Meeting 2 minutes for H2020-ITN THERACAT (765497)

Abstract

This document provides the minutes for the Meeting 2 of the THERACAT ITN project, held at University of Edinburgh (EDI) in Edinburgh, UK, on February 3rd, 2020.

Note: All presentations noted in the minutes are uploaded in the project website (intranet).

Issued by

Name	Lorenzo Albertazzi	**Partner**	IBEC	**Date**	17/02/2020

Reviewed by

Name	Asier Unciti-Broceta	**Partner**	EDI	**Date**	20/02/2020
Name	Rosa Miralles	**Partner**	IBEC	**Date**	29/04/2020
Name	All Attendees	**Partner**	All	**Date**	13/05/2020

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Barcelona, 13/05/2020

Lorenzo Albertazzi
Principal Investigator
IBEC

Rosa Miralles
Project Manager
IBEC

Contents

1. Attendees

IBEC: Lorenzo Albertazzi
TUE: Anja Palmans
GRO: Gerard Roelfes
BAS: Thomas Ward
EDI: Asier Unciti-Broceta
TAU: Galia Tiram (representing Ronit Satchi-Fainaro), Roey Amir
TEVA: Bianca Avramovitch
TAG: Marc Robillard
BGX: Chris Allan

Apologies: Rosa Miralles (IBEC) due to a medical leave

ESR Fellows:

Michela Vargiu (GRO)
Shreyas Wagle (TAU)
Krishna Vippala (TEVA)
Anjana Sathyan (TUE)
Stephen Croke (EDI)
Manos Arxontakis (TUE)
Alis Olea (IBEC)
Linlin Deng (TUE)
Africa Galvez (BGX)
Boris Lozhkin (BAS)
Melissa van de L'Isle (EDI)
Maria Vlastara (TAG)
Daniel Rodriguez (TAU)

2. Agenda

Monday 3rd February 2020

Schedule	Activity	Responsible	Attendees
09:00-10:15	Project Management: • General management issues • Training • Next meetings and events • Dissemination and communication actions • Deliverables and milestones alignment • Reporting Questions and doubts	Albertazzi	All
10:15-11:35	Fellows' individual reports, first round (for each ESR: 10 min presentation + 10 min questions): *ESR1, ESR2, ESR3, ESR4.*	All	All
11:35-11:50	Tea and Coffee	-	All
11:50-13:10	Fellows' individual reports, second round (for each ESR: 10 min presentation + 10 min questions): *ESR5, ESR6, ESR7, ESR8.*	All	All
13:10-14:10	Lunch (catering at University of Edinburgh)	-	All
14:10-15:50	Fellows' individual reports, third round (for each ESR: 10 min presentation + 10 min questions): *ESR9, ESR10, ESR11, ESR12, ESR13.*	All	All
15:50-16:15	Questions, doubts, conclusions + Tea and Coffee	Albertazzi	All
16:15-17:30	Assessment Commissions (AC): • AC1 (Tiram, Roelfes, Avramovitch) for students ESR4, ESR5, ESR6, ESR10 • AC2 (Palmans, Unciti-Broceta, Robillard) for students ESR1, ESR2, ESR7, ESR9 • AC3 (Ward, Albertazzi, Allan, Amir) for students ESR3, ESR8, ESR11, ESR12, ESR13	Turns of 3-4 PIs	ESRs
17:30-18:00	ESRs Meeting	ESRs	All
18:00	Closing Remarks	Albertazzi	All
19:00	*Network Dinner at Fazenda.* *https://fazenda.co.uk/edinburgh/*		*All*

3. Minutes

Asier (EDI) gave safekeeping information and Lorenzo (IBEC) apologised on behalf of Rosa (IBEC) for her absence (she had an accident and could not attend the meeting).

3.1 Project Management

GENERAL INFORMATION

IBEC reminded the key relevant information about the project (i.e. title, acronym, duration, project ID, funding body, funding scheme, topic, useful websites and relevant documents).

IBEC explained the new H2020 Funding & Tenders portal to ensure that beneficiaries are able to find the THERACAT project there to manage project.

IBEC explained in more detail the difference between periodic reporting (24 and 48 months reports) and continuous reporting (dynamic report, to be updated every 6 months) and where to find both type of reports within the Funding & Tenders portal. IBEC reviewed the calendar and status of all reports: Progress Report (Month 13, done and approved by the EC), 1st Periodic Report (Month 24) to be submitted by April 30th 2020 (IBEC will send template with instructions to all beneficiaries as soon as the Report is opened at the Portal) and 2nd Periodic Report (Month 48).

TRAINING

IBEC refreshed the THERACAT training programme, reviewing actions performed so far and planning future activities: (1) Local scientific activities, (2) THERACAT Conference, (3) Secondments and (4) Network-wide scientific/complementary skills courses (Training Events).

