Kick-off meeting minutes for H2020-ITN THERACAT (765497)

Abstract

This document provides the minutes for the Kick-Off consortium meeting for the THERACAT Marie Curie project, held at IBEC in Barcelona on 31st May 2018.

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

Issued by

Name	Javier Adrián	**Partner**	IBEC	**Date**	6th June 2018

Reviewed by

Name	Lorenzo Albertazzi	**Partner**	IBEC	**Date**	9th June 2018
Name	All Attendees	**Partner**	All	**Date**	15th June 2018

Document Control

Issue #	Date	Changed Pages	Cause of Change	Implemented by
---	---	---	---	---

Barcelona, 15/06/2018

Lorenzo Albertazzi
Principal Investigator
IBEC

Javier Adrián
Project Manager
IBEC

Contents

1. Attendees

IBEC: Lorenzo Albertazzi, Silvia Pujals, Javier Adrián.
TU/e: Anja Palmans.
GRO: Gerard Roelfes.
BAS: Tom Ward.
EDI: Asier Unciti-Broceta.
TAU: Ronit Satchi-Fainaro
TEVA: Bianca Avramovitch
TAG: Marc Robillard.
BGX: Elia Lopez.

2. Agenda

Thursday 31st May

	Consortium Management	
10:00-10:30	Tea and Coffee.	
10:30-10:45	Roundtable introductions.	All
10:45-12:45	Roles and Responsibilities: • Co-ordinator (10 min): IBEC. • Beneficiaries (10 min each): TUE, GRO, BAS, EDI, TAU, TEVA, TAG, BGX. • Partner organisations (5 min each): tbc. Questions and doubts.	All
12:45-13:30	Lunch.	
13:30-15:00	Project Management: • General aspects. • Boards – Meetings – Web. • Recruitment. • Training Courses – Skill Modules - Secondments. Questions and doubts.	IBEC (All)
15:00-15:15	Tea and Coffee.	
15:15-18:00	Project Management: • Dissemination and communication actions. • Milestones alignment and deliverables. • Reporting and Financial information. Questions and doubts.	IBEC (All)
18:00	AOB and Closing Remarks.	IBEC
20:00	Dinner*	

**Some of the attendees (Albertazzi, Palmans, Unciti-Broceta, Avramovitch, Robillard) came to the dinner (FARGA BEETHOVEN, Beethoven 11, 08021 Barcelona).*

3. Minutes

3.1 Introductions & Roles and Responsibilities

IBEC explained the meeting agenda.

All those present introduced themselves to the rest of the consortium team.

IBEC presented the spirit of the project (overview of the research part including work packages, preliminary results) but putting also big emphasis on the relevance of the training part to be implemented within the network.

IBEC pointed out that each Early Stage Researchers (ESR) recruited by each beneficiary will be the one responsible to present their research advances in future meetings (not the supervisor).

Beneficiaries presented their institution, the research group (focusing on those aspects related to the proposal) and their role within the Network (i.e. ESRs, deliverables, training, secondments, etc.). Main highlights of the presentations:

- IBEC presentation:
  - Main aim to understand how nanoparticles interact with biological environment using optical microscopy.
  - A lot of work is going on in instrumentation, labelling, dyes to at the end do imaging in vivo.
  - We take advantage of two colour imaging to study interactions.
  - Design and synthesis on materials (microscopy is the guide).
  - ESRs related to microscopy (ESR6: study of catalytic performance; ESR7: image cellular environment and ex-vivo).

- TU/e presentation:
  - Laboratory of macromolecular and organic chemistry.
  - Now working with amphiphilic catalysts in water.
  - Expertise: folding polymers with covalent bonds, reversible covalent bonds, non-covalent bond (use it as catalyst).
  - Working in the synthesis of different catalytic systems (for the moment two slow for the nanomedicine purpose). Comment from EDI: activation through flavin.
    - Length around 5 nm (they can be larger, around 20 nm. Relevant for tumour “accumulation”).
  - They can bring to the network: synthesis skills (small molecules, complex polymer stuff). Good collaboration with IBEC (know about folding and unfolding).
  - How to bring particles within cells, and improve long-term stability of catalyst and find new generation/complex catalyst (ESR4 and ESR8).

