presented at relevant scientific conferences, such as the European Association of Cancer Research bi-annual meeting, oncology-specific conferences (such as ASCO or ESMO) or speciality conferences relating to OOC, 'omics and diagnostic assay technology. Material presented and published will adhere to the IP process established for the project to ensure exploitable outputs are protected in advance of dissemination.

Open Science: The TRACT consortium are supportive of the Horizon 2020 strategic priority of Open Science. To maximise research impact and to help promote diversity in science across the EU, we will pursue the 'green' route to open access through self-archiving (such as the TARA repository in TCD) and publication in open-access peer-reviewed journals, wherever possible.

Other projects: TRACT will engage with other related projects, such as Project Cyclon, a Marie Curie ITN, which is working on the development of a sugar-based anti-cancer drugs, and the Marie Curie ITN "Cancer Diagnostics: Parallel Sensing of Prostate Cancer Biomarkers" (PROSENSE) and the FP-7-ICT project "Virtual Physiological Human based predictive model for oral cancer reoccurrence in the clinical practise" (OraMod). The consortium will also approach newly funded projects over the TRACT lifetime. A related projects page will be created on the website. Other anticipated engagements include sharing the e-newsletter and invitations to project events.

2.3.2 Exploitation of results and intellectual property

It is expected that TRACT will **identify 1) novel biomarkers for diagnosing OCC and monitoring therapeutic response and 2) develop novel chemical and biological therapeutics**. Project partners intend to use these outputs to train ESRs in intellectual property management and to pursue commercial opportunities. For example, TRACT will develop a saliva-based diagnostic kit for early detection of dysplasia in OSCC suspect patients, which would be of commercial interest to clinical laboratories globally and could be developed by Almac as discussed in Section 2.2.2. **Therapeutic benefits from the research programme are promising since potential molecular drug targets and biomarkers have already been identified by pilot studies.**

All academic TRACT beneficiaries have dedicated Technology Transfer Offices to help biomedical researchers realize the economic, societal and commercial impacts of their findings. Since each ESR project is linked to an industrial partner, this further provides a unique potential for the commercial development of the data and to enhance public-private sector collaboration. Outputs generated from this programme may be transferred for commercial development through our industrial partners or commercialised through new spin-out companies. The best commercialisation approach will be determined on a case-by-case basis. Transfer of IP may form the basis for developing and expanding projects, enhancing public-private sector collaborations and creating future jobs. Fostering stronger links between industry and research will not only open up broader career paths for TRACT ESRs, but will also drive more rapid, effective translation of research findings into products to enhance cancer diagnosis and management, and deliver growth in revenue and employment for European Life Science SMEs.

TRACT Marie Skłodowska-Curie ITN Exploitation Workshop: All ESRs will work together to organize a half-day Exploitation Workshop, held in conjunction with the Open Day for stakeholder engagement. Representatives from pharmaceutical companies and patient advocacy groups will be invited to attend the workshop. ESRs will deliver lectures to inform relevant commercial entities on the advantages of public-private collaborations and on the advances that have been made in OOC research through the programme.

In addition to generating commercialisable research outputs, TRACT will **advance the strategic research goals of all the host academic institutes**. For example, a major research priority in CCRCB in QUB is 'Biomarker discovery and validation that informs how patients are treated or predicts tumour sensitivity to therapeutic targets'. In addition, one of the 2014-2019 TCD strategic research goals is 'to focus on interdisciplinary research', such as that planned for TRACT. Furthermore 'Cancer' is a major research theme of TCD. TRACT, through its research outputs, will enhance the global reputation of the respective academic institutes as locations for knowledge creation.

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2.4 Quality of the proposed measures to communicate the project activities to different target audiences

Communication and public engagement strategy of the project: This has been developed with a number of key audiences in mind, including cancer patients, future PhD candidates and the general public. Involvement of the ESRs in communication and public engagement is central to the strategy - all ESRs will be involved in a minimum of two outreach activities per year. The aim will be to raise public awareness of cancer research and more generally increase public engagement with and understanding of science, as well as developing ESRs' understanding of public interest and science-related priorities. The impact of the outreach activities for both the public and ESRs will be assessed by a number of methods, including questionnaires and interviews.

Web-based outreach activities: A project website will be created as the central online dissemination tool. ESRs will regularly contribute content to the site, as well as contribute to a six-monthly e-newsletter aimed at informing the general public about OOC and about the project findings in particular. A Wikipedia page will also be created and maintained by the ESRs. Social media accounts (Facebook, Twitter) will be created and maintained by ESRs and each will contribute to regular blog posts giving an update on their research and training activities. The impact of these activities in raising awareness will be measured by numbers of hits to the website, and reach of the social media accounts. To measure the impact on increased engagement metrics will include numbers of retweets, comments and replies.

Media: Networks within the Communications Offices of all partners will be leveraged to establish a project presence in the popular media. For example, a press release will be issued at the project kick-off. Where publications are likely to attract wider public interest, authors will work closely with Communications Offices to maximise coverage in the popular media. Many TRACT investigators already have a proven track record in public engagement. For example, Prof. O'Neill (Opsona) currently has a weekly slot with a national Irish broadcaster. This impact will be measured by numbers of media articles and radio/television spots.

Outreach to OCC patient groups: The TRACT research programme is of particular relevance to OCC sufferers, their families and friends. Each year, QUB hosts an information day for members of the Oesophageal Patient Association and the Oesophageal Cancer Fund. Dr. Turkington (QUB) will chair an outreach session at this information day (M18), where all ESRs will present their research to a lay audience. This session will educate the public about the existence of European projects to improve OOC diagnosis and treatment, while also offering ESRs with an opportunity to engage with those who may benefit from their work, potentially inspiring a deeper interest in the field of cancer research. In addition, ESRs based at QUB will have the opportunity to engage with the public through the Northern Ireland Cancer Consumer Research Forum - ESRs will give lab tours and talks to members of the Forum in order to promote greater public understanding and involvement in cancer research.

Outreach to secondary school students*:* Inspiring the next-generation of PhD candidates requires early exposure of cutting-edge science. All the host beneficiaries will be involved in outreach programmes to secondary school students. For example, currently the School of Biochemistry & Immunology, TCD, run a 'transition year' programme where secondary school students (15-16 years old) spend a week in laboratories within TCD. Each secondary school student spends time participating in scientific activities and group activities with talks, quizzes and visits to other scientifically relevant sites on the TCD campus. Similar schemes will be set up by other beneficiaries. Impact of these outreach activities will be measured through questionnaires distributed to students before and after the events.

Science Gallery and related global network**:** TRACT is fortunate to have direct access to the world-leading Science Gallery (www.sciencegallery.com) based in TCD. Since 2008, the Science Gallery has attracted more than 1.9 million visitors to 34 exhibitions, ranging in theme from contagion to the future of fashion. It has recently partnered with Google to establish a global network of science galleries, modelled on the Science Gallery approach to engaging young people in science. TRACT will engage in debates and information events run by the Science Gallery. Science Gallery have considerable experience in measuring impact of science communication activities.

EU Researchers' Nights and other local events: Where possible, ESRs will participate in on-going initiatives run by the beneficiaries. For example, ESRs will participate in EU Researchers' Nights, such as those hosted by TCD and UNISI. Live links between Siena, Dublin and the other beneficiaries will allow all ESRs to participate in both Nights. TCD led by the Trinity Biomedical Sciences Institute, was awarded funding to host an 'EU Researchers' Night' event in 2014 and 2015. The event had over 7,000 attendees each year and features a wide range of interactive and hands-on activities for the general public that aim to challenge perceptions held by the general public about

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researchers, to promote research as an exciting career option, to demonstrate creativity and innovation in research across all disciplines and to show that researchers are dynamic contributors to society. It is anticipated that the event will continue to be held annually. Marie-Skłodowska Curie Fellows are central to the organisation of this event, and ESRs recruited to TRACT at TCD will organise events, present their research and have representation on the Steering Committee for future EU Researchers' Nights. Similarly, UNISI is partner in the Researchers' Night "Scientists are Humans: Interactive Night of Entertainment - SHINE!", and every year in September, UNISI organizes a number of initiatives dedicated to young researchers (http://www.unisi.it/shine), in which ESRs based at UNISI will participate. Impact assessment through qualitative and quantitative measures is a key deliverable of Researchers' Nights and TRACT ESRs will contribute to this.

***TRACT Marie Sklodowska-Curie ITN Open Day*:** All ESRs will organise and participate in the Open Day (M36), helping them develop project management and event organisation skills. Attendees will include the general public and other interested lay audiences, such as patient group representatives. The event will include presentations from the ESRs on their research results, as well as open question sessions. The aim of the Open Day is to communicate the project findings and give ESRs an opportunity to develop communication skills. Impact will be measured through numbers of attendees and quality of discussions.

3 Quality and Efficiency of the Implementation

3.1 Coherence and effectiveness of the work plan

Table 3.1 a Work Package Descriptions

Work Package Number	1	6-42
Work Package Title	Biomarker Discovery (research/training)	
Lead Beneficiary	UVEG (Jose Bagan)	
Objectives (A) To train ESRs in state of the art techniques related to biomarker discovery, (B) To identify novel panels of biomarkers for OOC, (C) To pursue an avenue of translational research utilising identified biomarkers as therapeutic targets, (D) To identify potential molecules for IP protection and patenting		
Description of Work and Role of Beneficiaries/Partners **Task 1.1. (Lead:** UVEG; **Participants:** TCD, NIBRT; **ESR 1). Identify differences in salivary glycan profiles in different disease stages of OSCC.** TCD will provide expertise in inflammatory markers analysis using flow cytometry and other immune assays. NIBRT will provide expertise in glycan analysis, ranging from isolation of salivary protein glycans through to glycan structural identification using liquid chromatography and mass spectrometry technologies. **Task 1.2.** (**Lead**: QUB; **Participants**: Almac Diagnostics and TCD; **ESR 2**). **Develop integromic biomarkers capable of predicting response to chemotherapy in early stage OAC.** QUB together with Almac will analyse whole genome sequencing, methylation and microarray data aiding in biomarker discovery. TCD will functionally analyse the underlying biology of predictive classifiers. **Task 1.3. (Lead:** UVEG; **Participants:** IME-SP; **ESR 3). Develop a diagnostic test based on salivary inflammatory markers as a predictor of an OSCC patient's response to radiotherapy.** IME-SP will utilise the Mesoscale discovery platform to determine the inflammatory cytokine profile of patient samples.		
Deliverables 1.1 Report on correlation of salivary inflammatory & glycan markers with stages of OSCC (M24) 1.2 Report on correlation of salivary marker level with tumour control in radiotherapy patients (M24) 1.3 Report on identification of molecular signatures predictive of response to chemotherapy (M24) 1.4 Report on retrospective validation of resultant predictive classifiers (M36) 1.5 Awarding of PhD degree to ESRs 1-3 (M48)		

Work Package Number	2	6-42
Work Package Title	Molecular Resistance Mechanisms (research/training)	
Lead Beneficiary	UNISI (Giuseppe Campiani)	
Objectives (A) To train ESRs in drug design, synthesis and testing in models of OOC; (B) To elucidate the genetic underpinnings of drug resistance in OOC; (C) To identify therapeutic targets and examine potential for arresting drug resistance; (D) To identify novel agents for treating and increasing the sensitivity of OOC to cell death		
Description of Work and Role of Partners:		

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Task 2.1. (Lead: TCD; **Participants:** QUB, Almac Diagnostics, IME-SP; **ESR 4**). **Analyse differentially expressed genes in responders and non-responders and identify novel drug targets for therapeutic intervention in OAC.** QUB and Almac will analyse RNA-seq & microarray data to determine expression profiles in responders and non-responders. TCD will functionally analyse the biology underlying drug resistance in OAC in order to identify potential drug targets. IME-SP will provide expertise in target selection and drug development.

Task 2.2. (Lead: TCD; **Participants:** QUB, Opsona; **ESR 5). Establish the involvement of inflammatory caspases in tumour progression and resistance in OAC.** QUB will perform expression analysis of inflammatory caspases in biopsies from OAC patients. TCD and Opsona will utilise co-culture and animal models of OAC to determine the efficacy of novel Opsona and caspase inhibitors.

Task 2.3. (Lead: UNISI; **Participants:** TCD,Exosomics; **ESR 6). Rationally design, synthesise and test novel Mcl-1 inhibitors for the treatment of OSCC**. UNISI will perform computational chemistry and organic synthesis of novel Mcl-1 inhibitors that will be biologically evaluated in OSCC models in TCD. With Exosomics the miRNA markers of cell resistance contained in exosomes extracted from the media of the treated cells will be evaluated.

Task 2.4. (Lead: TCD; **Participants:** OROBOROS, UNISI; **ESR 7). Generation of novel HAMLET derivatives for the treatment of OAC.** UNISI will design and synthesise novel HAMLET derivatives which will be biologically evaluated in OAC models in OROBOROS and TCD.

Task 2.5 (Lead: UNISI; **Participants:** TCD,Exosomics; **ESR 8). Develop highly effective novel autophagy modulators for the treatment of OSCC.** UNISI will perform bioinformatics analysis, computational chemistry and organic synthesis of novel autophagy modulators that will be biologically evaluated in OSCC models in TCD. With Exosomics the miRNA markers of cell resistance contained in exosomes extracted from the media of the treated cells will be evaluated.

Task 2.6 (Lead: TCD; **Participants:** UVEG, Andor; **ESR 9). Assess benefit of combining chemotherapeutics with autophagy inhibitors for the treatment of OSCC.** UVEG will provide OSCC patient samples and will perform immunohistochemistry and PCR analysis of autophagy markers. Andor will perform live cell imaging of autophagic processes using advanced fluorescent probes. Combinations of chemotherapeutics and autophagy modulators will be assessed in OSCC cell lines and mouse model by TCD.

Deliverables

2.1 Report on RNA-seq & microarray analysis of inflammatory/autophagy proteins in OAC (M24)
2.2 Report on inflammatory caspase expression profiles during OAC (M18)
2.3 Report on markers tested in OAC culture systems (M24)
2.4 Report on novel apoptotic/autophagic modulators synthesised (M24)
2.5 Report on identification of pathways governing drug resistance (M36)
2.6 Report on modulators tested in OSCC cell lines, biopsies or in vivo animal model (M36)
2.7 Awarding of PhD degree to ESRs 4-9 (M48)

Work Package Number	3	6-42
Work Package Title	Metabolic Transformation (research/training)	
Lead Beneficiary	Oroboros Instruments Corp (Dr. Erich Gnaiger)	

Objectives

(A) To train ESRs in the differential metabolic profiling of cells;
(B) To identify metabolic targets that may enhance chemotherapeutic sensitivity.

Description of Work and Role of Partners:

Task 3.1 (Lead: Oroboros; **Participants:** TCD; **ESR 10). Analyse the metabolic flux in defined stages of OSCC and correlate with chemotherapy sensitivity.** TCD will measure metabolic flux through glycolysis, pentose phosphate pathway and glutaminolysis using 2H/13C NMR. Oroboros will utilise high-resolution respirometry to measure real-time bioenergetics and metabolism in normal, dysplatic and cancerous oral cells.