Local scientific activities

These activities comprise all scientific, methodological and technical aspects relevant for the individual research project of the ESR and in which the host group is expert. All ESRs have received local training activities related to their scientific research and have attended complementary skills training sessions at their host institutions.

THERACAT Conference

THERACAT Conference is to be held in August-September 2021 in Barcelona. IBEC will try to organise it as a satellite of the NanoBio&Med conference co-organised yearly by IBEC (date to be confirmed). THERACAT PIs and ESRs are expected to give some lectures. Some external speakers will also be invited, and it will be open also to non-member students.

Secondments

IBEC reminded "Secondments" concept: it takes places in an institution different form the host institution (between partners with complementary expertise and nature), between 6 and 7 months for each ESR. Secondments are mandatory and must be done in accordance with the original project. Changes in secondments should be avoided, and only in justified cases can be requested to the Project Officer through a Formal Notification (no changes will be allowed until

the official approval of the Project Officer is received). Once secondment dates are agreed between fellow and supervisors (from host and receiving institution), details must be uploaded at the Funding & Tenders Portal by the beneficiary.

IBEC reminded all partners to define the work to be performed and specific dates of the secondment with the receiving institution in advance, if not done yet. Partners suggested to host secondments when the local ESR is not abroad doing his/her personal secondment, in order to increase networking opportunities.

Secondments and Brexit: UK beneficiaries advised that VISA rules to go to UK will not change until the end of 2020. UK secondments from 2021 on will need to follow new VISA rules (not yet agreed between EU and UK).

IBEC presented current calendar of secondments and revised one by one those secondments to be started within the next 12 months, to ensure that fellows and supervisors are all aligned. The only deviation identified was a change in the topic of ESR12-TAG secondment to EDI, with the aim of adapting it to ESR12 current status of research and future secondment of ESR5-EDI to TAG (i.e. pursuing to maximize benefit of the secondment both for the fellow and for the project); this modification will be properly justified in the Midterm Report.

Network-wide scientific/complementary skills courses (Training Events)

The organisation of future Training Events was reviewed (host institution, dates, duration, content). IBEC reminded that institutions hosting the Training Events are responsible to organise the program together with each course lecturer, to find room/spaces to perform the courses, to organise lunch and coffee breaks as well as to suggest potential accommodation for the attendees. IBEC (i.e. Coordinator and Project Manager) is supporting host institutions in the organisation of each event.

On the other hand, each course has a responsible who must define the specific details and content of the course, having on mind the main course topic presented to the EC. Course activities can be outsourced if necessary (related expenses can be charged to B1 cost category).

Next Training Event will be held by TAU in August 2020 and should be attended by all ESRs and PIs involved in the training sessions (TAU, CRUK, TAG). Roey Amir from TAU was given the contact details of Partner Organisation CRUK to organise the Event.

Assessment Commission

IBEC reminded general aspects of the Assessment Commission (AC) already established at the kick-off meeting: AC is composed of 3 members belonging to partners other than the host partner and with different profiles (academic/non-academic), to offer a broader perspective to the training and research carried out by the ESR; ACs meet with the ESRs coinciding with Network Meetings 1, 2 and 3; in-between these meetings (i.e. 6 months after the meeting), Assessment is performed on-line (ESRs have to send a short report describing the training received and research performed using a template will be provided by IBEC, and AC members assess them virtually).

IBEC explained the organisation of the AC evaluation for the afternoon session (about 15 minutes for each ESR, template with questions provided by IBEC), and reminded the composition of each AC:

- Assessment Commission 1 (TAU-b, GRO, TEVA): ESR4, ESR5, ESR6, ESR10.
- Assessment Commission 2 (TUE, EDI, TAG): ESR1, ESR2, ESR7, ESR9.
- Assessment Commission 3 (BAS, IBEC, BGX, TAU-a): ESR3*, ESR8, ESR11, ESR12, ESR13. **Roey Amir (TAU-a) will not be in the AC of ESR3 due to conflict of interest (he is his academic supervisor)*

AC members are reminded to give some feedback to the ESRs also based on their presentations during the Meeting and progress made since the last virtual Assessment (Month 18).

NEXT MEETINGS AND EVENTS

IBEC reviewed the calendar and attendees of all pending THERACAT meetings and events: 2 Training Events (Month 30, Month 36), 2 Meetings (Month 36, Month 48) and THERACAT Conference (Month 42).

DISSEMINATION AND COMMUNICATION ACTIONS

IBEC reminded differences between dissemination (i.e. scientific publications, conferences, etc.) and communication (i.e. THERACAT webpage, social media, blogs, videos, general press articles, science festivals, etc.).

Publications must follow the open access rule either gold way (extra costs that can be charged to B1 cost category) or green way (i.e. using repositories).