- GRO presentation:
  - Interface chemistry biology (main expertise catalyst).
  - Topics: design of (artificial enzymes, bio-orthogonal catalysts and catalytic chemistry in living cells).
  - Experience (ongoing) on transformation 1) diels-alder on dehydroalanine 2) photo-redox catalyst. To be proved on living cells (bacterial).
  - IBEC ask: where we want to catalyse (inside? Outside?). We’ll think about it.
  - ESR1: photo redox catalyst to be applied in living cells.

- X-Ray with synchrotron (current studies) – follow the metals (to avoid fluorophores when tracking "treatments"). Examples: Zn inside the nucleus, Fe mitochondria.

- BAS presentation:
  - Our approach:
    - Use bio orthogonal chemistry, accumulating metal catalyst on the surface of cancer cells.
    - Human Carbonic Anhydrase (HCA) IX overexpressed on the surface of various cancer cells.
    - Arylsulfonamides are high-affinity inhibitors for hCA IX.
    - Use hCA IX to localize and accumulate a metal catalyst on cancer cell to site-specifically uncage the drug.
  - They have proven to "accumulate" in side E. coli cells and mammalian cells.
  - hCA as host protein.
  - ESR10: Involved in Task 5.1, 5.3, 6.3. Secondments critical in TEVA and EDI (looking forward it).
  - RCM to produce a drug (EDI comments to include functional group in para position.
  - Contingency plan: rely on the CpRu-catalyzed de -allylation of doxorubicin.
  - Involved in Training Event 1 (we'll have to plan it within the following weeks).

- EDI presentation:
  - Laboratory is close to the "hospital" (for clinical trials).
  - They have RAMAN imaging for in vivo experiment.
  - Expertise: chemistry prodrugs, nanomaterials analysis, phenotypic assays, zebrafish models, glioma models, prostate cancer models, surgery glioma.
  - Concept proposed: inactive drug – catalyst (placing and implant, with minor surgery, where is the tumour) – active drug. Only activated where the Pd is accumulated.
  - Clinical challenge within the ITN project: In vivo LOCAL Activation of PROBE. Working in the "validation of the catalyst insertion".
  - Pd implantation is not a problem (working in Pd-Activated Prodrugs). Effort should be done in developing devices (nanoscale) to get to the places.
  - Beyond Pd (gold!!!).
  - ESR5 (prodrugs) / ESR11 (Pd implants).
  - Bioorthogonal bioresponsive a RSC Symposium (around june 2019).

- TAU:
  - Also representing Roey Amir (b TAU participant).
  - Presentation of CV + multidisciplinary laboratory: animal model, polymeric nanocarriers, supramolecular structure, targeting active entity, turn-on theranostic probes).
  - Mechanisms of molecular and cellular tumor-host interactions underlying tumor dormancy. How: model, omics (genomics-proteomics), function, theranostic nanomedicines, preclinical studies. Two years ago, they incorporated 2 surgery guys within the lab doing the inverse procedure.
  - Another aim: turn-on nanoprobes illuminate tumors during image-guided surgery leading to prolonged survival.
  - Example of mouse models of melanoma brain metastases: Ret-mCherry model, mCherry-5B1 model, patient-derived xenografts.

  - They use 3D – printed tumors for ex-vivo simulations of research, surgery and treatment (clinical specimen, MRI/CT, image analysis, 3D printer, Tissue culture). Simulating research surgery treatment. ·D-Bioplotter – envisiontec.
  - Tumor spheroids formation.
  - Tools: confocal microscopes, IncuCyte (migration, proliferation studies), LCM, whole animal imaging (SpectrumCT, Sequoia, Cell Vizio, Imager Biospace, among others), MRI. BLAVATNIK CENTER for Drug Discovery (BCDD).