Task 3.2 (Lead: TCD; **Participants:** Oroboros; **ESR 11). Correlate bioenergetics status and chemotherapy sensitivity of defined stages of OSCC to mitochondrial function.** Oroboros will utilise high-resolution respirometry to measure mitochondrial respiration in normal, dysplatic and cancerous oral cells. Confocal microscopy to observe rates of mitochondrial fission, fusion and mitophagy will be performed in TCD.

Deliverables

3.1 Report on metabolic flux pathways in normal/cancer cells (M24)
3.2 Report on chemotherapy sensitivities & mitochondrial functions (M36)
3.3 Report on identification of novel metabolic targets for oral cancer cells (M36)
3.4 Awarding of PhD degree to ESRs 10-11 (M48)

Work Package Number	4	1-42

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Work Package Title	Training
Lead Beneficiary	TCD (Emma Creagh)

Objectives

(A) To organise secondments, network events and travel,
(B) To monitor quality of supervision and progress of ESRs against PDPs.

Description of Work and Role of Partners:

Task 4.1 Project Meetings (Lead: TCD; **Participants:** All**)**: Project-wide meetings will be held at M6 (TCD), M18 (QUB), M30 (TCD) and M45 (UNISI), and will be an opportunity to foster multidisciplinary and intersectoral exposure. TCD will oversee organisation of the training carried out at the meetings (workshops/discussion sessions, presentations (ESRs, PIs, external keynote speakers etc.).

Task 4.2 Training Events (Lead: TCD; **Participants:** UNISI, UVEG, Seahorse, Oroboros, QUB, Andor, NIBRT**)**: A number of technical and complementary skills training events are planned during the project (section 1.2.1). TCD will oversee the general organisation of these events, while the local logistics, content and delivery will be the responsibility of the event organisers. In order to ensure the highest quality training, the agenda for each training event will be submitted to the Supervisory Board for review 4 weeks in advance of the meeting. In addition, TCD will collect ESR feedback after each event and summarise the findings for the Supervisory Board to allow continuous improvement of training events.

Task 4.3 Quality and Progress Monitoring (Lead: TCD; **Participants:** All**)**: The Support Team and PDPs described in section 1.3 are central to the training of all ESRs. Together, the Support Team and ESRs will be responsible for their relevant PDPs, with PDP approval granted by the Supervisory Board. TCD will ensure that the PDPs of all ESRs are approved in a timely fashion and that progress monitoring is on-going by each Support Team. TCD will ensure that six-monthly updates for each ESR are provided to the Supervisory Board and that the Supervisory Board provides timely feedback. At M18, and M30, TCD will also collect ESR feedback on the quality of supervision for presentation to the Supervisory Board.

Deliverables

4.1 Report on ESR Training (including training events and Progress, Year 1 (M18)
4.2 Report on ESR Training and Progress, Year 2 (M36)
4.3 Report on ESR Training and Progress, Year 3 (M44)

Work Package Number	5	1-45
Work Package Title	Dissemination and Exploitation	
Lead Beneficiary	QUB (Richard Turkington)	

Objectives

(A) To effectively communicate and disseminate the project findings to key stakeholders, including the general public, patient groups, cancer researchers, pharmaceutical/diagnostics companies,
(B) To involve ESRs in dissemination and exploitation activities associated with a European research project,
(C) To effectively manage intellectual property generated during the project.

Description of Work and Role of Partners

The planned dissemination and exploitation activities are described in detail in section 2.3.

Task 5.1 Online Dissemination (Lead: QUB; **Participants:** All): A project website and social media accounts will be launched at M1, and regularly updated throughout the project with content contributed by all partners. ESRs will be expected to participate actively in online dissemination activities.

Task 5.2 Media (Lead: QUB; **Participants:** All**):** A press release will be issued by TCD at M1, and will form the basis for local press releases by all partners. PIs will interact with their local Press Offices to promote the project through their existing media networks. Additional press releases will be issued to promote project findings and outward facing events over the course of the project.

Task 5.3 Dissemination and Exploitation Events (Lead: QUB; **Participants:** All**):** A number of outward-facing events are planned during the project (section 2.3), including outreach events for students and OOC patients, Researcher Nights, Open Day and Exploitation Workshop. Responsibility for the planned events will rest with the local organisers and involved ESRs, with QUB providing overall oversight and support.

Task 5.4 Publications/presentations (Lead: QUB; **Participants:** All**):** Publication of results in peer-reviewed journals and presentation at academic conferences are envisaged. A publication policy will be agreed at the start of the project, and will include processes for authorship decisions and intellectual property protection.

Task 5.5 IP Management (Lead: QUB; **Participants:** All**):** QUB will work with all partners to ensure adherence to the IP management processes established in the Consortium Agreement and Description of Work.

Deliverables

5.1 Online dissemination (M2)
5.2 Dissemination diary (publications, events, etc.), year 1 (M18)
5.3 Dissemination diary (publications, events, etc.), year 2 (M36)
5.4 Dissemination diary (publications, events, etc.), year 3 (M44)

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Work Package Number	6	1 – 45
Work Package Title	Project management	
Lead Beneficiary	TCD (Daniela Zisterer)	

Objectives

A) To ensure effective collaboration across the project and effectively manage project risks,
B) To support recruitment processes across all sites,
C) To ensure on time submission of high quality contractual deliverables,

Description of Work

Details of the implementation strategy are presented in section 3.2.

Task 6.1 Oversight and integration (Lead: TCD; **Participants:** All**):** Integration of activities across all WPs is key to achieving intended research and training objectives, as well as project impact. The Coordinator (Prof. Zisterer), supported by the Project Manager will oversee all project activities and promote integration.

Task 6.2 Communications (Lead: TCD; **Participants:** All**):** TCD will establish clear internal communication mechanisms, which are essential for ensuring effective collaboration. The Project Manager (TCD) will establish a project contact list and project calendar. A process for document sharing will also be established and maintained.

Task 6.3 Risk Management (Lead: TCD; **Participants:** All**):** Implementation risks have already been identified (Table 3.2a) and will be monitored on an on-going basis by the Coordinator and Project Manager. PIs will be responsible for identifying new risks should they arise, as well as proposing mitigation measures.

Task 6.4 Recruitment (Lead TCD; **Participants:** All**):** Recruitment will be carried out through a joint, pooled strategy (D6.1) building up a previously developed successful ITN model implemented by TCD and augmented by other partner requirements. Further detail is given in section 3.2.3.

Task 6.5 Reporting (Lead: TCD; **Participants:** All**):** Deliverables and formal reports (scientific and financial) will be delivered to the Commission, as required by the Grant Agreement. TCD will be responsible for ensuring that accurate, high-quality reports are delivered on time by all beneficiaries.

Deliverables

6.1 Recruitment strategy including recruitment of Project Manager (M2)
6.2 Consortium agreement in place (M4)
6.3 Researcher declarations (M7)
6.4 Interim reports (M12,36)
6.5 Periodic reports (M24, 48)

Table 3.1 b Deliverables List

Scientific Deliverables						
Deliverable No.	**Deliverable Title**	**WP No.**	**Lead Beneficiary Short Name**	**Type**	**Dissemination Level**	**Due Date**
1.1	Correlation of salivary inflammatory & glycan markers with stages of OSCC	1	UVEG	R	CO	24
1.2	Correlation of salivary marker level with tumour control in radiotherapy patients	1	UVEG	R	CO	24
1.3	Identification of molecular signatures predictive of response to chemotherapy	1	UVEG	R	CO	24
1.4	Retrospective validation of resultant predictive classifiers	1	UVEG	R	CO	36
1.5	Awarding of PhD degree to ESRs 1-3		UVEG	OTH	PU	48
2.1	Expression analysis of inflammatory caspases in OAC completed	2	UNISI	R	CO	24
2.2	Novel apoptotic/autophagic modulators designed	2	UNISI	R	CO	18
2.3	HAMLET derivatives tested in OAC models	2	UNISI	R	CO	24
2.4	Novel apoptotic/autophagic modulators synthesised	2	UNISI	R	CO	24
2.5	Identification of pathways governing drug resistance	2	UNISI	R	CO	36
2.6	Modulators tested in OSCC models	2	UNISI	R	CO	36
2.7	Awarding of PhD degree to ESRs 4-9		UNISI	OTH	PU	48

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3.1	Metabolic flux pathways in normal/cancer cells identified	3	Oroboros	R	CO	24
3.2	Chemotherapy sensitivities & mitochondrial functions	3	Oroboros	R	CO	36
3.3	Identification of novel metabolic targets for OSCC	3	Oroboros	R	CO	36
3.4	Awarding of PhD degree to ESRs 10-11		Oroboros	OTH	PU	48
Management, Training, Recruitment and Dissemination Deliverables						
Deliverable Number	**Deliverable Title**	**WP No.**	**Lead Beneficiary Short Name**	**Type**	**Dissemination level**	**Due date**
4.1	ESR Training and Progress, Year 1	4	TCD	R	PU	18
4.2	ESR Training and Progress, Year 2	4	TCD	R	PU	36
4.3	ESR Training and Progress, Year 3	4	TCD	R	PU	44
5.1	Online dissemination	5	QUB	R	PU	2
5.2	Dissemination diary, Year 1	5	QUB	R	PU	18
5.3	Dissemination diary, Year 2	5	QUB	R	PU	36
5.4	Dissemination diary, Year 3	5	QUB	R	PU	44
6.1	Recruitment strategy	6	TCD	R	PU	2
6.2	Consortium agreement	6	TCD	R	CO	4
6.3	Researcher declarations	6	TCD	R	CO	7
6.4	Interim reports	6	TCD	R	CO	12,36
6.5	Periodic reports	6	TCD	R	CO	24,48

Table 3.1 c Milestones List

Number	Title	Related WP (s)	Lead Beneficiary	Month	Means of verification
1.1	Salivary glycan assay development	1	UVEG	24	HPLC and Mass Spectroscopy assays for salivary glycan profiles established
1.2	Whole genome sequencing, methylation & microarray development	1	UVEG	24	Generation of whole genome sequencing, methylation & microarray data from early stage OAC
1.3	Salivary immune based assay development	1	UVEG	12	Immune based assay for salivary inflammatory markers established
2.1	RNA-seq & microarray analysis of responders vs non-responders	2	UNISI	24	Combined RNA-seq & microarray analysis of differentially expressed/frequently mutated genes in OAC completed
2.2	Inflammatory caspases as biomarkers for OAC assessed	2	UNISI	24	Inflammatory caspase-1, -4 and -5 expression in OAC progression/resistance determined
2.3	Synthesis of pro-apoptotic and autophagy modulators	2	UNISI	24	Synthesis of Mcl-1 inhibitors and autophagy modulators completed
2.4	Screening of novel HAMLET derivatives	2	UNISI	24	Screening of novel HAMLET derivatives in OAC models completed
3.1	Development of high-resolution respirometry assay	3	OROBOROS	12	High-resolution respirometry to assay real time bioenergetics and metabolism in oral cancer cells established
3.2	Metabolic profiling of OSCC cells	3	OROBOROS	24	Metabolic profiles of normal, dysplastic and cancerous oral cells identified.
4.1	PDPs completed, approved	4	TCD	8	PDPs approved by SB
5.1	Website, social media live	5	QUB	1	Online assets established
5.2	Review of dissemination/ exploitation	5	QUB	24	Interim internal assessment
6.1	Recruitment	6	TCD	5	11 ESRs and Project Manager recruited
6.2	Internal communications	6	TCD	6	Internal communications established

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6.3	Risk management	6	TCD	12	Risk assessments completed
6.4	Mid-term review with REA PO	6	TCD	18	Review complete
6.5	Interim reports	6	TCD	12, 36	Reports submitted
6.6	Periodic reports	6	TCD	24, 48	Reports submitted; all training events complet

Table 3.1 d: Fellows Individual Research Projects

ESR1	**Host institution (UVEG)**	**PhD enrolment Y**	**Start date (Month 6)**	**Duration (36 months)**	**Deliverables *(1.1, 1.5)***
Project Title: Inflammatory response elements and glycan profiles as salivary biomarkers for the early diagnosis of oral cancer (WP1; Task 1.1))					
Objectives: Complete a research training programme in: • Translational clinical research • Molecular and biochemical techniques for the study of inflammatory activation and regulation • Molecular and biochemical techniques (e.g. LC-MS) for the study glycan profiles					
Expected Results: • Identification of significant differences in salivary and serum glycan profiles, inflammatory markers, homeostatic chemokines amongst patients with potentially malignant disorders (group 1), with OSCC (group 2) and age/gender matched controls (group 3). • Identification of differences in salivary and serum glycan profiles, inflammatory markers, homeostatic chemokines between OSCC patients in early stages (stage I and II) and those with advanced stages (stage III and IV) and examination of any gender differences					
Planned secondment(s): NIBRT, (Rudd, 3 months from M14) - glycan analysis.					

ESR2	**Host institution (QUB)**	**PhD enrolment Y**	**Start date (Month 6)**	**Duration (36 months)**	**Deliverables *(1.3, 1.4, 1.5)***
Project Title: Identification of Novel Molecular Biomarkers Predictive of Benefit to Neo-adjuvant Chemotherapy in Oesophageal Adenocarcinoma (WP1; Task 1.2)					
Objectives: Complete a research training programme in: • Development of integromic biomarkers capable of predicting response to chemotherapy in early stage OAC • Analysis of high-dimensional whole genome sequencing, methylation and microarray data					
Expected Results: • Identification of molecular signatures predictive of response to chemotherapy in OAC • Retrospective validation of resultant predictive classifiers • Discovery of the biology underpinning the predictive classifier					
Planned secondment(s): Almac Diagnostics, (Davison, 3 months from M9)- biomarker development. TCD, (Creagh, 5 months from M25)- functional analysis of the underlying biology of predictive classifiers.					

ESR3	**Host institution (UVEG)**	**PhD enrolment Y**	**Start date (Month 6)**	**Duration (36 months)**	**Deliverables *(1.2, 1.5)***
Project Title: Modulation of salivary inflammatory markers in patients undergoing radiotherapy for OSCC. A potential tool for identifying toxicity to irradiation (WP1; Task 1.3)					
Objectives: Complete a research training programme in: • Translational clinical research • Molecular and biochemical techniques for the study of inflammatory activation and regulation					
Expected Results: • Correlation of salivary inflammatory marker levels with tumour control in patients undergoing radiotherapy • Examination of saliva as a putative prognostic test as a predictor of a patient's response to radiotherapy • Potential for IP and bedside test development					
Planned secondment(s): IME-SP, (Windshügel, 3 months from M13) - biomarker discovery, inflammatory cytokine profile from patient samples utilising the MesoScale Discovery platform.					

