

Training Event 2 minutes of H2020-ITN THERACAT (765497)

Abstract

This document provides the minutes for the Training Event 2 of the THERACAT ITN project, held at University of Basel in Basel (Switzerland) on September 23rd – 27th 2019.

Note: All presentations noted in the minutes are uploaded in the project website (intranet) with the exception of those that could not be distributed by the speaker due to confidentiality issues.

Issued by

Name	Rosa Miralles	Partner	IBEC	Date	05/12/2019
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Name	Lorenzo Albertazzi	Partner	IBEC	Date	06/12/2019
Name	All Attendees	Partner	All	Date	19/12/2019

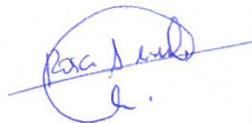
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Barcelona, 20/12/2019



Lorenzo Albertazzi
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1. Attendees

TUE: Anja Palmans

BAS: Thomas Ward

EDI: Asier Unciti-Broceta

TEVA: Bianca Avramovitch

External trainers: Fabrice Gallou (Novartis), Christof Sparr (BAS), Olivier Baudoin (BAS), Andreas Pfaltz (BAS), Konrad Tiefenbacher (BAS), Florian P. Seebeck (BAS), Cornelia Gabriela Palivan (BAS), Michael A. Nash (BAS), Heinz Mueller (Swiss Federal Institute of Intellectual Property)

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)

** Have attended all week. The supervisors have attended the day of their training session.*

2. Agenda

Training Event 2: Chemical Synthesis & Catalysis

Monday 23rd September 2019: Safety in chemical laboratories and research in industry and academia			
Schedule	Activity	Responsible	Attendees
09:00-10:15	Safety in the lab (Part 1)	Palmans	ESRs
10:15-10:30	Break	-	ESRs
10:30-12:00	Safety in the lab (Part 2)	Palmans	ESRs
12:00-13:00	<i>Lunch</i>	-	<i>ESRs</i>
13:00-17:30	Novartis' tour	Gallou (Novartis)	ESRs

Tuesday 24th September 2019: Prodrugs – design principles, synthesis and preliminary evaluation			
Schedule	Activity	Responsible	Attendees
09:00-09:15	Introduction	Unciti-Broceta	ESRs
09:15-10:45	Lecture 1 (Historical overview of prodrugs)	Unciti-Broceta	ESRs
10:45-11:00	Break	-	ESRs
11:00-12:30	Lecture 2 (Bioorthogonal prodrugs 1)	Unciti-Broceta	ESRs
12:30-13:30	<i>Lunch</i>	-	<i>ESRs</i>
13:30-15:00	Lecture 3 (Bioorthogonal prodrugs 2)	Unciti-Broceta	ESRs
15:00-15:30	Break	-	ESRs
15:30-17:00	Lecture 4 (Challenges to progress metal-activated prodrugs into the clinic)	Unciti-Broceta	ESRs

Wednesday 25th September 2019: Catalysts and catalysis – from the synthetic utilization to artificial enzymes

Schedule	Activity	Responsible	Attendees
08:30-08:45	Introduction	Ward	ESRs
08:45-09:45	Reaction- and Stereocontrol by Organocatalytic Activation Strategies	Sparr (BAS)	ESRs
09:45-10:45	Constructing rings by Pd-catalyzed C-H activation	Baudoin (BAS)	ESRs
10:45-11:00	Break	-	ESRs
11:00-12:00	Asymmetric catalysis with chiral metal complexes: general strategies and ligand design	Pfaltz (BAS)	ESRs
12:00-13:00	Catalysis inside the Supramolecular Resorcinarene Capsule	Tiefenbacher (BAS)	ESRs
13:00-14:15	<i>Lunch</i>	-	<i>ESRs</i>
14:15-15:15	Enzyme Catalyzed C-S Bond Forming Reactions	Seebeck (BAS)	ESRs
15:15-16:15	Catalytic reactions in nano-microcompartments: How to build a bio-synthetic lego?	Palivan (BAS)	ESRs
16:15-16:30	Break	-	ESRs
16:30-17:30	Directed evolution of oxidoreductases using single-cell hydrogel capsules	Nash (BAS)	ESRs
17:30-18:30	Artificial Metalloenzymes: Challenges and Opportunities	Ward	ESRs
18:30-18:45	Concluding remarks	Ward	ESRs