  - Roey J. Amir (school of chemistry).
  - Goals for ESR2:
    - Develop synthetic methodology for amphiphilic polymers with a ligand.
    - Metal complexation and self-assembly of micelles.
    - Demonstrating catalytic capability and its optimization.
  - Possibility to tune amphiphilicity with high molecular precision.
  - Labeled polymeric assemblies designed to self-report their activation.
  - Lab:
    - Polymer synthesis and characterization: chemistry, Schlenk lines, preparative LC, GPC HPLC, microwave reactor.
    - Caracterizing self-assembly: DLS, TEM, Fluorimeter, Automated sample preparation.
    - Others: NMR, MALDI-TOF, TEM.

- TEVA presentation:
  - Micro spectroscopy and imaging: new products designs are being developed based on the new available technologies, e.g. OROS.
  - Raman imaging (product): nasal spray mapping by micro Raman → in vitro characterization of the API specific particle size distribution (PSD) and polymorphism in the nasal spray drug product. CHALLENGE: control the product efficacy, quality and IP through its particle size distribution.
  - IBEC: Raman technique can be a very useful tool for catalyst experiments.
  - Goals: Deliver platform for researchers, enrich consortium with practical knowledge.
  - When developing drug products (take care of):
    - At the molecular chemistry level (impurities), at the physical structure level (polymorphism), at the powders level characteristics (particle size & shape), at the formulative level for optimal bioavailability (minimum dosage for desired efficacy), at the final drug product level (packaging and stability).
  - IMMS: Ion Mobility Mass Spectroscopy (TAU: very potential tool to be used when working with tissues (their expertise is on materials right now but working on it)).

- TAG presentation:
  - Concept (click release): On-target actuation of tagged antibodies.
  - Now very focused on drug realise (antibody-drug conjugates – ADC). Currently systems are based on intracellular toxin release by enzymes or thiols.
  - Click-to-image-release (before/after treatment).
  - Plans with THERACAT:
    - Click: image catalyst in vivo.
    - Unclick: activate catalyst / release the catalyst as carrier.
    - Neither click or unclick: imaging probe (substrates for the catalysts).
  - EDI: Triacines less reactive than tetracines (yes!).

- BGX presentation:
  - Main propertie peptide hydrogels: 3D, 99% water, nanoscale matrix structure, short peptides self-assemble into fibers, suitable surface for cell adhesion, animal-free.
  - EDI: used in vivo? YES in animals (not yet in humans).
  - Great property: mechanically tuneable – A Gel for Every cell.
  - Can be tuned mechanically and chemically (this approach in house).
  - Product Range: but can do customized products.
  - Participation in the THERACAT: peptide hydrogels used as a vehicle and/or model.
  - Possibility to use them with 3D printing (collaboration with TAU).
  - IBEC: Are they self-healing? No (we'll check).

3.2 Project Management

GENERAL ASPECTS

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

BOARDS

Constitution of the Supervisory Board and definition of the responsibilities:

IBEC: Dr. Albertazzi (coordinator).
TU/e: Dr. Palmans.
GRO: Dr. Roelfes.
BAS: Dr. Ward.
EDI: Dr. Unciti-Broceta.
TAU: Dr. Satchi-Fainaro.
TEVA: Dr. Avramovitch.
TAG: Dr. Robillard.
BGX: Dr. Goldie.

This board will meet once a year coinciding with the Network meetings.

The Supervisory Board agreed the Training and Recruitment Committee to be a consultant Board only in case of conflicts. TEVA proposes to include a non-academic partner within the Training Committee (everybody agreed to include TEVA). The consortium agreed the Recruitment Plan elaborated by IBEC (including information about eligibility criteria, recruitment procedure, instructions to select candidates, templates for interview assessment, etc.). IBEC pointed out the importance to keep evidences of the recruitment procedure for future audits.

Fellows Committee will be formed in the next Network Meeting (month 12) when all ESRs are recruited.

MEETINGS, WEBSITE and OTHER ISSUES

IBEC explained the Network Meetings format (1.5 – 2 days):

- Meeting 2 (month 12) host by BAS. Supervisory Board agreed think the dates for meeting in case has more sense to delay it a little bit or modify the order with EDI (considering potential congresses to be launched on 2019).
- Meeting 3 (month 24) host by EDI (maybe it will be changed by BAS, see previous comment).
- Meeting 4 (month 36) host by IBEC.
- Meeting 5 (month 48) host by IBEC.
  IBEC will prepare all meeting minutes.