ESR4	**Host institution (QUB)**	**PhD enrolment Y**	**Start date (Month 6)**	**Duration (36 months)**	**Deliverables *(2.5, 2.7)***
• Project Title: A Pathways-based Approach to Identify Determinants of Drug Resistance in Oesophageal Adenocarcinoma (OAC). (WP2; Task 2.1)					

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Objectives: Complete a research training programme in:

- Combined RNA-seq and microarray analysis of differentially expressed/ frequently mutated genes in responders/non-responders
- Pathways-based analysis using Gene Set Enrichment Analysis and Gene Ontology analysis to determine pathways governing drug resistance. Preliminary data analysis has identified the MAPK and glycolytic pathways as potential targetable pathways
- Construction of siRNA screens of candidate genes
- Validation of potential novel drug targets in suitable panel of in vitro cell lines, primary tumour-derived cell lines and patient-derived xenograft models

Expected Results:

- Discovery of the molecular pathways regulating drug resistance in OAC
- Validation of drug targets to develop strategies for overcoming resistance to chemotherapy
- Discovery of the molecular pathways regulating drug resistance in OAC

Planned secondment(s): IME-SP (Windshügel, 3 months from M9) - industry experience in target selection and drug development. Almac Diagnostics (Davison, 3 months from M15) - ontological analysis of microarray datasets. TCD (Zisterer, 5 months from M23) - biological functional analysis of drug resistance in OAC.

ESR5	**Host institution (TCD)**	**PhD enrolment Y**	**Start date (Month 6)**	**Duration (36 months)**	**Deliverables *(2.1, 2.7)***

Project Title: Inflammatory caspase expression during oesophageal carcinoma. (WP2; Task 2.2)

Objectives: Complete a research training programme in:

- Immunohistochemical (IHC)-based profiling and analysis of OAC patient biopsies
- Molecular and biochemical techniques for the study of inflammasome activity and inflammation
- Screen novel inflammatory modulators/caspase inhibitors in co-culture and animal models of OOC

Expected Results:

- Establish the expression profiles of human inflammatory caspase-1, -4 and -5 during OAC tumour progression/resistance
- Examine the influence of inflammatory caspase expression on inflammatory, growth and angiogenic markers in a co-culture model system
- Target inflammatory caspase expression using novel anti-inflammatory modulators and caspase inhibitors, in co-culture and animal models of OOC.

Planned secondment(s): QUB (Turkington, 4 months from M13) - IHC analysis of inflammatory caspases in OAC (responder/non-responder) biopsies. Opsona Therapeutics (O'Neill, 3 months from M30) - screen efficacy of novel anti-inflammatory drugs in OOC cell culture and mouse models.

ESR6	**Host institution (UNISI)**	**PhD enrolment Y**	**Start date (Month 6)**	**Duration (36 months)**	**Deliverables *(2.2, 2.4, 2.6, 2.7)***

Project Title: Novel Mcl-1 inhibitors for the treatment of OSCC (WP2; Task 2.3)

Objectives: Complete a research training programme in:

- Computational chemistry and rational drug design
- Organic synthesis of novel chemical entities and scale up procedures
- Screening of compounds in OSCC models
- Profiling of exosomes/EVs in OSCC models prior and after treatment with Mcl-1 inhibitors

Expected Results:

- Synthesis of novel Mcl-1 inhibitor(s)
- Identify lead compound which induces cell death in OSCC
- Identification of EV associated molecules as stratification markers for targeted therapies and/or surrogate markers for therapy monitoring

Planned secondment(s): TCD (Zisterer, 3 months from M28) - testing of drugs on OSCC models; Exosomics (Chiesi, 3 months from M31)- extraction of exosomes from OSCC cells and miRNA/DNA/protein content evaluation

ESR7	**Host institution (TCD)**	**PhD enrolment Y**	**Start date (Month 6)**	**Duration *(36 months)***	**Deliverables *(2.3, 2.7)***

Project Title: HAMLET derivatives as a pre-operative therapy in oesophageal cancer (WP2; Task 2.4)

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Objectives: Complete a research training programme in: • Chemical design and synthesis • NMR (nuclear magnetic resonance) metabolite analysis • Analysis of metabolic changes by respirometry • CRISPR and next generation sequencing
Expected Results: • Development of highly effective tumouricidal HAMLET derivatives. Identification of their mode of action in oesophageal cell lines by genome scale CRISPR-Cas9 knockout
Planned secondment(s): UNISI (Campiani, 5 months from M7) - chemical design and synthesis and Oroboros (Gnaiger, 3 months from M21) - analysis of metabolic changes.

ESR8	**Host institution (UNISI)**	**PhD enrolment Y**	**Start date (Month 6)**	**Duration (36 months)**	**Deliverables *(2.2, 2.4, 2.6, 2.7)***
Project Title: Development of novel autophagy modulators to improve sensitivity of OSCC to chemotherapy (WP2; Task 2.5)					
Objectives: Complete a research training programme in: • Bioinformatics and computational drug design • Synthesis of novel compounds to specifically inhibit autophagy processes • Biochemical techniques for the study of mechanisms of cell death • Quantitative and qualitative analysis of OSCC released EVs for monitoring of autophagy modulating therapy in mouse model					
Expected Results: • Development of highly effective novel autophagy protein modulators for OSCC • Identify their efficacy in OSCC cell lines and in a mouse model • Identification of surrogate markers for novel compound screening in OSCC cell and mouse model(s)					
Planned secondment(s): TCD (Zisterer, 3 months from M25) - testing of drugs on OSCC cell lines and on a mouse *in vivo* model of OSCC; Exosomics (Chiesi, 3 months from M28)- extraction of exosomes from OSCC lines and mouse samples and miRNA/protein content evaluation					

ESR9	**Host institution (TCD)**	**PhD enrolment Y**	**Start date (Month 6)**	**Duration (36 months)**	**Deliverables *(2.6, 2.7)***
Project Title: Pre-clinical evaluation of targeting autophagy for the treatment of OSCC (WP2; Task 2.6)					
Objectives: Complete a research training programme in: • Molecular, biochemical and genetic techniques, imaging techniques relevant to autophagy/apoptosis • Analysis of expression of autophagy proteins as potential biomarkers in OSCC patient samples • Testing pharmacological and genetic inhibition of autophagy as a chemosensitising strategy for OSCC.					
Expected Results: • Identify clinically relevant biomarkers of OSCC disease that can be used for earlier disease detection, • Determine whether combining existing OSCC chemotherapy strategy with autophagy inhibition represents a better treatment strategy that could be translated into benefit for OSCC patients.					
Planned secondment(s): UVEG (Bagan, 3 months from M13) - immunohistochemistry and PCR analysis of OSCC patient samples. Andor (Hanrahan, 3 months from M25) - live cell imaging of autophagy using advanced fluorescent probes.					

ESR10	**Host institution (Oroboros)**	**PhD enrolment Y (Univ. of Innsbruck)**	**Start date (Month 6)**	**Duration *(36 months)***	**Deliverables *(3.1, 3.3, 3.4)***
Project Title: Metabolic profiles in normal, dysplastic and cancerous oral cells (WP3; Task 3.1)					
Objectives: Complete a research training programme in: • High-resolution Respirometry to measure real-time bioenergetics and metabolism • NMR metabolomics					
Expected Results: • Comparison of oxygen consumption, extracellular acidity and metabolic flux in different cell types under normoxic and hypoxic conditions and correlate with chemotherapy sensitivity • Identify differential novel drug targets in the cancer cells					
Planned secondment(s): TCD (Porter, 9 months from M13) - measure metabolic flux through (a) glycolysis, (b) pentose phosphate pathway and (c) glutaminolysis using 2H/13C NMR.					

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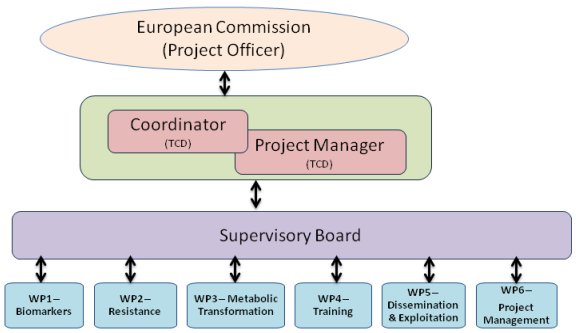
ESR11	**Host institution (TCD)**	**PhD enrolment Y**	**Start date (Month 6)**	**Duration *(36 months)***	**Deliverables *(3.2, 3.3, 3.4)***
Project Title: Mitochondrial morphology linked to metabolic differences in normal, dysplastic and cancerous oral cells (WP3; Task 3.2)					
Objectives: Complete a research training programme in: • High-resolution respirometry to measure real-time bioenergetics and metabolism • Confocal microscopy to observed mitochondrial fission/fusion/mitophagy • Immunoblotting & quantitative RT-PCR					
Expected Results: • Correlate bioenergetics status and cisplatin sensitivity of the cells over a range of glucose/galactose ratios to mitochondrial morphology • Identify the functional proteins involved in mitochondrial dynamics.					
Planned secondment(s): Oroboros (Gnaiger, 6 months from M10) - measure real-time cellular bioenergetics, metabolism					

3.2 Appropriateness of the management structure and procedures

3.2.1 Network Organisation and Management Structure

Management of the project will depend on robust management principles that incorporate strong leadership from the project **Coordinator** Dr. Zisterer. Dr. Zisterer has over ten years experience in participating in large multi-centre projects. She was recently the Coordinator of the cancer stream of the PRTLI structured PhD programme (2011–2015) entitled 'Molecular and Cellular Mechanisms underlying inflammatory processes,' which included 4 partner Universities with a budget of 7.2 million euro. Trinity Research & Innovation and the Financial Service Division at TCD will provide overall legal and financial management of the project. Both Offices have considerable experience in large multinational and European projects - TCD currently successfully coordinates in excess of 20 FP7 projects and has been involved in over 200 FP7 projects. A dedicated **Project Manager** will be hired to oversee day-to-day operations of the project. Specifically, the team at TCD will be responsible for the overall management of the project, communication between all partners and the Commission, distribution of funds, collation of annual reports and financial statements for the Commission, overseeing recruitment and risk management. TCD will also provide a virtual communication centre to advance the mutual exchange of knowledge through internet forums, a wiki, communication/conferencing tools and websites.



Financial management strategy: As Coordinator, TCD will be responsible for dispersal of funding to all beneficiaries and overall financial management of the project, including submission of cost claims. Each beneficiary will adhere to their local financial management practices and requirements of the H2020 programme.

Scientific misconduct: Research integrity is a priority of all TRACT partners. ESRs will be briefed on the importance of ethics and integrity in research during induction to their recruiting institution, and bioethical research will be discussed at the Kick-off meeting (M6). ESRs and Support Teams will report suspected misconduct of any project participant to the SB who will ensure relevant local procedures are followed.

WP leaders have been assigned to each WP - each WP leader will be responsible for ensuring all activities are delivered according to plan. The Coordinator and Project Manager will hold monthly virtual meetings with each WP leader, organising cross-WP virtual meetings as needed to promote synergies between the research themes.

3.2.2 Supervisory Board

A Supervisory Board (SB) will be established to support the Coordinator and Project Manager in overseeing the research, training and dissemination activities of the project. The SB will be composed of **representatives from all beneficiaries and partner organisations** (Chair: Zisterer (TCD), Members: Bagan (UVEG), Campiani (UNISI), Turkington(QUB), Gnaiger (Oroboros), Hanrahan (Andor), Davison (Almac Diagnostics), Rudd (NIBRT), Liversage (Seahorse), O'Neill (Opsona), Windshügel (IME-SP), Chiesi (Exosomics)). An **ESR representative** will also be nominated to join the SB at the Kick-off meeting. An **External Advisor,** Prof. Gavin Davey (TCD, Coordinator of the FP7-funded ITN TINTIN), will also sit on the SB. The SB will strive for consensus in decision-making - in the event consensus cannot be reached, the Coordinator will hold the deciding vote.

Importantly, the SB will be involved in monitoring ESR progress, through initial approval of all PDPs (M7) and on-

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going review of progress with the designated Support Teams through six-monthly reports. The SB will monitor:

- **Training planning/content** - by ensuring the PDP for each ESR includes challenging, yet achievable, training goals with a balance between scientific/technological and complementary skills training; by ensuring that emerging needs of both academic and non-academic sectors are being addressed by the project and amending the training, as required, and that the project is maximizing potential synergies,
- **ESR progress** - through assessment of ESR research presentations at annual meetings and six-monthly progress reports summarising research, training and dissemination activities against PDPs/research plans,
- **Training quality** - by ensuring consistent quality of training across all sites, reviewing training agenda/content in advance of training events and obtaining feedback after training events to support future improvements,

Conflict resolution - The SB will also act to resolve conflicts between ESRs and their ESR Support Team, individual ESRs or PIs should the need arise. The SB will offer robust 'Adaptable Conflict Resolution' pathways, such as facilitated dialogue and shuttle negotiation. The ESR representative on the SB will not be involved in any conflict resolution or progress reviews of their peers.

3.2.3 Recruitment strategy

Recruitment of suitably trained, motivated researchers will be central to success of the project and will be carried out as per the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers.[36] The academic institutions TCD, UNISI, QUB and Medical University of Innsbruck (where ESR10 will be registered) have officially endorsed the Charter and Code. As further evidence of the consortium commitment to the principles, partner QUB has been granted permission to use the "HR Excellence in Research" logo.

A **centralised recruitment strategy** will be implemented. The recruitment strategy will be aligned with the Charter and Code and consistent with local practices, and be developed as a priority in M1 by the SB. The strategy will also be informed by the Erasmus Mundus Handbook of Excellence – Doctoral Programmes[37]. Recruitment will begin as soon as possible to capture the attention of the best students. A professional project website and social media accounts will be developed as a priority. Marketing of the programme is critical to ensure that excellent international doctoral candidates are motivated to apply for TRACT. To ensure openness and transparency and maximum reach, positions will be widely advertised on accessible websites and journals (www.findaphd.com, www.researchgate.com, New Scientist, Nature, Science) and the pan-European Researcher's Mobility Portal.[38]

The call for applications will clearly describe the minimum requirements (BSc/Master or equivalent in science and meet the mobility and selection criteria of the ITN scheme) , the selection criteria (including relevance of research training and experience and level/quality of degrees awarded), the information that applicants must provide (CV, completed application form and at least two letters of reference from professionals involved in their previous training) and a description of the working conditions and entitlements, including career development prospects. A selection committee will be established with inter-sectoral representation and gender balance. Shortlisted candidates will be interviewed either face to face or via Skype if required. Candidates will be scored according to the published selection criteria - a minimum threshold score will be agreed in the recruitment strategy. Fellowships will be offered to the first ranked candidates and, should they not accept, to the next ranked candidate meeting the threshold score. The closing date for applications will be the end of M2, with recruitment completed by M5.

Equal opportunity will apply to the recruitment process with no discrimination on the basis of gender, age, ethnic, national or social origin, religion or belief, sexual orientation, language, disability, political opinion, social or economic condition. As recommended by the Charter, this will not take precedence over quality and competence criteria. The Human Resources Offices in the recruiting beneficiaries will provide advice to the recruitment process on all aspects of local employment law. All ESRs will be employed on a full time contract by their host organisation (36 months) and be entitled to social security provision, including sickness, parental benefits, pension and unemployment benefits. International Student Offices at the host institutions and the SB, will support recruited researchers on mobility issues. Candidates will also be directed to national mobility portals, such as www.euraxess.ie, for practical support.