IBEC revised all dissemination and communication activities to be performed; regarding THERACAT video (D8.4), some ESRs (ESR4, ESR6, ESR7 and ESR13) will be involved on its preparation in collaboration with the ICMS/TUE animation studio; general press articles will need to be prepared (Month 30 and 48), IBEC asked for involvement of supervisors and/or ESRs; IBEC encouraged ESRs to participate in communication activities through public events (e.g. European Researchers' Night).

IBEC asked the consortium to be always informed about any dissemination and communication activity performed to upload it in the project website and include it in reports and deliverables. Before the meeting, IBEC had sent a template regarding dissemination and communication actions to be filled in by each beneficiary (in the meeting IBEC reminded pending contributions to those beneficiaries that had not provided any feedback yet).

IBEC reminded how beneficiaries must acknowledge the project in publications and presentations: *This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No. 765497 (THERACAT)* – or equivalent structure. Logos for presentation are already available in the THERACAT intranet.

DELIVERABLES AND MILESTONES ALIGNMENT

IBEC went through the project planning and all the deliverables and milestones for the next 12 months to make sure that timescales were sensible and aligned. IBEC always informs deliverable's/milestone's leader 2 months in advance of its submission date to better plan its preparation.

- Deliverables:
  - Deliverables already submitted to the EC (most of them are still under revision by the EC): D2.1, D2.2, D2.3, D8.1, D7.1, D1.1, D1.2, D1.3, D2.4, D2.5, D7.2, D7.3, D8.2, D2.6, D3.1, D4.1, D5.1, D6.1, D7.4, D7.5 and D6.2.
  - Deliverables requiring imminent submission, Month 24 (IBEC is preparing a first draft): D2.7, D7.6, D7.7, D7.8, D8.3, D8.4.
    IBEC reminded fellows to update their PCDP (D7.8) together with their supervisors, based also on the feedback received by the AC during the meeting.
  - Deliverables to be submitted Month 28 - 36: D4.2, D3.2, D5.2, D7.10, D8.5, D7.9, D5.3, D8.6, D2.8, D7.12, D7.13, D6.3, D7.11.
- Milestones:
  - Milestones already reached: MS1, MS2, MS3, MS4, MS5, MS6, MS7, MS8, MS9, MS11, MS12, MS13.
    MS10 still on-going, delay will be informed and justified in the Midterm Report.
  - On-going milestones to be achieved by end of Month 24: MS14, MS15, MS16.
  - Milestones to be achieved Month 28 – 36: MS17, MS18, MS19, MS20.

FINANCIAL REPORTING INFORMATION

IBEC explained the connection between Researcher Declaration (RD) data uploaded by each beneficiary at the Funding & Tenders Portal with the corresponding EC payments once periodic report is accepted. All beneficiaries confirmed information uploaded regarding RD is correct (screenshot of the RD at the Portal was showed).

IBEC reminded what to do in case of a change in the employment contract in terms of updating the RD, situations related to paternity/maternity or sick leaves (IBEC should be contacted before).

IBEC reminded the information/records that all beneficiaries need to keep proving the number of units declared (evidence of open, transparent recruitment, evidence of the eligibility of the fellow, employment contract, etc.). Such records must be kept for 5 years after the final payment.

3.2 Fellows' individuals reports

ESRs presented the work performed so far (10 minutes presentation + 10 minutes questions/discussion). *Presentations for further details are uploaded on the THERACAT intranet.*