IBEC showed THERACAT web structure (final version of general and intranet approaches will be ready along June). We propose to include more figures and pictures from the beneficiaries to make the web more attractive. We will put effort in including all relevant events (congresses, etc.) within the project website.

IBEC explained that most of the information included in the MGT presentation comes from a coordinator's info day hold last December 12th 2016. Important: contact with the Project Officer must be done through the coordinator.

RECRUITMENT

IBEC explained the Eligibility Criteria (i.e. mobility rule, definition of ESR, date of recruitment, etc.), the Recruitment Procedure (i.e. publish vacancies in EURAXESS jobs portal, gender equality, avoid conflict of interest, European Charter and Code of Conduct, create a pool of candidates by sharing candidates not selected) and Working Conditions (i.e. employment contract, rights and obligations, secondments, don't's, etc.).

IBEC explained the Researcher Declaration action: to be done by each beneficiary within the 20 days of start date of recruitment using the participant portal. It contains personal data of the candidate.

IBEC explained the recruitment costs. Funding mechanism based on units costs (1 unit = 1 month of eligible ESR).

- Living allowance: Monthly salary for the fellow before any deductions. Monthly rate (3110€) is affected by country correction coefficient. We cannot pay less to the candidates (we can pay more). Progressive salary and/or 13-14 month pay regime is accepted.
- Mobility allowance: For all recruited fellows (600€ month) to cover private costs not professional costs (e.g. secondments). This cost is usually taxed but depends on national taxation rules.
- Family allowance: For recruitment fellows who have family at the time of recruitment (i.e. being officially married equivalent (or equivalent) and/or having children). Evidences are needed. Family allowance units will be returned to EC in case fellows don't fulfill this requirement.

IBEC proposed that each beneficiary has to explain the salary conditions at the end of the recruitment phase, in particular defining the taxes applied following the national rules as well as the possible differences (due to coefficient country factor) with other ESRs within the Network. Doing this at the very early stage will avoid future problems or misunderstood.

TRAINING

IBEC explained the different training actions:

- Local Scientific Training Activities: Provided by host institutions along the project.
- Secondments: takes places in an institution different form the host one, from 6 to 7 months for each ESR. Secondments are mandatory and must be done in concordance to the original project (some flexibility is agreed if it improves project performance. Big changes will be communicated to the Project Officer). All secondments are reviewed.
- Training Events: network-wide scientific/complementary skills courses. The Training Committee will define in advance and more in detail the course content, since courses are not detailed in the proposal. Course duration 1-2 days, Training Event duration 4-5 days. Beneficiaries can subcontract the courses in case they are not able to impart the course.

- Training Event 1 (month 12) host by BAS. Coincide with the Network Meeting 2.
- Training Event 2 (month 18) host by TUE.
- Training Event 3 (month 24) host by EDI. Coincide with the Network Meeting 3.
- Training Event 4 (month 30) host by TAU.
- Training Event 5 (month 36) host by IBEC. Coincide with the Network Meeting 4.

IBEC explained the network objective regarding the PhD: ESRs of the Network end up by defending a PhD thesis and being awarded a Doctoral Degree. All beneficiaries pointed out the difficulties to finish a PhD in 3 years. BGX explains difficulties to finish the project having a ESR with a PhD (companies will have more flexibility in this respect).

Assessment Commission was established. It is composed by 3 members belonging to partners other than the host partner and with different expertise to offer a broader perspective to the training and research carried by the ESR. It will meet in the Network Meetings.

- Assessment Commission 1 (TAU, GRO, TEVA): ESR4, ESR5, ESR7, ESR10.
- Assessment Commission 2 (TUE, EDI, TAG): ESR1, ESR2, ESR6, ESR9.
- Assessment Commission 3 (BAS, IBEC, BGX) ESR3, ESR8, ESR11, ESR12, ESR13.

DISSEMINATION AND COMMUNICATION

IBEC explained differences between dissemination (i.e. scientific publications, conferences, participation in other networks, final network meeting, webpage, newsletter (4), applications notes (3), etc.) and communication (i.e. webpage, social media, blogs, videos, general press articles, science festivals, local media, 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).