3.2.4 Progress Monitoring and Evaluation of Individual Projects

The PDPs developed by each ESR with their Support Team are at the core of training progress monitoring - the **PDPs will detail the training planned for each ESR and mechanisms for on-going assessment of progress**. PDPs will also include a detailed research plan, including deliverables and milestones, which will be used to monitor

36 http://ec.europa.eu/euraxess/index.cfm/rights/whatIsAResearcher

37 http://eacea.ec.europa.eu/erasmus_mundus/tools/documents/repository/handbook_of_excellence_2012_doctoral_en.pdf

38 http://ec.europa.eu/euraxess/index.cfm/jobs/index

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progress. As all ESRs will be enrolled in a PhD programme, progress against any local programme requirements will also be tracked by the Support Team and SB. For example, in TCD there is a requirement for all PhD students to submit a progress report 18 months into their degree. Students must also give a formal research talk followed by a viva voce examination by two independent examiners within TCD with experience in the field of research. A formal report with suggestions for future studies is then provided to the students and their supervisor(s).

Progress monitoring for all ESRs will be overseen by the ESR Support Team (see 1.3.2) on a regular basis. Each ESR will meet weekly with their Primary Supervisor when at the recruiting institution and the relevant Secondary Supervisor while on secondment. Monthly meetings will take place between ESR and their full Support Team (virtually or face-to-face) where they will be provided with informal feedback. The SB will also monitor progress (research, training, dissemination) on a six-monthly basis based on reports from each ESR and their Support Team. The SB will provide formal written feedback on progress after ESR presentations at the annual meetings.

3.2.5 Risk Management

Any large, multinational research and training programme carries risk. However, the experimental procedures and technologies involved in TRACT are well established in the partner laboratories - the novelty of the application is in the integration of multidisciplinary research to combat oral and oesophageal cancers. The research programme has been structured to include several strands of development, which converge at points, such as identification of novel biomarkers or novel therapeutics, but do not depend on each other. Even if some ESR projects do not yield the intended results, the overall project will still advance research in OOC, as well as successfully deliver high-quality, intersectoral training to a multidisciplinary cohort of ESRs. Furthermore, key personnel within the consortium have extensive experience with managing risk in large, multinational projects.

The TRACT consortium has formally identified the key risks to the project, along with agreed mitigation measures (Table 3.2a). The SB will review the risks identified in Table 3.2a at each meeting. The Coordinator and SB will be informed of new risks as soon as they arise to allow mitigation measures to be put in place.

Table 3.2a Implementation Risks

Risk No.	Description of Risk	WP	Proposed Mitigation Measures
1	ESR research projects not completed on time.	1, 2, 3	ESR projects will run for three years, while the project duration is four years, allowing a six-month buffer period in case of unforeseen delay (e.g. breakdown of equipment, illness of researcher). The ESR projects are not interdependent - delays in one project will not affect others.
2	ESRs do not achieve requisite competences	1, 2, 3, 4	Experimental procedures and technologies are well established in the partner laboratories so this risk is minimal. Furthermore, recruited ESRs will have a demonstrated track record in experimental research. If required, affected ESRs will receive intensive training.
3	Partners do not collaborate effectively.	6	A dedicated Project Manager will be engaged to monitor all project activities (research and training) on a monthly basis, and flag any potential issues to the Coordinator and SB. The consortium will strive for consensus, but the Consortium Agreement will detail a clear process for conflict resolution, should the need arise. Many partners have long standing collaborations and common research goals (e.g. Zisterer group in TCD and Campiani group in UNISI have collaborated effectively for 20 years with 33 joint publications).
4	Difficulty recruiting high-quality ESRs.	6	Vacancies will be advertised widely and well in advance. A list of ranked reserve candidates will be held in the event that the highest ranked candidates withdraw. All PIs have a successful recruiting history with 165 PhD students supervised to completion.
5	Dispute between ESR and Support Team.	6	Conflict resolution mediated by the SB will be adhered to in the event of a dispute between an ESR and their Support Team. Non-academic conflicts can be dealt with by both formal and informal procedures with the Graduate Studies Office in the host institution. Academic conflicts will be highlighted to the SB.
6	ESR fails to complete PhD programme.	6	TRACT has extensive support mechanisms to enable ESRs to successfully meet the requirements of local PhD programmes. If an ESR wishes to leave the project early, it will be possible to award an MSc degree after 1.5 years.

3.2.6 Intellectual Property Rights (IPR)

IPR management will be detailed in a Consortium Agreement (CA) agreed and implemented by all partners before the project starts. The CA will specify the processes for management of IPR, including appropriate management of knowledge (protection of know-how, exclusion of background, access rights, etc.). The CA may set out specific rights and obligations of the partners, which may integrate or supplement, but which will under no circumstance be in conflict with those of the Grant Agreement. IPR disputes that cannot be resolved within the consortium shall be finally settled under the Rules of Arbitration of the International Chamber of Commerce by one or more arbitrators. The award of the arbitration will be final and binding upon the partners. The Technology Transfer Office (TTO) in each beneficiary will look after any potential IP generated in that beneficiary and will liaise with the TTO in other beneficiaries should joint IP arise.

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Following the generation of potential IP, PIs will work with the relevant ESR to submit invention disclosure forms to the Technology Transfer Office in the relevant host institution and inform the Coordinator. From a **training perspective**, ESRs will be introduced to the issues and actions associated with quality assessment, early identification and protection of intellectual property from modules given at the Innovation Academy. From a **commercialisation perspective**, TRACT beneficiaries and partners have an exceptional track record in the successful patenting and commercial exploitation of research. TCD has produced more entrepreneurs than any other university in Europe over the last five years, according to The Universities Report by private equity and venture capital-focused research firm, PitchBook. TRACT Co-ordinator, Dr. Daniela Zisterer has two patents on novel anti-cancer drugs and Prof. Giuseppe Campiani has 15 patents on pro-apoptotic and anti-psychotic drugs in collaboration with Sigma-Tau and Eurosearch/GSK. Prof. Richard Kennedy's group has extensive experience in developing microarray-based biomarkers having identified a 634-probe set prognostic signature in Stage II colon cancer and a 44 gene signature predictive of response to DNA-damaging chemotherapy by characterising DNA damage response-deficient primary breast tumours. Both of these biomarkers have been licensed to global biotech companies (one to Genomic health (US) for $9 million plus royalties) for validation and are scheduled to enter clinical usage shortly. ESRs in the programme will benefit from this experience, directly through their supervision arrangements and indirectly through project events, such as the project-wide meetings.

Training in IPR will be included in the PDPs for all ESRs. In addition, the IP policies and practices of each employer/host will be set forth in detail to each incoming ESR before any grant-supported work begins. ESRs will sign a non-disclosure agreement regarding all research activities, if specifically requested by the associated partners' institutions. ESRs will be expected to retain first author rights on publications of their research. ESRs working at private-sector partners will be advised of their legal rights to their results before commencing work.

3.2.7 Gender Aspects

The consortium recognises the advancement of gender equality: representation, progression and success for all as detailed in the Athena Swan charter (https://www.tcd.ie/diversity-inclusion/athena-swan/). QUB is the recipient of an Athena Swan award.

Decision-making: The SB will be responsible for overall decision making for the project. There will be an adequate gender balance on the SB, aiming to reach the Commission's target of 40% of the under-represented sex.

Recruitment: During recruitment of ESRs, an equal opportunity policy will be implemented. However, this will not take precedence over quality and competence criteria in line with the European Charter for Researchers and Code of Conduct for Recruitment. Shortlisting panels and interview committees will have adequate gender balance to ensure equal treatment of candidates. Project supervisors will promote gender balance in their research teams, through equal opportunity hiring, flexible working conditions and work-life balance initiatives wherever possible. For example, the host institutes will provide compulsory annual leave, flexible working hours and will foster an environment that encourages ESRs to engage in social/leisure/family activities.

3.3 Appropriateness of the infrastructure of the participating organisations

There are 12 legal entities participating in the TRACT programme, each of which have the required infrastructure to support the main tasks attributed with their involvement in the programme, as summarised below.

Institution	*PhD programme*	*Innovation training*	*Science communication*	*Cell imaging/microscopy*	*Metabolic analysis*	*Drug discovery*	*Biomarker discovery*	*Biomarker development*	*Mito. respiration*	*Exosome isolation/analysis*	*Glycobiology analysis*	*Bioinformatics*	*Patient perspective*	*IP management*	*Project Management*
TCD	X	X	X	X	X									X	X
QUB	X	X	X										X	X	X
UNISI	X		X			X								X	X
UVEG	X		X				X	X						X	X
Oroboros	X		X						X					X	X
Andor				X										X	X
Opsona						X								X	X
ALMAC							X	X				X		X	X
NIBRT							X	X			X			X	X
IME-SP						X	X	X						X	X
Exosomics						X				X				X	X
Seahorse					X									X	X

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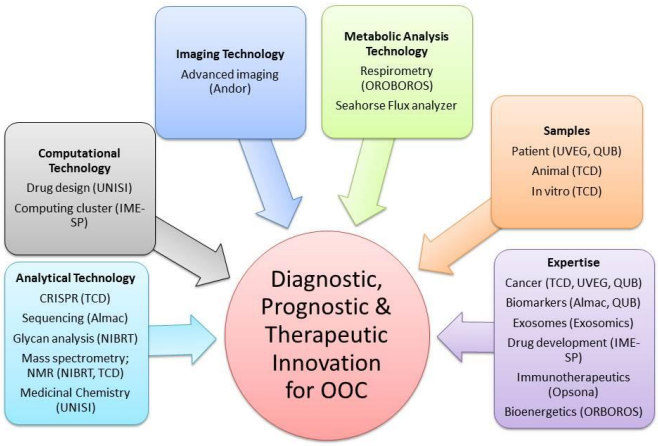
3.4 Competences, experience and complementarity of the participating organisations and their commitment to the programme

3.4.1 Consortium Composition and Exploitation of Partners' Complementarities



Research expertise: Delivering diagnostic, prognostic and therapeutic innovation for OOC requires expertise in a number of research domains as summarised here diagramatically. **Access to samples:** The discovery work planned for the project relies on in vitro, in vivo and ex vivo samples, all of which will be provided from within the consortium - animal models (TCD) and patient samples (UVEG, QUB). **Access to technologies:** Our research innovation relies on information obtained from leading edge technologies, that are all available within the consortium including Seahorse Flux analyser (Seahorse), qPCR, array and next-generation sequencing platforms (Almac), in silico drug development (UNISI), advanced imaging (Andor), glycan assays (NIBRT), exosome purification and analysis (Exosomics), mass spectrometry (NIBRT, UNISI), biomarker assays (QUB), NMR (TCD), high throughput drug screening (IME-SP), computing cluster (IME-SP), high-resolution respirometry (OROBOROS), whole genome sequencing (QUB), CRISPR generated cancer models (TCD) & analytical chemistry assays (HPLC, etc.) (UNISI, NIBRT).

3.4.2 **Commitment of beneficiaries and partner organisations to the programme**

Beneficiary	**Research Activities**	**Training Activities**
TCD (IE)	Autophagy & Inflammation; autophagy as a target; pre-operative therapies; and metabolic analysis, of oral and oesophageal cancer patients and models (ESR 5, 7, 9, and 11)	Research Ethics; Tumour histology; Antibody technology; CRISPR generated cancer models; drug discovery; Whole body imaging in xenograft cancer models; Innovation academy and career development workshops (All ESRs)
QUB (UK)	Novel biomarkers and drug resistance pathways specific to OAC patients (ESR 2, 4)	Science communication; Computational biology; OOC patient outreach; Career development workshop; Introduction to OOC workshop (All ESRs)
UVEG (ES)	Inflammatory and glycan profiles as markers of oral cancer severity and patient responses (ESR 1, 3)	An introduction to OOC workshop; Biomarker Discovery workshop (All ESRs)
UNISI (IT)	Anti-apoptotic protein inhibitors, autophagy modulators as potential therapies (ESR 6, 8)	Drug Discovery and Medicinal Chemistry workshop (All ESRs)
OROBOROS (AT)	Metabolic profiles in normal, dysplastic and cancerous oral cells (ESR 10)	Training in mitochondrial and cellular respiratory physiology (All ESRs)
Partner	**Research Activities**	**Training Activities**
IME-SP (DE)	Gene profiling in OAC responder/non-responder groups and OSCC patient samples	Biomarker discovery – via multiplex analysis systems (ESR 3; ESR 4)
Almac Diagnostics (UK)	Analysis of potential biomarkers in molecular pathways differentially activated in OAC patients	Biomarker development (ESR 2; ESR 4)
Opsona Therapeutics (IE)	Testing immunomodulatory drugs in OOC cell culture & mouse models	Training in cancer immunology (ESR 5)
Exosomics(IT)	Exosome analysis from OSCC cell lines untreated/treated with Mcl1-inhibitors or autophagy inhibitors	Exosomes extraction/purification from cells and DNA/protein/miRNA analysis (ESR 6; ESR 8)
Andor (UK)	Live cell imaging of autophagy in OSCC models	High resolution confocal microscopy (ESR 9)
NIBRT (IE)	Analysis of serum/salivary glycan profiles in OSCC patient samples	Glycoanalytics (ESR 1)
Seahorse Biosciences (UK)	Metabolic analysis in normal, dysplastic and cancerous oral cells	Use of Metabolic Flux Analyzer (ESR 10 (OROBOROS); ESR 7, 11 (TCD))

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4 Gantt Chart

	Months	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
	ESR 1														S	S	S																								T						A
	ESR 2									S	S	S														S	S	S	S	S												T						A
	ESR 3													S	S	S																										T						A
	ESR 4									S	S	S				S	S	S						S	S	S	S	S														T						A
	ESR 5													S	S	S	S														S	S	S									T						A
	ESR 6																												S	S	S	S	S	S								T						A
	ESR 7							S	S	S	S	S										S	S	S																			T						A
	ESR 8																									S	S	S	S	S	S												T						A
	ESR 9													S	S	S										S	S	S															T						A
	ESR 10													S	S	S	S	S	S	S	S	S																					T						A
	ESR 11										S	S	S	S	S	S																											T						A
Training	Scientific Training																																																
	Complementary Skills Training																																																
	Conference																C												C																				
	Visiting Scientist						V												V											V															V				
M'ment																																																	
	Project Meetings						K												1												2														3			E
Dissem. / Public e'ment	Dissemn.																																										P	P	P			
	Public engagement										RN			SS					PT				RN			SS					PT				RN	OD		SS										

S = Secondment; T = PhD thesis submission; A = Award of PhD; K = Kick-off meeting; E = End of project; C = annual cancer conference; P = Publications submitted/patents filed; RN = Researchers' Night; PT = OCC Patient Info Day; SS = school student intern programmes; OD = Open Day

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5 Capacity of the Participating Organisations