Thursday 26th September 2019: How can we do better in bringing new molecules to the market – scaling up, formulations, regulations, procedures and economical aspects

Schedule	Activity	Responsible	Attendees
09:00-10:15	A drug product pathway to the market (Part 1)	Avramovitch	ESRs
10:15-10:30	Break	-	ESRs
10:30-12:00	A drug product pathway to the market (Part 2)	Avramovitch	ESRs
12:00-13:00	Lunch	-	ESRs
13:00-14:15	A drug product pathway to the market (Part 3)	Avramovitch	ESRs
14:15-14:30	Break	-	ESRs
14:30-16:30	A drug product pathway to the market (Part 4 & quiz)	Avramovitch	ESRs
16:30-17:00	Summary of the day, gaps and planning ahead	Avramovitch	ESRs
19:15	Dinner at Aroma , Auf der Lyss 14, 4051 Basel	-	All

Friday 27th September 2019: IP and commercial exploitation

Schedule	Activity	Responsible	Attendees
08:30-10:15	Part 1 (Introduction, objectives of the workshop & overview of day; Basic concepts of intellectual property)	Mueller (IPI)	ESRs
10:15-10:30	Break	-	ESRs
10:30-12:00	Part 2 (Copyright, design, trademarks; Patents, basic concepts)	Mueller (IPI)	ESRs
12:00-13:00	Lunch	-	ESRs
13:00-14:30	Part 3 (Patent rights in biotech / pharma; Understanding the content of a patent (exercise: writing a claim))	Mueller (IPI)	ESRs
14:30-15:00	Break	-	ESRs
15:00-16:30	Part 4 (Patenting strategies; Patent information as knowledge source; Q&A)	Mueller (IPI)	ESRs

3. Minutes

3.1 Safety in chemical laboratories and research in industry and academia

The course has been focused on giving practical tips and real examples for students to avoid accidents in the laboratory and raise their awareness on safety issues (including theory about hazard ratings of chemicals, safety measures in the laboratory, examples of real accidents, etc. and practical exercises).

- Performed by: Anja Palmans (TUE)
- Content:
 - How to prepare before you do an experiment in the lab
 - Illustrative examples of lab accidents and lessons learned
 - What could possibly go wrong in a lab (also for biology oriented people)?

In the afternoon all ESRs have visited the Novartis facilities guided by Dr. Fabrice Gallou from the company.

3.2 Prodrugs – design principles, synthesis and preliminary evaluation

The course has been focused on giving basic concepts about prodrugs and their mode of action, key factors to design prodrugs against cancer, biorthogonal chemistry, metal catalysis (in vitro/in vivo), and practical exercises.

- Performed by: Asier Unciti-Broceta (EDI)
- Content:
 - Historical overview of prodrugs
 - Bioorthogonal prodrugs 1
 - Bioorthogonal prodrugs 2
 - Challenges to progress metal-activated prodrugs into the clinic

3.3 Catalysts and catalysis – from the synthetic utilization to artificial enzymes

The course has given a broad overview about catalysis, thanks to the know-how of the 8 experts invited to give a lecture (all of them from the University of Basel).

Reaction- and Stereocontrol through Organocatalytic Activation Strategies

- Performed by: Sparr (BAS)
- Organocatalytic activation modes, enamine catalysis and chemistry, advances in catalyst design, carbenes as organocatalysts, urea catalysts, stereoselective aldol condensation, catalyst-controlled stereodivergent synthesis, noncanonical polyketide cyclization, acridinium fluorophores

Constructing rings by Pd⁰-catalyzed C-H activation

- Performed by: Baudoin (BAS)
- Current research (Pd-catalyzed C–C bond formation, transition metal-catalyzed C–H bond functionalization, intramolecular organometallic C(sp³)–H activation), ring construction, general reaction mechanism, site-selectivity of the C–H activation step, synthesis of b-lactams, enantioselectivity.