Before dissemination and communication, research results will be evaluated by the Supervisory Board to determine its possible protectability (consortium agreed will agree on the Consortium Agreement to send the publications or in advance before it is published to be reviewed.

IBEC ask the consortium to be informed about any dissemination and communication activities to be uploaded on the project website and on the participant portal.

FINANCIAL AND REPORTING INFORMATION

IBEC explained costs for institutions:

- B1 research, training and network costs (1800€ per unit cost): consumables, courses, conferences, secondments, visa, tuition fees, etc.
- B2 management and overheads: IBEC reminded the previous agreement where overheads will be calculated according to the 10% of direct costs while the management will be redistributed (coordinator retains the largest share to address the management activities). Distribution included in the Consortium Agreement (under preparation).

IBEC explained the possibility to transfer institutional costs to costs for researchers for example to increase candidate's salary or for example using overheads costs to pay part of the 4th year contract when necessary (host institution must be agreed).

IBEC repeated that records of recruitment of the fellows and the fulfilment of eligibility criteria must be kept for 5 years after last payment of the project (see examples in the presentation). Timesheets are not an obligation for fellows but can be used if in line with local practices.

Parental/maternal and sick leaves must be informed to the coordinator to support you with different subsequent actions (e.g. update researcher's declaration, adapt salary conditions, etc.). IBEC proposed to evaluate case by case when it happen.

IBEC informed how partner organisations are paid (e.g. travel costs and training activities) and the potential costs related to the advisory board if it's finally formed (IBEC, EDI, and BAS will "refresh" the contacts to involve again Prof. David Cameron (Director of Cancer Services in NHS Lothian and Clinical Cancer Research Champion for Scotland), Dr. John Dixon (Director of JD Consulting and former VP of Drug Discovery in AstraZeneca Charnwood) and Prof. Wolfgang Meier (Full Professor of Chemistry at Basel University) within the project). The coordinator will pay all these costs using the management category costs. Minor tasks (e.g. courses) can be subcontracted following internal institutional and national practices.

IBEC informed about the project payments:

- Pre-financing 80%: IBEC has already transferred the budget received (75%) proportional to budget agreed in the consortium agreement. 5% was kept by the Commission as guarantee fund.
- Interim payment (up to 10%): based on unit claimed in the first periodic report.
- Payment of balance: based on the final accepted costs.

Financial statements are calculated in EURO but beneficiaries using another currency must convert the costs into euro at the average of the daily exchange rated published in the Official Journal of the European Union, calculated over the corresponding reporting period.

IBEC explained the reporting periods:

- Progress report (month 13): technical.
- 1st reporting period (month 24): technical and financial.
- 2nd reporting period and final report (month 48): technical and financial.
  Financial statements are individual and submitted to the coordinator before being submitted to the Commission.
  CFS are not required for ITN projects but financial distribution report might be requested in some specific cases (audit, recovery, etc.).
- Continuous reporting to the participant portal: deliverables, dissemination/communication activities, publications, patents, publishable summary, milestones, risks, questionnaires (gender, innovation, etc.).

IBEC explained how the beneficiaries must acknowledge the project in publications and presentations: This work has received funding from the **European Union's Horizon2020** research and innovation programme under the Marie Sklodowska-Curie **grant agreement No. 765497 (THERACAT)** – or equivalent structure. Logos for presentation will be uploaded on the THERACAT intranet.

IBEC showed the importance to avoid amendments along the project. Any trouble, change, etc. must be consulted with the coordinator to try to find a solution before contacting the Project Officer.

IBEC will monitor ethical issues along the project. The Commission created a specific work package and deliverables for all H2020 projects. In case your ethical issues change, please inform the coordinator.

IBEC introduced the Responsible Research and Innovation (RRI) concept requested by H2020. The Network will fulfil all the requirements (i.e. public engagement, open access, gender, ethics, science education).

MILESTONES ALIGNMENT AND DELIVERABLES

All beneficiaries went through the project planning and the short-term (i.e. within the first 12 months) deliverables to make sure the timescales were sensible and aligned. An Excel file will be shared to the consortium to detect potential future issues. If necessary, modifications will be considered.