Beneficiary– Trinity College Dublin (Trinity Biomedical Sciences Institute)	
General description	Trinity College Dublin is recognised internationally as Ireland's premier university and is ranked 78th in the top 100 world universities by the QS World University Rankings 2015 and 48th in the world for Biological Sciences. The Trinity Biomedical Sciences Institute (TBSI) is a state-of-the-art research facility built around the areas of immunology, cancer and medical devices and linked directly to both medical education and industrial collaboration. The multi-disciplinary facility currently accommodates 65 principal investigators (PI's) and their research groups (approx. 520 researchers) from five TCD schools: Biochemistry & Immunology, Chemistry, Pharmacy & Pharmaceutical Sciences, Bioengineering and Medicine. The eleven-storey development contains 17,000 m^2 academic research space, 3,000 m^2 for industry-academia collaborative research and 4,000 m^2 purpose-built teaching space. Since 2011, TBSI researchers have published eleven papers in Nature and two in Science, with five of these having TBSI investigators as lead author. During this period, there have over 78 interdisciplinary publications between the participating Schools.
Role and commitment of key persons (including supervisors)	Coordinator, Dr Daniela **Zisterer** (Cell Death Mechanisms & Anti-Cancer Therapeutics) (12% time commitment] Supervisor of ESR 9; Dr Emma **Creagh** (Immunology & Cancer Biology) (10% time commitment) Supervisor of ESR 5; Dr Vincent **Kelly** (Biochemistry & Cancer Biology) (10% time commitment) Supervisor of ESR 7; Dr Kenneth **Mok** (Biochemistry & NMR Metabolomics) (10% time commitment) Co-supervisor of ESR7; Dr James **Murray** (Metabolism & Enzymology) (10% time commitment) Co-supervisor of ESR 5; Dr Jeff **O'Sullivan** (Oral Cancer) (10% time commitment) Co-supervisor of ESR 7; Dr Richard **Porter** (Bioenergetics & Metabolism) (10% time commitment) Supervisor of ESR 11.
Key Research Facilities, Infrastructure and Equipment	**TSBI** is equipped with a strong range of major research equipment, mostly funded from research sources, including a Protein X-ray crystallography facility, FACScan, Taqman, a confocal microscope, a DNA sequencer, sophisticated spectroscopy instruments, a molecular graphics facility, a gamma irradiator, MALDI ToF and QTRAP Mass Spectrometers and extensive cell culture and biohazard suites. The School runs a 800 MHz NMR with a cryoprobe.
Independent research premises?	**Yes**
Previous Involvement in Research and Training Programmes	TCD has a successful track record in securing and managing large training and research programmes. Two programmes in Neuroscience and Molecular Medicine were the first funded programmes in Ireland (Health Research Board, Ireland). TCD is also involved with developing a national PhD programme under the auspices of Molecular Medicine Ireland. TCD supervisors have together supervised 50 PhD and 7 MSc projects to completion.
Current Involvement in Research and Training Programmes	The supervisors listed above are currently supervising 19 PhD and 2 MSc projects. The TBSI is also currently involved in three doctoral programmes; an FP7 funded ITN (TINTIN), a PhD programme in Immunology (Health Research Board, Ireland) and one in Molecular and Cellular Mechanisms Underlying Inflammation in the disciplines of Neuroscience, Infection and Immunity and Cancer (funded by PRTLI, Ireland). The coordinator (Zisterer) has over ten years of experience in participating in large multi-centre projects. She was recently the coordinator of the cancer stream of the PRTLI structured PhD programme (2011–2015) entitled 'Molecular and Cellular Mechanisms underlying inflammatory processes,' which included 4 partner Universities with a budget of 7.2 million euro.
Relevant publications and/or research/innovation products	1) Coll et al., (2015) A small molecule inhibitor of the NLRP3 inflammasome for the treatment of inflammatory diseases. Nature Med 21(3):248-55 2) Netea et al., (2015) Innate immune memory: a paradigm shift in understanding host disease. Nature Immunol. 16(7):675-9.3) 3) Flood B et al., (2015) Altered expression of caspases-4 and -5 during inflammatory bowel disease and colorectal cancer: diagnostic and therapeutic potential. Clin Exp Immunol. 181(1):39-50. 4) Lynam-lennon et al., (2014) Excess visceral adiposity induces alterations in mitochondrial function and energy metabolism in esophageal adenocarcinoma**.** BMC Cancer.14:907 5) Lennon et al., (2014) The novel pyrrolo-1,5-benzoxazepine, PBOX-6, synergistically enhances the apoptotic effects of carboplatin in drug sensitive and multidrug resistant neuroblastoma cells Biochem. Pharmacol. 87(4):611-24.

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Beneficiary– UNISI-NatSynDrugs	
General description	The University of Siena (UNISI) is almost 800 years old and is composed by 15 Departments, including the School of Pharmacy to which the Department of Biotechnology, Chemistry and Pharmacy (DBCP) belongs. Within FP6 and FP7, the University was granted 60 projects and there are about 180 EU projects currently active, while 7 projects were granted to UNISI within the H2020 framework. . The research focus of the DBCP is in bioinformatics, design and synthesis of bioactive compounds, natural products, pharmacology, enzymology & parasitology. The DBCP includes the European Research Centre for Drug Discovery and Development (NatSynDrugs. www.natsyndrugs.org), an international multidisciplinary research network that encompasses Universities and Institutes that have a major commitment to the development of innovative drugs. NatSynDrugs will facilitate the transfer of knowledge and innovative technologies among Italian and European groups.
Role and commitment of key persons (including supervisors)	Coordinator, Prof. Giuseppe **Campiani** (Medicinal Chemistry & Bioinformatics) [10% time commitment]; Supervisor of ESR 6 & 8; Prof. Stefania **Butini** (Medicinal Chemistry & Drug design) (8% time commitment); Dr. Margherita **Brindisi** (Synthetic methodologies & NMR studies) (8% time commitment).
Key Research Facilities, Infrastructure and Equipment	UNISI-NatSynDrugs is equipped with a range of **equipment for synthesis, characterization and purification of compounds**: Microwave Peptide Synthesizer "Liberty" CEM, Microwave CEM, Syncore Büchi for parallel synthesis, "SPOT liquid chromatography" for flash-chromatography, HPLC (LaPrep, VWR), HPLC/MS-MS Varian Apparatus, Analytical/semipreparative Merck HPLC, PARR reactor with hydrogen generator CLAIND (HG2600), GC/MS Varian Saturn 2000 Apparatus, Capillary electrophoresis Beckman Coulter, NMR 400 MHz Bruker, NMR 300 MHz Varian, Varian IR, Varian polarimeter. Full instrumentation to **characterize protein samples** is available (SDS-GE, SEC, LS; ITC, UV-Vis, CD, MS, NMR, XRD). Access to synchrotron sources for data collection on protein crystals is also granted. UNISI-NatSynDrugs provides access to **one laboratory fully equipped with hardware and software**: one Cooler Master Centurion 5 (Intel Core2 Quad CPU Q6600 @ 2.40 GHz; 4GB RAM) workstation with Ubuntu 10.04 LTS (long-term support) operating system; two Cooler Master Centurion 5 (Intel Core i5–2500 CPU @ 3.30 GHz Quad; 8GB RAM) workstations with Ubuntu 10.04 LTS (long-term support) operating system and equipped with NVIDIA GeForce GT 440 and GT 520 as graphic cards for GPU computing by means of CUDA technology with GROMACS and OpenMM (NCBC) software. **Proprietary molecular modeling software** as Maestro Molecular Modeling Environment Suite (Schrödinger, LLC, NY), G.O.L.D. (Genetic Optimization for Ligand Docking, CCDC, UK), Molecular Dynamics software as Desmond (DESRES), NAMD (TCB) are installed on these workstations.
Independent research premises?	Yes
Previous Involvement in Research and Training Programmes	The supervisors listed above have together supervised 28 PhD, and 2 Marie Curie PhD students (EU-InterMalTraining and EU-Antimal). UNISI-NatSynDrugs has a successful track record in securing and managing large training and research programmes, such as a European PhD School in Malaria.
Current Involvement in Research and Training Programmes	The supervisors listed above are currently supervising 6 PhD students that are part of a PhD training programme in Pharmaceutical Sciences. Prof Campiani delivers two taught modules on this PhD training programme: 'New frontiers for antitumor agents' – 2 ECTS, 16 hours and 'Drug Discovery for Neuropsychiatric and Neurodegenerative Disorders' – 1 ECTS, 8 hours. Prof Butini delivers a taught module of "Medicinal Chemistry Features" as a part of an integrated course of the "CNS therapies" in the Specialization School of Hospital Pharmacy at the University of Siena (1 ECTS, 8 hours).
Relevant publications and/or research/innovation products	1) O'Callaghan, K., et al. (2015) Induction of apoptosis in oral squamous carcinoma cells by pyrrolo-1,5-benzoxazepines. Mol Med Rep. 12, 3748-3754. 2) Greene, L.M., et al. (2013) Inhibition of late-stage autophagy synergistically enhances pyrrolo-1,5-benzoxazepine-6-induced apoptotic cell death in human colon cancer cells. Int. J. Oncol., 43, 927-935. 3) McElligott, A. M. et al. (2009) The Novel Tubulin-Targeting Agent Pyrrolo-1,5-Benzoxazepine-15 Induces Apoptosis in Poor Prognostic Subgroups of Chronic Lymphocytic Leukemia. Cancer Res., 69: 8366-8375. 4) Ferlini, C. et al. (2009) Paclitaxel Directly Binds to Bcl-2 and Functionally Mimics Activity of Nur77. Cancer Res., 69, 6906-6914. 5) Ferlini C.et al. (2005) The Seco-Taxane IDN5390 Is Able to Target Class III Beta-Tubulin and to Overcome Paclitaxel Resistance, Cancer Res., 65, 2397-2405.

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Beneficiary– Queen's University Belfast, Centre for Cancer Research and Cell Biology	
General description	The Centre for Cancer Research and Cell Biology (CCRCB) is increasingly recognised on the national and international stage for both its basic and translational research programmes in addition to its rapidly evolving clinical trial expertise. The CCRCB forms the hub of the Belfast Cancer Research UK (CRUK) Centre and the Experimental Cancer Medicine Centre in Belfast. The integrated clinical and basic scientific research programmes funded by Cancer Research UK, MRC, BBSRC, EPSRC, Wellcome Trust and other major cancer charities address clinically-relevant questions and areas of strategic priority, the outputs of which are underpinning improved patient outcomes in high incidence, solid tumours of Gastro-intestinal, Prostatic, Breast and Ovarian origin. The CCRCB provides a unique environment where researchers in basic science can work alongside and interact with clinical scientists in a variety of laboratory programmes. Our unifying research theme is to develop translational outputs, i.e. biomarkers and/or novel therapeutic strategies that enable CCRCB to be at the forefront of personalized cancer medicine in these prevalent diseases. The major impact of our research upon patient outcomes in Northern Ireland resulted in Queen's and CCRB receiving Her Majesty's Jubilee Anniversary Prize in 2012.
Role and commitment of key persons (including supervisors)	**Prof. Richard Kennedy** (10% time commitment) and **Dr. Richard Turkington** (10% time commitment) will supervise 2 students (ESR 2 & 4). They have supervised 10 PhD students over the last 10 years. **Dr. Nuala McCabe and Dr Leanne Stevenson,** senior research fellows will contribute to PhD training in bioinformatics techniques and will also contribute to overall network training.
Key Research Facilities, Infrastructure and Equipment	CCRCB has molecular biology expertise, molecular pathology facilities, genomic platforms, bioinformatics platforms, animal facilities and access to bioengineering and hospital facilities. The Northern Ireland Molecular Pathology laboratory is also housed at CCRCB and provides access to a range of pathological and next-generation sequencing techniques. CCRCB also runs a Phase I clinical trial unit at Belfast City Hospital. In combination with our established biobanking of pre-chemotherapy biopsies and post-treatment resection specimens in OOC these capabilities provide a comprehensive platform for the translation of laboratory discoveries into clinical practice.
Independent research premises?	Yes
Previous Involvement in Research and Training Programmes	From 2004-2007, Prof. Kennedy was an instructor in Oncology at Harvard Medical School, USA and formed a spin-out company - DNAR. 2007 - present Prof. Kennedy is Head of Research Almac Diagnostics. Developed and commercialised 3 biomarkers. 2011 - present Prof. Kennedy is Professor Medical Oncology,QUB. Manages a lab group of 12 people. 2014 – present Dr Turkington is a Clinical Senior Lecturer, QUB, Manages a lab group of 4 people
Current Involvement in Research and Training Programmes	R. Kennedy is Director for undergraduate academic training in medicine, which incorporates the intercalated BSC, summer studentship and academic foundation year programmes. He leads a research group of 12 people at Queen's University. R Turkington is Academic lead for postgraduate academic training in medicine. r. Kennedy holds a £4 Million Invest Northern Ireland grant to develop novel biomarkers between Almac Diagnostics and Queen's University of Belfast. In Nov 2013 one of these was out-licensed to Genomic Health (USA) for $9 million and royalties. Postgraduate students in QUB are enrolled on a number of taught modules which Prof Kennedy and Dr Turkington are involved in delivering including: **1. Generic Skills for Life Sciences** 2. **Cancer Biology Module**- This module provides a comprehensive overview of the fundamental principles of carcinogenesis highlighting how normal control processes are bypassed during tumour formation. The pathogenic mechanisms to be discussed will range from genomic alterations in key gene families, to epigenetic mechanisms of gene control, alterations in kinase activities or protein turnover, or activation of aberrant phenotypes such as invasion and angiogenesis. In taught sessions the students will learn about our current knowledge of the molecular basis of cancer, the signalling mechanisms underpinning cancer pathogenesis and a brief introduction to drug discovery including examples of novel targets have been identified for cancer treatment 3. **Generic Skills in Communicating Science** **4. Translational Cancer Medicine** 5. **Medical Statistics**
Relevant publications and/or research/innovation products	1. Mulligan JE et al. Identification and Validation of a DNA Damage Response Deficiency Assay for Breast Cancer. The Journal of The National Cancer Institute 2014 Jan 1;106(1)82-6 2. Kennedy RD et al , Development and Independent Validation of a Prognostic Assay for Stage II Colon Cancer using Formalin Fixed Paraffin Embedded Tissue. Journal of Clinical Oncology 2011 10;29:4620-6 3. Kennedy RD et al. Fanconi anemia pathway-deficient tumor cells are hypersensitive to inhibition of ataxia telangiectasia mutated. Journal of Clinical Investigation. 2007 (5):1440-9. 4. Turkington RC, Allen WL, Stevenson L, McLaughlin K, Dunne P, Blayney J, Salto-Tellez M, Longley DB Schaeybroeck S, and Johnston PG. Fibroblast Growth Factor Receptor 4 (FGFR4) as a novel determinant of resis to chemotherapy in colorectal cancer. Cell Death and Disease 2014 Feb 6; 5:e1046 5. Allen WL*, Turkington RC*, Stevenson L, Carson G, Coyle VM, Hector S, Dunne P, Van Schaeybroeck S, Lo DB, Johnston PG. Pharmacogenomic Profiling and Pathway Analyses Identify MAPK-Dependent Migration as an Response to SN38 in p53 Null and p53-Mutant Colorectal Cancer Cells. Mol Cancer Ther 2012; 11(8): 1724-34 first authors