Asymmetric Catalysis with Chiral Metal Complexes: General Strategies and Ligand Design

- Performed by: Andreas Pfaltz (BAS)
- Asymmetric catalysis (early results), chiral ligands, C₂-symmetric semicorrin ligands, phosphinooxazolines ligands, catalytic cycles and mechanistic models.

Catalysis Inside the Supramolecular Resorcinarene Capsule

- Performed by: Konrad Tiefenbacher (BAS)
- Total synthesis vs. biosynthesis, terpene cyclizations, how to mimic an enzyme?, catalytic cycle, where is the reaction taking place?, sesquiterpenes.

Enzyme Catalyzed C-S Bond Forming Reactions

- Performed by: Florian P. Seebeck (BAS)
- Acid/base catalyzed C-S bond formation, metal catalyzed C-S bond formation, metal mediated radical C-S bond formation.

Catalytic Reactions in Nano- Micro-Compartments: How to Build A Bio-Synthetic Lego?

- Performed by: Cornelia Gabriela Palivan (BAS)
- Challenges for today's medicine, hybrid systems, amphiphilic copolymers, bio-synthetic assemblies, catalytic nanocompartments, catalytic nanocompartments in tandem, artificial organelles, artificial organelles with triggered activity.

Directed evolution of oxidoreductases using single-cell hydrogel capsules

- Performed by: Michael A. Nash (BAS)
- Creation of new enzymes, cell-gel encapsulation technology, characterization techniques (confocal microscopy, SEM imaging), methods for isolating/enriching encapsulated cells.

Artificial Metalloenzymes: Challenges and Opportunities

- Performed by: Thomas Ward (BAS)
- Definition of catalysis, homogeneous/heterogeneous/enzymatic catalysis and catalysts, design of catalysts, historical perspective, examples of catalysts used in our daily life, artificial metalloenzymes.

3.4 How can we do better in bringing new molecules to the market – scaling up, formulations, regulations, procedures and economical aspects

The course has been focused on giving an overview of the drug product pathway to the market, including concepts about technological and knowledge impact, drug product development process, generic drugs, safety and efficacy, dosage forms, scaling up and pharmaceutical development, case studies, supply chain and clients, life cycle management, impurities, data integrity, 3D printing, followed by a final practical exercise and quiz.

- Performed by: Bianca Avramovitch (TEVA)
- Contents:
 - Part 1:
 - a. From early medicine to digital inhalers and personalized medicine, from blockbusters to kitchen drugs printing – the technological and knowledge impact.
 - b. What does it mean to develop a drug product? The regulatory and scientific pathway to develop an efficient and safe drug, worth to be marketed.
 - c. Innovative versus generic drugs, toxicological and clinical studies.
 - Part 2:
 - a. Formulative development: processes, excipients, controls, stability programs.
 - b. Manufacturing scale up and optimization.
 - c. Case Studies: reverse engineering, processes optimization
 - Part 3:
 - a. The special story: “Run for a First to file”, the story of a bioequivalence study
 - b. The analytical complexity of an impurity profile
 - c. Integrity of data and people - information technology impact
 - Part 4:
 - a. 3D Printers in Drug Products Manufacturing
 - b. Quiz
 - c. The students voice: what can you do differently, what do you need to elaborate more and when?

3.5 IP and commercial exploitation

The course has been focused on how to make the most out of the ESRs research in terms of IPR with the aim that ESRs gain sufficient understanding of IP rights, know the basic does and don'ts and make use of the patent system for advancing in their research (including real examples of patents, application routes and practical exercises).

- Performed by: Heinz Mueller (Swiss Federal Institute of Intellectual Property)
- Contents:
 - Basic concepts of intellectual property
 - Copyright, design, trademarks
 - Patents, basic concepts
 - Patent rights in biotech/pharma
 - Understanding the content of a patent (exercise: writing a claim)
 - Patenting strategies
 - Patent information as knowledge source
 - Q&A