- **ESR1 (Michela).** She gave a background of the project and catalyst-based prodrug activation. N4Py was the ligand first used to coordinate metals and perform catalytic activations. Palladium and ruthenium based catalysts were tested. Ru complexes were successfully made and probe deprotection (bisAllocRho) tested. Uncaging did not work. Two different new projects were proposed. One was based on the reduction of N3 to NH2 to trigger drug release. The other was based on the generation of a new ligand: N5Py.
- **ESR2 (Shreyas).** He explained the design of amphiphilic molecules labelled with metal ligands to generate micelles that can be loaded with Pd. The protocol was described and the test results. Substrate was consumed during the reaction with Pd loaded micelles, regardless the presence or not of ligand. The stability of the micelles is studied with a FRET system. He explained that he was interviewed in his home town and spoke about THERACAT.
  Discussions about the use of micelles was followed by the THERACAT members.
- **ESR3 (Krishna).** He explained his project, which is based on the preparation of micelles to encapsulate drugs. Different polymeric structures containing "cleavable" tumour-targeting peptides will be made and tested in TEVA.
  The consortium discussed the use of targeted ligands to deliver to tumours. P-selectin was recommended as a good tumour-associated antigen to be targeted.
- **ESR4 (Anjana).** SCPNs for bio-orthogonal catalysis. She presented the technology and the design of the catalysts (Pd). 10 nm NPs are formed and Pd complexation. NPs showed good catalytic activity in water and PBS but not in DMEM. Encapsulated hydrophobic palladium catalyst works well in DMEM.
  A discussion was initiated by Tom, Gerard, Asier and Lorenzo about issues of intracellular metals inducing reactive oxygen species that would be the actual responsible of probe / prodrug activation. Then, the PIs discussed the problem of testing different probes and prodrugs. It was decided to make a list of all the probes used to test the catalytic properties of the catalysts.
- **ESR5 (Stephen).** He works on targeting cancer making PROTACs in a locally controlled fashion. He worked in the synthesis of a dasatinib-thalidomide construct containing a triazole in the spacer to demonstrate protein degradation. The compound led to degradation of ABL but not SRC. Same strategy was used to make a second PROTAC with a selective SRC inhibitor. Training in organic synthesis and cell culture assays.
- **ESR6 (Manos).** Use of microscopy to study SCPNs. The polarity of the pocket using solvatochromic dyes. Using super resolution microscopy and fluorimetry. Spectrally resolved single molecule microscopy and wavelength to study SCPNs showed different spectral shifts (20 nm), indication that they have different sizes and then different hydrophobic pockets, which may affect catalysis. Wide range of training and attended conference in Veldhoven.
- **ESR7 (Alis).** She explained the aim of looking into the distribution and imaging of different catalysts to understand their capacity to reach the tumour. She explained the methods she is employing, including microfluidics, FRAP and single particle tracking. Model molecule was dextran-FITC with different sizes. Smallest molecules could cross the gels easily but the

largest got stuck in the gels (Biogelx) or collagen. Side project on ratiometric imaging with TAU was also described. She explained technical trainings and dissemination.

- **ESR8 (Linlin).** She explained the concept of developing SCPNs to activate prodrugs. She has studied the stability of the system in biological media. If the NPs unfold, modified Nile Red dyes (solvatochromic dye) will change its physical properties. They studied covalent and non-covalent strategies. NPs show similar fluorescence properties in water, buffer or DMEM. In the presence of serum remains inconclusive, although it seems that serum have influence in the NPs stability.
- **ESR9 (Africa).** She explained the 3D in vitro cancer model she is working on. She is working on synthetic hydrogels non-functionalised or functionalised with RGD. She is working with MCF7 and MDA-MB-231 cells, seeding them on the gels. She will continue with 3D when the 2D models are optimised. She was interviewed and video uploaded in her company's website and will be involved in CRUK 10K run event.
- **ESR10 (Boris)**. He described the goal of using metathesis catalysts to activate prodrugs. The catalysts will be bound to human carbonic anhydrase (hCA) IX by an arylsulphonamide (known binders of this enzyme). Arylsulphonamide tagged Grubbs Ru catalysts were made and also deallylation cofactors. Prodrugs strategies were also described. He received various trainings in Basel.
- **ESR11 (Melissa).** She described the background and goal of the project: to obtain devices that allows performance of local bioorthogonal reactions. Copper ligands that can been coupled to resins to capture Cu(I) and performed click reactions. Project 2 is based on the generation of Pd or Au NPs and entrap them inside dialysis bags. Preliminary results showed that probe can penetrate the bags and get activated. She has been involved in LEAP, to promote university career in high schools from areas with low university registration rates.
- **ESR12 (Maria).** She explained the background of the click-to-release approach. Antibodies tagged with radioactive imaging metals that stay too long in blood. They will be connected to the Ab with TCO and cleaved by tetrazines after the scanning has been done. She explained the current stage of the synthetic part of the project and dissemination update.
- **ESR13 (Daniel).** Triple negative BRCA1/2 mutated breast cancer possess synthetic lethality with PARP inhibitors. EMT-6 cells were used as disease model. Talazoparib is one of the most potent PARPi but increases expression of PDL1. Combination of PDL1 inhibitor and talazoparib in the same micelles showed good activity. Micelles of different sizes were screened in spheroids. Training on nanoscience and scientific writing and FACS.

3.3 Assessment Commissions

All THERACAT ESRs were interviewed by the corresponding Assessment Commission (AC, composition previously detailed in page 7) using a template prepared by IBEC with some questions to evaluate the evolution of the individual Research Project, main obstacles and contingency plans, implementation of PhD studies at university, alignment of local/THERACAT training with their research and interests, and future perspectives.

More details will be provided in the corresponding deliverable D7.7.

3.4 ESRs Meeting

ESR2 (Shreyas Wagle) keeps representing the ESRs. ESRs gave some feedback to the THERACAT Supervisory Board regarding their experience as PhD students in the framework of the project. They are in general very satisfied of the training received and secondments planned, but some of them are afraid that 3 years may not be enough to finish and defend the thesis, especially considering that they will spend some months in laboratories abroad (secondments).