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Beneficiary– Valencia University and University General Hospital, Valencia, Spain.	
General description	Valencia University (UVEG) was founded over five centuries ago by the Juries of Valencia, and has become a modern, public university that teaches all areas of knowledge: social, economic and legal sciences, experimental sciences, engineering, health sciences, educational sciences and the humanities. More than 45,800 undergraduate students and 8,600 postgraduate students take classes taught by more than 3,300 professors, lectures and researchers with the support of over 1,700 administration and service staff. Our University is committed to being a university of reference: we are ranked second in Europe in receiving Erasmus students and fourth among Spanish universities in research. According to the most prestigious international rankings, we are the ranked fourth in Spain. The National Registry of Childhood Tumours is located in the Faculty of Medicine of the University of Valencia, and aims to carry out epidemiological research that contributes to improving care for infants suffering from cancer in Spain and to study the fundamental mechanisms underlying this disease.
Role and commitment of key persons (including supervisors)	Prof Jose V. Bagan, Professor of Oral Medicine at Valencia University (time commitment 10%). Supervisor of ESRs 1 & 3. Head of Service of Stomatology and Maxillofacial Surgery at University General Hospital, Valencia, Spain. Technical and laboratory staff are on site to assist all ESRs undergoing training in this institute.
Key Research Facilities, Infrastructure and Equipment	The Research Unit University General Hospital offers access to sate of the art facilities utilizing “In vivo” and “In vitro” techniques encompassing biochemistry and molecular biology including real time fluorescence microscopy, HPLC with multiple detector types e.g. fluorescence, UV-visible, refractive index. Molecular biology facilities include, qRT-PCR, high-throughput screening using Fluidigm technologies, PCR based microarrays, nucleic acid sequencing, pharmacogenetic analysis. Flow cytometry, cell culture and standard laboratory facilities are also available.
Independent research premises?	Yes
Previous Involvement in Research and Training Programmes	Prof. Bagan has supervised 43 PhD and is currently involved in several projects focused in potentially malignant disorders and oral cancer. Prof Bagan has published 326 articles indexed in PubMed most of which are derived from supervised PhDs and have been published in journals indexed in Journal Citation Report. (Search in Pubmed as: Bagan J or Bagan-Sebastian J)
Current Involvement in Research and Training Programmes	Dr. Bagan is currently supervising 3 PhD students and he is also the general Coordinator of the doctoral programme in Clinical Dentistry in the Department of Stomatology at Valencia University, which recruits 30 students per year.
Relevant publications and/or research/innovation products	1) Bagan J, Sáez GT, Tormos MC, Gavalda-Esteve C, Bagan L, Leopoldo-Rodado M, Calvo J, Camps C. Oxidative stress in bisphosphonate-related osteonecrosis of the jaws. J Oral Pathol Med. 2014 Jan 23. doi: 10.1111/jop.12151. [Epub ahead of print] PubMed PMID: 24450511. 2) Bagan J, Saez G, Tormos C, Gavalda C, Sanchis JM, Bagan L, Scully C. Oxidative stress and recurrent aphthous stomatitis. Clin Oral Investig. 2014 Jan 10. [Epub ahead of print] PubMed PMID: 24407552. 3) Bagan J, Sáez G, Tormos M, Hens E, Terol M, Bagan L, Diaz-Fernández J, Lluch A, Camps C. Interleukin-6 concentration changes in plasma and saliva in bisphosphonate-related osteonecrosis of the jaws. Oral Dis. 2013 Jun 25. doi: 10.1111/odi.12150. [Epub ahead of print] PubMed PMID: 23837828. 4) Bagan J, Sheth CC, Soria JM, Margaix M, Bagan L. Bisphosphonates-related osteonecrosis of the jaws: a preliminary study of salivary interleukins. J Oral Pathol Med. 2013 May;42(5):405-8. doi: 10.1111/jop.12021. Epub 2012 Nov 15. PubMed PMID: 23157469. 5) Bagan JV, Mata-Roig M, Cortio-Gimeno J, Murillo-Cortes J, Hens-Aumente E, Poveda-Roda R, Bagan L. Epidermal growth factor receptor copy number in potentially malignant oral disorders and oral squamous cell carcinoma: a short communication and preliminary study. J Oral Pathol Med. 2012 Oct;41(9):662-6. Epub 2012 Mar 14. PubMed PMID: 22417006.

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Beneficiary– SME: OROBOROS INSTRUMENTS Corp	
General description	Erich Gnaiger is founder and CEO of the SME OROBOROS INSTRUMENTS Corp. (www.oroboros.at) with world-wide technological leadership in high-resolution respirometry (>1600 Oxygraph-2k publications) and reference laboratories in 42 countries. The cooperation between academia (Medical University of Innsbruck) and industry (OROBOROS INSTRUMENTS) is formalized in the MitoFit Centre of Excellence by Erich Gnaiger.
Role and commitment of key persons (including supervisors)	Erich Gnaiger (time commitment 10%) has scientific and technical expertise in the fields of mitochondrial physiology and pathology, microcalorimetry and biological thermodynamics, contributing fundamentally to the understanding of mitochondrial respiratory control, and development and application of high-resolution respirometry to cellular bioenergetics and the diagnosis of mitochondrial defects. Apart from being CEO of the SME OROBOROS INSTRUMENTS Corp, Erich also has a faculty position at the D. Swarovski Research Laboratory, Department of Visceral, Transplant and Thoracic Surgery, Medical University of Innsbruck, Austria. The Medical University of Innsbruck has a strong pedigree in Oncology. His focus in TRACT will be on cellular bioenergetics (10% time commitment).Supervisor of ESR 11.
Key Research Facilities, Infrastructure and Equipment	Application of high-resolution respirometry to cellular bioenergetics and the diagnosis of mitochondrial defects. The apparatus central to these studies is the OROBOROS Oxygraph-2k, a respirometer, which is also suitable for studying cultured cells.
Independent research premises?	Yes. Erich Gnaiger's research laboratory is situated in the Mitochondrial Research Lab of OROBOROS INSTRUMENTS which provides state-on-the art equipment for high-resolution respirometry on 12 fully upgraded Oxygraphs-2k.
Previous Involvement in Research and Training Programmes	He is initiator and chairman of the Mitochondrial Physiology Society (MiP*society*; www.mitophysiology.org), and has organized numerous conferences (particularly MiP2003, MiP2005, MiP2010, MiP2013 and MiP2014 in Austria), workshops (more than 100 international workshops on high-resolution respirometry), and training courses on mitochondrial physiology, bioenergetics and biological thermodynamics, and is editor of several proceedings of international meetings. The international teaching activities range from non-equilibrium thermodynamics for chemical engineers (EU-level training; previous member of the IUPAC steering committee on biological thermodynamics) to mitochondrial physiology. E. Gnaiger participated at international scientific expeditions taking high-resolution respirometry to climatic extremes in Northern Greenland, Alaska and high altitude (Monte Rosa, Italy; Mt. Chacaltaya, Bolivia; Everest Base Camp, Nepal). Visiting scientists have stayed at the OROBOROS MitoLab within the framework of the following training programmes (ERASMUS, Aktion Österreich-Slowakei, ASEA-UNINET, innovabalt). Erich Gnaiger is initiator of 'Gentle Science' (http://www.bioblast.at/index.php/Gentle_Science).
Current Involvement in Research and Training Programmes	Erich Gnaiger has supervised 10 Ph.D students to completion and is currently supervising three Ph.D students. Ongoing involvement in workshops and training course on mitochondrial physiology, bioenergetics and biological thermodynamics.
Relevant publications and/or research/innovation products	Innovation products: » http://www.bioblast.at/index.php/O2k-Fluo_LED2-Module 1) Harrison DK, Fasching M, Fontana-Ayoub M, **Gnaiger E** (2015) Cytochrome redox states and respiratory control in mouse and beef heart mitochondria at steady-state levels of hypoxia. J Appl Physiol Aug 6:jap.00146.2015. doi: 10.1152/japplphysiol.00146. 2015. 2) **Gnaiger E** (2014) Mitochondrial pathways and respiratory control. An introduction to OXPHOS analysis. 4th ed. Mitochondr Physiol Network 19.12. OROBOROS MiPNet Publications, Innsbruck: 80 pp. ISBN 978-3-9502399-8-0 – Open Access, see: http://www.bioblast.at/index.php/Blue_Book 3) Krumschnabel G, Eigentler A, Fasching M, **Gnaiger E** (2014) Use of safranin for the assessment of mitochondrial membrane potential by high-resolution respirometry and fluorometry. Methods Enzymol 542: 163-81. 4) Boushel R, Ara I, **Gnaiger E**, Helge JW, Gonzalez-Alonzo J, Munck-Andersen T, Sondergaard H, Damsgaard R, van Hall G, Saltin B, Calbet JA (2014) Low intensity training increases peak arm VO2 by enhancing both convective and diffusive O2 delivery. Acta Physiol (Oxf) 211:122-34. 5) Kristiansen G, Hu J, Wichmann D, Stiehl DP, Rose M, Gerhardt J, Bohnert A, ten Haaf A, Moch H, Raleigh J, Varia MA, Subarsky P, Scandurra FM, **Gnaiger E**, Gleixner E, Bicker A, Gassmann M, Hankeln T, Dahl E, Gorr TA (2011) Endogenous myoglobin in breast cancer is hypoxia-inducible by alternate transcription and functions to impair mitochondrial activity: a role in tumor suppression? J Biol Chem 286: 43417-43428. 6) Eberhart K, Rainer J, Bindreither D, Ritter I, **Gnaiger E,** Kofler R, Oefner PJ, Renner K (2011) Glucocorticoid-induced alterations in mitochondrial membrane properties and respiration in childhood acute lymphoblastic leukemia. Biochim Biophys Acta 1807: 719-725. 7) Scandurra FM, **Gnaiger E** (2010) Cell respiration under hypoxia: Facts and artefacts in mitochondrial oxygen kinetics. Adv Exp Med Biol 662: 7-25.

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Partner Organisation	Seahorse Biosciences
General description	Manufactures Seahorse Flux Analyzers XF^{e}24, XF^{e}96 and XFp, along with kits and reagents that provide easy access to gold standard applications in the field of cancer metabolism. Seahorse also collaborates with many academic and industrial laboratories around the globe.
Key Persons and Expertise	**David Ferrick, Ph.D.** (Chief Scientific Officer) has over 20 years of R&D experience in drug discovery, clinical development and life science applications. **Andy Neilson** (Founder, Chief Technology Officer) brings over twenty years of engineering management and design experience focused on complex electro-optical systems. He is the primary inventor of the Seahorse extracellular flux measurement technology. **Brian P. Dranka, Ph.D.** (Manager of Biology) leads the development of new kits and reagents at Seahorse Bioscience. His main research focus has been to increase understanding of cellular metabolism and bioenergetics in human disease for nearly 15 years. He has experience taking new products from concept to development and commercialization, most recently completing a new application for metabolic fuel dependency in cancer and other diseases. He has published 19 highly cited peer-reviewed manuscripts in the field of mitochondrial dysfunction. **Dr Alex Liversage** (Seahorse UK), expert in Seahorse extracellular flux technology, delivers training workshops within Europe such as 'Experimental design for intact cells, isolated mitochondria and permeabilized cells using the Seahorse XF Stress Test kits.' Dr Liversage will deliver a training course to ESRs in TRACT specifically ESR 7, 10 & 11.
Key Research facilities, infrastructure and Equipment	The research space at Seahorse Bioscience has laboratories of approximately 1500 sq. ft. and office space of approximately 1000 sq. ft. located at the Seahorse Bioscience headquarters in Billerica, MA, US. This space is dedicated to the biological validation of Seahorse Bioscience's current instrumentation, and also supports research and development of future products. All current product development activities are led from this main office. Training activities will occur on site at Trinity Biomedical Science Institute at Trinity College Dublin.
Previous and Current Involvement in Research and Training Programmes	Seahorse Bioscience consistently conducts workshops and training for customers and users. Training typically occurs onsite at the users laboratory. Additional workshops are offered 4-6 times per year at various locations around the world. Recent examples include: XF User Group Meeting at University of Alabama at Birmingham Birmingham, AL, USA http://www.seahorsebio.com/support/meeting-reg.php Mitochondrial function in T cells at University of Amsterdam http://www.seahorsebio.com/support/training/courses/advanced-uamsterdam.php
Research/innovation product	Seahorse Bioscience Extracellular Flux Analyzers XF^{e}24, XF^{e}96, and XFp.

Partner Organisation NIBRT	
General description	NIBRT is a company whose mission is to provide a continuum of world class research and training solutions for the bioprocessing industry with a specific focus on the design, development & optimization of bioprocess for the safe and efficacious production of biopharmaceutical products
Key Persons and Expertise	Prof. Pauline Ruud (BSc, PhD, FRSM) Secondary supervisor of ESR 1. Dr Jayesh Kattla–glycan biomarker development, Dr Stephen Quinn–Glycan markers in neurodegenerative diseases, Dr Naobh O'Donoghue , Lab manager.
Key Research facilities, infrastructure and Equipment	The Rudd laboratory has extensive knowledge and experience in the field of Glycobiology, specifically *N*- and *O*-glycan analysis. Using state-of-the-art, high-throughput, high-resolution HPLC methodology for *N*-glycan analysis allowing quantitative comparisons of glycan structures between clinical samples. In addition, mass spectrometry analysis of released glycans is used to further elucidate structures. NIBRT has extensive research contracts with major pharmaceutical and analytical companies and provides bespoke training courses for industry scientists
Previous and Current Involvement in Research and Training Programmes	NIBRT provides training such as "Introduction to Glycobiology", "Analytical Techniques in Glycobiology: Applications to biomarker discovery" and is involved in other training courses such as in "State-of-the-art Protein Analysis and Regulatory Science" at Barnett Institute in Northeastern University in Boston and in the EuroCarb Workshop. Prof Rudd is involved in a number of grants including EuroGlycoArrays Network. **NIBRT** provides training programmes for the fast growing Biopharmaceutical Industry within Ireland and overseas with an emphasis on Glycobiology. NIBRT is currently an associated partner in an FP-7 funded ITN entitled TINTIN and is providing training courses and hosting ESR secondments.
Relevant Publications and/or research/innovation product	1) Albrecht S et al. (2014) Cancer Biomark. Jan 1;14(1):17-28 2) Saldova R et al. (2013) PLoS One. Aug 30;8(8):e71159 3) Dempsey E et al. (2012) Ann N Y Acad Sci. Apr;1253:122-32.

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Partner Organisation Fraunhofer Institute for Molecular Biology and Applied Ecology IME	
General description	The Hamburg site of Fraunhofer Institute for Molecular Biology and Applied Ecology IME has four main areas of activity: Drug Discovery – covering all stages from target validation via small molecule screening to candidate selection; Biomarker and Translational Research – support biomarker discovery studies for clinical and pre-clinical research projects; Enabling Technologies – develop and benchmark novel assay and screening technologies; R&D Information Technologies – using "Big data" approaches to improve efficiency in antibiotic drug discovery and Computational Chemistry approaches for hit finding and optimisation.
Key Persons and Expertise	Dr. Björn Windshügel, Head of Bioinformatics, 4 years of postdoctoral and 4 years of industrial experience at IME-SP. He will act as secondary supervisor to ESR 3 & 4. Dr. Philip Gribbon, CSO/COO, altogether 9 years of industrial experience at Pfizer and GSK.
Key Research facilities, infrastructure and Equipment	High-throughput and high-content screening facility, large compound libraries (~500,000 cpds.), multiple readout systems including label-free technologies. State-of-the-art chemoinformatic and computational chemistry software, 3D workstations, computing cluster.
Previous and Current Involvement in Research and Training Programmes	Since the setup of the IME-SP antecessor European ScreeningPort in 2007, the institute has participated in two completed Neu2 projects, financed by the Federal Ministry of Education and Research (BMBF) in Germany as well as four other BMBF-financed projects (e.g. HepaChip, NanoBioComp). The IME-SP is participating in several ongoing FP7 (*e.g.* EuRythDia, MARINE NMTrypI, FUNGI, CVGenes@Target) and IMI projects (K4DD, TRANSLOCATION). Moreover, IME-SP is involved in two ongoing Neu2 projects funded by the BMBF and participates in a EuroTransBio project. IME-SP regularly hosts and trains undergraduate students (internships, Bachelor and Master thesis) as well as professionals (workshops) and is participant in the Marie Curie ITN projects TRANSLOCATION, TINTIN and INTEGRATE (start in 2015).
Relevant Publications and/or research/innovation product	1) Küblbeck J. *et al*. (2011) New *in vitro* tools to study human constitutive androstane receptor (CAR) biology: discovery and comparison of human CAR inverse agonists. *Mol. Pharm.* 8, 2424-2433 2) Halley F. *et al*. (2011) A bioluminogenic HDAC activity assay: validation and screening. *J. Biomol. Screen.* 16, 1227-1235 3) Burk O. *et al.* (2012) Differential effects of clinically used derivatives and metabolites of artemisinin in the activation of constitutive androstane receptor. *Br. J. Pharmacol.* **167**, 666-681.

Partner Organisation Andor	
General description	Andor Technology plc. (Andor) is a world leader in Scientific Imaging and Microscopy Systems. Located in Belfast, Andor employs over 300 people in 16 offices worldwide and distributes its products to 10,000 customers in 55 countries. Andor acquired Bitplane (Switzerland) which incorporated Bitplane's focus on 3D/4D imaging to Andor's existing business. Andor acquired Photonic Instruments (USA) who developed the revolutionary Mosaic/Micropoint products and are the market leaders in fluorescence imaging and laser ablation for Confocal and widefield microscopy.
Key Persons and Expertise	Dr Andrew Dennis (BSc PhD), director of product management and is responsible for global Product Management & Marketing activities. Dr. Orla Hanrahan, Life Science Application Specialist at Andor Technology holds a PhD in Biochemistry and joined Andor from TCD where she was the Cell Imaging Facility manager. She will act as secondary supervisor to ESR 9. Andor has invested heavily in software and offers a range of world-class software solutions targeting imaging and multi-dimensional microscopy.
Key Research facilities, infrastructure and Equipment	ESRs will be hosted at the largest Andor facility, based in Belfast, Northern Ireland. The facility is a new, purpose-built 5,000sqm premises, which includes state of the art optical, electronic and mechanical workshops, a 300sqm clean room, vacuum and electronic processing facilities. Andor operates a quality management system and complies with the requirements of BS EN ISO9001:2000 and has other accreditations including Investors in People and ISO14001 environmental compliance.
Previous and Current Involvement in Research and Training Programmes	1. Andor technology works with QUB as part of their Engineering Leadership Programme (ELP). Engineering students are selected in their first year at Queens from a mechanical engineering discipline to participate in the programme which aims to develop the students business acumen and will look at the areas of communication, team building, problem solving, leadership, lean manufacturing, project management and leadership. Andor are also a participant in an FP7 funded ITN entitled TINTIN, where they are hosting an ESR secondment and delivering a training course to all ESRs.
Relevant Publications and/or research/innovation product	1) Hanrahan O, Harris J, Egan C. (2011) Methods Mol Biol. 784:169-80 2) Spitznagel D et al. (2010) PLoS One.5(8):e12282. 3) Hanrahan O et al. (2009) PLoS Pathog. 6:e1000468. Epub 2009 Jun 5.

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Partner Organisation	Almac Diagnostics
General description	Almac Diagnostics has 80 staff and scientists focused on the discovery, development, validation and delivery of predictive and prognostic biomarkers. The bioinformatics and biostatistics department include 5 PhD and 6 MSc level scientists.
Key Persons and Expertise	Dr. Timothy Davison (TD) (8% time commitment) will support the supervision and training of ESRs 2 & 4. He will act as their secondary supervisor. He has led teams including a total 17 PhD and 11 Masters level scientist bioinformaticians and statisticians in the biotech, pharmaceutical and diagnostics industries over the last 9 years.
Key Research facilities, infrastructure and Equipment	Almac Diagnostics is a personalized medicine company focused on the discovery, development and delivery of biomarkers with bioinformatics, statistics and biostatistics data analysis expertise, and experience analyzing data and developing, validating and delivering biomarkers from qPCR, array and next-generation sequencing platforms.
Previous and Current Involvement in Research and Training Programmes	2006 – 2009 TD was Steering committee member and Co-Chair of the Regulatory Biostatistics Working Group in the Food and Drug Administration (FDA) Microarray Quality Control Consortium (MAQC-II) 2011- Present TD is Head of Bioinformatics and Biostatistics at Almac Diagnostics. Developed and commercialised 5 biomarkers. TD is an honorary senior lecturer at CCRCB in QUB. Through Almac Diagnostics, the bioinformatics group participates in an MSc student internship program with University College Cork.
Relevant Publications and/or research/innovation product	1) Identification and validation of an anthracycline/cyclophosphamide-based chemotherapy response assay in breast cancer. Mulligan JM, et al., J Natl Cancer Inst. 2014 Jan;106(1):djt335. doi: 10.1093/jnci/djt335. 2) Model selection for prognostic time-to-event gene signature discovery with applications in early breast cancer data. Ahdesmäki M, et al., Stat Appl Genet Mol Biol. 2013 Oct 1;12(5):619-35. doi: 10.1515/sagmb-2012-0047. 3) Implications for powering biomarker discovery studies. Dibben SM, et al., 2012 Mar; 14(2):130-9. Epub 2012 Jan 15.

Partner Organisation Opsona Therapeutics	
General description	Opsona Therapeutics is one of Europe's most innovative and dynamic drug development companies. We are at the forefront of drug development in immunology research, with particular focus on the innate immunity pathways. Since its founding in 2004, Opsona has validated and developed a series of exciting new drug candidates and strategies which modulate the human innate immune system. Opsona are located in Dublin, Ireland.
Key Persons and Expertise	Prof. Luke O'Neill (BA, PhD) is a Director and the Chief Scientific Officer of Opsona Therapeutics. He will act as secondary supervisor to ESR 5. Dr. Brian Keogh and William McCormack are head scientists at the Opsona research facility, where novel agents are being screened and validated.
Key Research facilities, infrastructure and Equipment	The Opsona research laboratory has extensive knowledge and experience in the field of Immunology, specifically in the identification and validation of novel immunomodulatory drugs for the treatment and prevention of disease. Infrastructures relevant to this collaboration include Tissue culture and animal facilities, FACS cell sorter and Confocal microscope facility. Opsona has extensive research contracts with major pharmaceutical and analytical companies.
Previous and Current Involvement in Research and Training Programmes	In 2010, Opsona was awarded €5.9m to lead an EU FP7 consortium of research and clinical groups, termed MASBOT (Monoclonal Antibody Solid Organ Transplantation) in the advancement of clinical trials for its lead drug candidate OPN-305 in solid organ transplantation. Opsona is also partaking in an innovation partnership with Trinity College Dublin, the aim of this programme, which is co-funded by Enterprise Ireland and Opsona, is to assess the potential of Opsona's TLR2 antibody as a novel therapeutic in Alzheimer' disease (AD).
Relevant Publications and/or research/innovation product	1) Reilly M. et al. (2013) Randomized, double-blind, placebo-controlled, dose-escalating phaseI, healthy subjects study of intravenous OPN-305, a humanized anti-TLR2 antibody. Clin. Pharmacol. Ther. 94:593-600. 2) Keogh B et al. (2011) Toll-like receptors as targets for immune disorders. Trends Pharmacol Sci. 32; 435-42. 3) McCormack WJ et al. (2009) Toll-like receptors and NOD-like receptors in rheumatic diseases. Arthritis Res Ther. 11(5):243.

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Partner Organisation Exosomics	
General description	EXOSOMICS (EXS) was founded in 2011 and is located within the Toscany Life Science (TLS) Biomedical Park in Siena – Italy. EXS' R&D activities focus on the development of: 1) assays for diagnosis, prognosis and monitoring of prostate and colorectal cancer 2) assays for personalized medicine
Key Persons and Expertise	Antonio Chiesi (MD) with 20 years of experience in translational and clinical research at the Italian ISS, CEO of Exosomics. Natasa Zarovni (PhD), EXS Head of R&D, responsible for projects management and team training and supervision, EXS product development, biomarker validation. Davide Zocco, (PhD), PI in Molecular Diagnostics, works with clinical partners to implement EV platforms for personalised medicine.
Key Research facilities, infrastructure and Equipment	EXS offers office and laboratory space and it is equipped with routine instrumentation for cell and molecular biology and biochemistry and dedicated technologies for EV research i.e. NTA.. EXS has access to core TLS facilities for FACS and mass spectrometry and next-generation sequencing platforms (Ion Torrent and SOLiD) and bioinformatics services through strategic partnerships
Previous and Current Involvement in Research and Training Programmes	EXS core 5 year R&D programme is focused on validation of exosome associated tumour markers and development of novel generation of diagnostic tools. EXS was a *coordinator* of Tuscany region strategic project (UNICO) EXONANODI (Identification of multifunctional nanomaterials suitable for capture quantification and characterisation of circulating exosomes) a*nd is a national representative in* COST Action (BM1202) MEHAD. EXS also participateds in Children Tumor Foundation Clinical Research Award ("Identification of neurofibroma and MPNST specific exosome-associated markers as early detectors of malignant transformation.") and in ongoing STW Perspectief Project ("New Technology for monitoring Cancer therapy through extracellular vesicle Identity (Cancer-ID) ").
Relevant Publications and/or research/innovation product	1. A new method to measure and characterize microvesicles in the human body fluids – AU2009207927 (A1) (US12/321,412; PCT/EE2009/000001) 2. Method and a kit to detect malignant tumors and provide a prognosis – US2012058492 (A1) (US13/290207) 3. Exosomes as intercellular signaling organelles involved in health and disease: basic science and clinical applications. Corrado C, Raimondo S, **Chiesi A,** Ciccia F, De Leo G, Alessandro R. Int J Mol Sci. 2013 Mar 6;14(3):5338-66. 4. Emerging technologies in extracellular vesicle-based molecular diagnostics. Jia S, **Zocco D**, Samuels ML, Chou MF, Chammas R, Skog J, **Zarovni N**, Momen-Heravi F, Kuo WP. Expert Rev Mol Diagn. 2014 Apr;14(3):307-21 5. Integrated isolation and quantitative analysis of exosome shuttled proteins and nucleic acids using immunocapture approaches. **Zarovni N**, **Corrado A**, Guazzi P, **Zocco D**, Radano G, Muhhina J, Fondelli C, Gavrilova J, **Chiesi A**. Methods 2015 Jun 2

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6 Ethics Issues

Relevant national legal and ethical requirements

Patient biopsy samples are required for the research projects described in WP 1-3 and it will be necessary to distribute biopsy samples, or derivative thereof, to TRACT partners across European borders. Regulations covering the use of human tissue are set out in **The European Union Tissue and Cells Directives** (EUTCD). The EUTCD is made up of three Directives, the parent Directive (**2004/23/EC**), which provides the framework legislation and two technical directives (**2006/17/EC and 2006/86/EC**), which provide the detailed requirements of the EUTCD. Directive 2004/23/EC sets the standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells. TRACT beneficiaries and partners will ensure that all activities, imports and exports of human tissues.

Each of the ESR projects which requires the use of human samples will apply to local Ethics committees for approval in advance of applying to the respective national competent authorities (Office for Research Ethics Committees Northern Ireland, UK; Irish Medicines Board, Ireland; Organización Nacional de Trasplantes, Spain) in order to obtain individual authorisation.

Both local statutory instruments and EU Directives stipulate that for human participants involved in research, the autonomy of the potential research participant must be respected by providing, in clear and accessible format, the maximum information on the implications of participation in a project and allowing independent and informed decision-making on whether to participate. The information will include written details of risks and benefits in participating, and a guarantee of confidentiality. Where possible this will be ensured through implementation of a controlled scheme for participant anonymisation. It is expected that participants will sign a consent form to agree to take part in the research and in all cases the participants will be made aware of their right to withdraw from the research without penalty at any time.

The study of molecular biomarkers and mechanisms of drug resistance in early stage oesophageal adenocarcinoma has already received ethical approval from the Office of Research Ethics Committees of Northern Ireland (ORECNI). National Health Service Research and Development approval has been obtained from all four health trusts in Northern Ireland for participation in the project and provision of biopsy materials.

The research described in WP6 involves the use of animal models of oesophageal squamous cell carcinoma in Trinity College Dublin. In accordance with **DIRECTIVE 2010/63/EU** all animal work will be pre-approved through ESR individual authorization with the national competent authority (Irish Medicines Board, S.I. No. 543 of 2012) and approval by the college Animal Research and Ethics Committee.

Addressing issues in the ethical issues table

Ethical issues of the research objectives: TRACT intends to define new biomarkers in OOC and their relationship to disease progression and response to therapeutic intervention. Such data could have potential impact on OOC patients. Patients in the University Hospital Valencia will be recruited on a voluntary basis and be made aware of the likely outcome of the research and will be required to give written consent. The biopsy samples will be anonymised after harvesting and records that identify particular participants will be retained only for as long as may be needed for cross-reference during the study. Published data will not be provided to third parties. With respect to the animal based tumour models it is not expected that the research objective (to assess new tumouricidal drugs) will give rise to ethical issues.

The primary objective of the research projects of ESR 2 and 4 based in QUB is to identify a molecular biomarker predictive of benefit from neo-adjuvant chemotherapy in early stage oesophageal adenocarcinoma. The secondary objective is the identification of genes and pathways associated with resistance to neo-adjuvant chemotherapy in oesophageal adenocarcinoma. Given the poor prognosis and the majority of patients for whom tissue samples will be utilised will be deceased. However, for surviving patients there is a potential for their tissue sample to be required for testing to guide the use of targeted therapeutic agents in the event that they experience a relapse. Therefore it will be mandatory that no tissue samples are exhausted during this study and that sufficient material be retained for possible future testing.

Ethical issues related to research methodology: The **biopsy samples** provided by the OCC patients in University Hospital Valencia will be harvested as part of a normal diagnosis schedule. The sample will be anonymised at the commencement of the study by allocation of a code number. This number will be used in all subsequent stored data records. A written guarantee of confidentiality will be provided. Participants will be given the option to withdraw from the study.

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In QUB, Belfast, the Clinical Oncology Information System (COIS) will be used to identify patients who have received neo-adjuvant chemotherapy from 2004-2012. The relevant clinical information will be collected from the COIS system and pathology reports obtained from the LabCentre system. All confidential data will be held in password protected and encrypted files on a computer and external hard drive in the locked office of Dr Richard Turkington at the Centre for Cancer Research and Cell Biology, Queen's University Belfast. All data will be held in accordance with the NHS code of Confidentiality and the Data Protection Act. Given the high relapse rate and poor survival associated with oesophageal adenocarcinoma the majority of patients will have died prior to this study beginning and so it will not be possible to obtain consent for the use of tissue samples. Surviving patients may well have relapsed or be undergoing subsequent treatment so we do not think it would be appropriate to obtain consent from surviving patients due to the potential of causing unnecessary distress. This plan of research has been granted ethical approval by the Office for Research Ethics Committees Northern Ireland (ORECNI).

Tumor models in mice require the use of immune-compromised strains and can suffer from inadvertent ulceration, metastasis and necrotic sepsis. ERSs participating in animal based experiments will have been trained on the LAST Ireland course, which is recognised by the national competent authority, the Irish Medicines Board. Local technical and veterinary staff will provide training in the use of tumour models. Prior to conducting the research the project will be required to be approved by the local AREC committee and for the individual ESR to be registered with the Irish Medicines Board. Ethical issues that may arise during the course of the animal studies will be brought to the attention of the Animal Welfare Body (a statutory body) who will advise and monitor the progression of the project and ensure project alternations and registered with the Irish Medicines Board.

Potential ethical impact of the research: Patients will be providing biopsy samples with the potential to diagnose disease and therapeutic outcome. Therefore, participants will be provided with the maximum information on the implications of participation in a project, in clear and accessible format, and be allowed independent and informed decision-making on whether to participate. The information will include written details of risks and benefits in participating, and a guarantee of confidentiality. Each of the national competent bodies, in accordance with legislation, have established reporting systems for the notification of suspected Serious Adverse Reactions (SARs) and Serious Adverse Events (SAEs) associated with human tissues and cells.

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7 Letters of Commitment

Please use this section to insert scanned copies of the required **Letters of Commitment from partner organisation**

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Seahorse Bioscience
A part of Agilent Technologies

TO: Richard K. Porter, FTCD, Ph.D. December 4, 2015
RE: Marie Curie Innovative Doctoral Programme proposal –
TRAining in Cancer metabolism Therapeutics (TRACT)

Seahorse Bioscience was founded in 2001 and is headquartered in Billerica, Massachusetts, U.S., with regional offices in Copenhagen, Denmark and Shanghai, China. Seahorse Bioscience metabolic analyzers and stress test kits are the industry standard in cell metabolism measurements. Scientists worldwide are using Seahorse technology to advance their research in understanding the role of cell metabolism in many diseases; however cancer metabolism is a specific focus.

A key hallmark of cancer cell metabolism is deregulated switching between oxidative phosphorylation and glycolysis. Seahorse XF technology is particularly useful in cancer metabolism because both of these key pathways are measured in parallel in real time. Over 500 peer-reviewed publications in the cancer field now include Seahorse data, and that number is rising quickly.

Seahorse is delighted to be a part of the Marie Curie Innovative Doctoral Programme proposal entitled – TRAining in Cancer metabolism Therapeutics (TRACT). In collaboration with The School of Biochemistry and Immunology at the Trinity Biomedical Science Institute at Trinity College, Dublin, Seahorse will provide training on the use of XF Analyzers and applications.

During the introductory 2-day course, each ESR will learn the importance of measuring cellular bioenergetics, how to effectively use XF technology to quantify cellular bioenergetic function, and how to perform and analyze XF data. Specifically, each person will:

- Spend two days with a Field Applications Scientist or Product Specialist
- Gain hands on experience with XF technology and applications in a wet lab environment
- Use current model XFe Analyzers and Reagent Kits
- Learn Standard Operating Procedures and Best Practices for sample preparation, sample handling, cell culture, and data analysis.
- Learn how to maximize the value of each experiment
- Form relationships and network with other scientists who study cancer cell metabolism

Advanced Training is also available and will be structured to expand beyond the typical introductory training in areas of experimental design and data interpretation. Seahorse offers advanced training courses typically in collaboration with regional experts in the field of interest. For example, recent courses in cancer metabolism have included Navdeep Chandel, Ph.D. (Northwestern University). An upcoming course in immunometabolism is being hosted in Amsterdam and features Erika Pearce, Ph.D. (Senior Group Leader and Director at the Max Planck Institute of Immunobiology and Epigenetics). A similar course will be created based on the needs of the TRACT programme and hosted at Trinity College Dublin.

Best regards,

Brian P. Dranka, Ph.D.
Manager of Biology
Seahorse Bioscience – a part of Agilent Technologies

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Prof Daniela Zisterer
School of Biochemistry & Immunology
Trinity College Dublin

7th December 2015

Dear Dr Zisterer

We are delighted to be part of your TRACT network and look forward to a successful collaboration in the training of young European scientists in the area of glycan biomarkers & cancer therapeutics. NIBRT is an SME that specializes in running bespoke training courses for students and industry-based scientists. NIBRT will run advanced training courses in the area of protein characterisation and glycoanalytics. Glycoanalytics is an increasing area of importance for cancer biomarkers and one that we have much experience, especially in relation to developing high throughput analysis for large numbers of patient samples. We have built a world-renowned company that specializes in training industry & academia researchers in the area of quantitative glycoanalytics. NIBRT will oversee a training course & workshop specifically in this area for TRACT researchers. Our expertize in this area will ensure that TRACT researchers will receive comprehensive training and transfer of knowledge, that will equip them with valuable experience for future employment in this area.

With respect to research training, we look forward to receiving a TRACT ESR for a 6 month research secondment in NIBRT. The ESR will receive intensive training in the area of glycoanalytics assay of cancer tissue samples. This secondment will synergise research training activities with Prof O'Sullivan's group in Trinity and ensure that the ESR will uncover important scientific discovery that will be patented, published in research papers, and part of their final PhD thesis.

Pauline M. Rudd

Pauline Rudd
Glycobiology Laboratory
National Institute for Bioprocessing Research and Training

Chairman: Joe Harford Board of Directors: Jeremy Bird, Martin Conry, Declan Farrell, Des Fitzgerald, Barry Heavey, Terry Lambe, David Lloyd, Paul Logue, Anita Maguire, Mary Martin, Eucharia Meehan, Gerard O'Mahoney.

Registered Office: Engineering Building, Room 125, Belfield, Dublin 4, Ireland NIBRT is a Company Limited by Guarantee (No 413711) VAT No: IE6433711D

This proposal version was submitted by **Daniela ZISTERER** on **11/01/2016 17:32:48** Brussels Local Time. Issued by the Participant Portal Submission Service.

Fraunhofer
IME

Fraunhofer Institute for Molecular Biology and Applied Ecology IME

Senior Executive Director
Prof. Dr. Rainer Fischer

Schnackenburgallee 114
22525 Hamburg

Prof. Dr. Carsten Claussen
Head
Fraunhofer IME ScreeningPort

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Fraunhofer IME | Schnackenburgallee 114 | 22525 Hamburg

Dr. Daniela Zisterer
School of Biochemistry and Immunology
Trinity College Dublin
Dublin
Ireland

Hamburg, November 30 2015

Letter of Support

Dear Dr. Zisterer,

hereby we confirm that the Fraunhofer-Institute for Molecular Biology and Applied Ecology IME is highly interested in participating in the Marie Curie ITN consortium "TRACT".
Our institute has a long standing and documented expertise in drug discovery approaches and biomarker research. We will contribute actively to this ITN and host two young researchers from the network in our facilities. The reserachers will be trained in target selection and drug discovery as well as biomarker research.
We understand that the sending institutions will provide funds for salary, travel and health insurance for the young researcher, whereas our institution will provide the necessary working environment.

Sincerely,

(Carsten Claussen)

Fraunhofer-Gesellschaft zur Förderung der angewandten Forschung e. V., München
Executive Board
Prof. Dr.-Ing. habil. Prof. E. h. Dr.-Ing. E. h. mult. Dr. h. c. Dr. h. c. Reimund Neugebauer, President
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Prof Daniela Zisterer
School of Biochemistry &
Immunology
Trinity College Dublin
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15th December 2015

Re: Marie Curie Initial Training Network

Dear Prof Zisterer

Andor Technology PLC would like to continue supporting your research and hereby declares their full commitment to act as an associate partner in the Initial Training Network "TRACT" (Training in cancer metabolism therapeutics). We are willing to play an active role in the training of the ESRs in the area where we have strong expertize. We are also willing to act as the host for 2 x 6 month secondments of the ESRs to our laboratories.

Our expertize that is of particular relevance to the activities of this programme includes the use and enhancement of 3D analysis software used to process microscopy images. This is relevant to the work of many of the ESR projects carried out in TRACT.

We also comit to organise an Andor Academy for the ESRs and ERs of TRACT at our labs in Belfast. The Andor Academy involves a three level training program relating to product optimisation, calibration and related applications. Level one of the Andor Academy takes place on-line, levels two and three take place at our facilities in Belfast, NI, UK.

Kind Regards

Dr Andrew Dennis
Director of Product Management

OHSAS 18001:2007 ISO9001:2008 ISO14001:2004

Offices in:

North America
Japan
China

Co. Reg. No. NI 22466
VAT No. GB 517 1829 44

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W www.almacgroup.com

Prof Daniela Zisterer
School of Biochemistry & Immunology
Trinity College Dublin

Dear Prof Zisterer,

I am delighted to be part of your Marie Sklodowska-Curie ITN TRACT network and look forward to training of early stage researchers in the area of biomarker discovery. Almac Diagnostics is a personalized medicine company focused on the discovery, development and delivery of biomarkers with bioinformatics, statistics and biostatistics data analysis expertise, and experience analyzing data and developing, validating and delivering biomarkers from qPCR, array and next-generation sequencing platforms.

As a collaborator of **Prof Richard Kennedy**, I am familiar with his successful activities pioneering the identification of molecular mechanisms underlying cancer subtypes and subsequently utilising this information to discover, develop and validate prognostic and predictive tests. He commands the resources necessary to produce the highest quality molecular data and subsequent characterisation through appropriate and unbiased analyses.

With respect to research training, we look forward to receiving TRACT ESRs for research secondments in Almac Diagnostics. These ESRs will receive intensive training in bioinformatics and biostatistics. These secondments will synergise research training activities with Prof Kennedy's group at Queen's University Belfast and ensure that the ESRs uncover novel results that will be published in research papers and may be commercialised

In my ten years' experience in the field of biomarker discovery, and my recent capacity as co-chair of the Regulatory Biostatistics working group of the Microarray Quality control Consortium (MAQC-II), an FDA-led collaboration characterising approaches for development and validation of classifiers utilizing DNA microarray data for the purpose of diagnostic, prognostic, or therapeutic applications, I have designed, implemented, reviewed and evaluated dozens of successful biomarker discovery efforts in a prognostic setting. In addition, I have led a number of projects translating biomarkers discovered on array platforms to clinically applicable tests using qRT-PCR and IHC technologies. Over the last 9 years, I have led teams including a total 17 PhD and 11 Masters level scientist bioinformaticians and statisticians in the biotech, pharmaceutical and diagnostics industry.

I give the proposed TRACT ITN application my full support. Please contact me if I can be of any further assistance.

Regards,

Timothy Davison
VP, Head of Bioinformatics & Biostatistics Almac Diagnostics
Honorary Senior Lecturer, CCRCB, Queen's University Belfast

This proposal version was submitted by **Daniela ZISTERER** on **11/01/2016 17:32:48** Brussels Local Time. Issued by the Participant Portal Submission Service.

Opsona Therapeutics Ltd,
Second Floor, Ashford House,
Tara Street, Dublin 2.

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Web: www.opsona.com

Opsona Therapeutics

Dr Emma Creagh,
School of Biochemistry & Immunology,
Trinity Biomedical Sciences Institute,
Pearse Street,
Dublin 2.

December 17th 2015.

Dear Dr. Creagh,

I am pleased to provide a letter of intent from Opsona Therapeutics as the industrial partner for your application in your Horizon 2020 European Training Network (ETN) application, 'TRACT' Training in Cancer metabolism and Therapeutics.

Opsona Therapeutics is a leading clinical stage biopharmaceutical company focused on the treatment of autoimmune/inflammatory diseases and cancers. We are innovators in the field of innate immunity research and are actively identifying new ways to prevent and treat these diseases. Our drug discovery and development is focused on the role of Toll-Like Receptors (TLRs) and Inflammasome signaling in human immunology.

Opsona Therapeutics has developed a proprietary fully humanised IgG4 anti-TLR2 antibody, OPN-305, which has been shown to be a potent inhibitor of TLR2-mediated pro-inflammatory immune responses. OPN-305 is a humanized IgG4 antibody derived from the murine IgG1 parent molecule OPN-301. OPN-305 has been shown to be biologically equivalent to the murine parent, OPN-301.

OPN-305 has successfully completed the first part of a Phase II study I to prevent delayed graft function following kidney transplantation and is also being tested in an open-label phase I/II study in second line lower risk myelodysplastic syndrome (a hematological cancer disease).

Opsona is committed in principle to engaging in this collaborative research initiative and intends to provide support in a PhD student on secondment for a period of 3 months and provide them with training regarding protocols involved in screening of a novel TLR2 inhibitor in oral cancer cell culture and animal models.

It is clear from the TRACT proposal that the ESR will receive excellent training from the TRACT programmes combined with the specific technical training that they will receive in microarray anaJysis from the Turkington/Kennedy laboratories in Queen's University; and Molecular biological techniques, Cell culture and Animal training from your laboratory. This training will provide the student with a range of valuable skills that will be applicable to their secondment at Opsona Therapeutics, such as cell culture, animal cancer models and several molecular biological techniques.

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We look forward to collaborating with you in the future and affirm our interest in ESR training through the Horizon 2020 ETN, 'TRACT'.

On behalf of Opsona Therapeutics on this 17th day of Dec 2015

Mary Reilly
VP Pharmaceutical Development & Operations
Opsona Therapeutics.

This proposal version was submitted by **Daniela ZISTERER** on **11/01/2016 17:32:48** Brussels Local Time. Issued by the Participant Portal Submission Service.

LETTER OF COMMITMENT as an Associate Partner in the Marie Curie Innovative Training Network - TRACT

Dear Dr. Daniela Zisterer,

We hereby confirm that ***Exosomics Siena S.p.A (EXS)*** is interested to join the TRACT project as an associated partner and actively collaborate with the coordinator and with other members of the network according to the objectives and schedule provided in the Project Proposal.

To this purpose we agree to provide ESR secondment opportunities, aimed at transferring skills in the field of ***exosome/EV isolation and analysis*** ultimately aimed at development of new generation of complementary diagnostic and research tools in oncology field.

We understand that expenses for travel and subsistence of the students, as well as costs related to particular students activities related to the planned TRACT training programme will be covered by host institutions.

Exosomics is interested in the formation and availability of the fully competent research profiles having proficiency in inter-connected biomedical disciplines and endowed with scientific and management capabilities necessary to comply with the advances in tumor diagnostics and their rapid transfer to the clinics and release on the market.

We are looking forward to the success of this programme.

Yours sincerely,

Antonio Chiesi ***December 15th 2015, Siena***
(CEO, Exosomics Siena S.p.A)

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53100 Siena
ITALY

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ENDPAGE

MARIE SKŁODOWSKA-CURIE ACTIONS

Innovative Training Networks (ITN)
Call: H2020-MSCA-ITN-2016

PART B

"TRACT"
TRAining in **C**ancer Mechanisms & **T**herapeutics

This proposal is to be evaluated as:

[ETN]

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