**ISOTOPICS: Isotopic labeling for drug innovation**

ISOTOPICS is a highly interdisciplinary project which started in January 2016. It is expected to have a profound beneficial impact on drug innovation in Europe by providing innovative isotopic labeling chemistry. This H2020 – Marie Skłodowska Curie Action – Innovative Training Network gathers 5 academic partners and 3 pharmaceutical companies in 5 European countries.

The main objective of the ISOTOPICS project will be to train 15 Early Stage Researchers (ESRs) during 3-year PhD fellowships to meet the need of industry by providing new researchers specialized in labeling chemistry with a dual academic/industrial culture.

Website: www.isotopics-project.eu

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**1st Training Session**

The ISOTOPICS ESRs (13 PhD fellows recruited at that date) met each other for the first time in November 2016 during the 1st Training. They were welcomed at CEA premises (Saclay, France) for a 3-day programme giving an overview of the several radioisotope chemistries investigated by the ISOTOPICS project. They also got some advice and guidelines for the successful achievement of their PhD.

**Day 1**

An external trainer (Ray HORN, ALM Formation) provided the ESRs hints and tips on the implementation of a PhD project and also on public speaking. The trainer tackled several topics and ESRs had to face situational scenarios about:
- General framework of communication for academics
- Two language features: pronunciation and word stress
- Non-verbal communication
- Content (organisation, structure)
- Preparing and managing a presentation.

"Personally, I believe that the introduction course that Mr. HORN gave us on the first day of the ISOTOPICS training was an eye-opening experience that will benefit all of us on a long term perspective. My take-home messages from that day relate mostly to several very interesting aspects such as: networking effectively, time-management (rituals and automation) and last but not least, personal branding and presentation skills.” **ESR8 - Alexandra GAFITESCU (UOXF)**

**Day 2**

The PhD fellows attended a workshop on the Intellectual Property Rights in H2020 projects to focus on dissemination and exploitation issues in a research project funded by the European Commission. Then, they were given information about radioactivity and safety requirements regarding chemical and radiologic hazards in laboratories. They also had the opportunity to visit the Molecular Labeling and Bio-Organic Chemistry unit (CEA Saclay/DRF/IBITECS/SCBM) to learn about the techniques and equipment used for the tritium and carbon-14 handling by CEA teams.

It was followed by 2 taught courses about deuterium/tritium and carbon-14 labeling given by two CEA group leaders, Dr. Gregory PIETERS and Dr. Davide AUDISIO.

At the end of the second day, Prof. Bruno CHAUDRET (CNRS/INSA Toulouse, France) provided to the ESRs an overview of the nanoparticles formation and their use for the isotopic labeling of organic molecules.

"Dr. Davide AUDISIO gave a very interesting overview about the use of Carbon-14 during the history and modern times, underlining possible applications and synthetic routes. Dr. Grégory PIETERS shared the most recent achievements in isotope exchange reactions in his group. These new rapid labeling methods will be a great asset for drug development. The experience in radioactive labeling of the two CEA members led to numerous comments and raised a vigorous discussion among the PhD candidates.” **ESR3 - Antonio DEL VECCHIO (CEA)**

"Prof. Bruno CHAUDRET did not only demonstrate how manifold the world of nanoarchitectures can be, he also put the emphasis on the versatility of the products synthesized in his interdisciplinary team. Young chemists being able to handle the sensitive nanoparticles for catalytic purposes, reveal to be equally indispensable at the nanotechnologies job market.” **ESR1 - Viktor PFEIFER (CEA)**

**Day 3**

There were 2 sessions on the last day of training. The first one explored the development of PET radioligands with an emphasis on carbon-11 labeling reactions. This course was given by Prof. Christer HALLDIN (Director of Karolinska Institute PET Center, Sweden) and Dr. Magnus SCHOU (AstraZeneca, Sweden).

The second session was animated by Prof. Veronique GOUVERNEUR (University of Oxford, UK) who extensively described the fluorine chemistry and Fluorine-18 labeling.

"Prof. Christer HALLDIN and Dr. Magnus SCHOU works are very interesting, with fine and delicate Carbon-11 chemistry. Moreover, their applications to neuro-imaging showed us how radiochemists can actually be near to everyday clinical practices” **ESR2 - Alberto PALAZZOLO (CEA)**

"The “Fluorine-18 labeling” course given by Prof. Véronique GOUVERNEUR provided a clear and thorough understanding of the relevance of fluorine-18 chemistry in the production of radiopharmaceuticals for Positron Emission Tomography (PET) imaging. Moreover, Prof. GOUVERNEUR’s presentation highlighted the different synthetic chemical strategies for ¹⁸F-labeling, in particular the late-stage fluorination strategy, of utmost importance in the development of PET radiotracers with potentially high specific activity.” **ESR12 – Agostinho LEMOS (ULG)**
**1st ISOTOPICS Meeting**

All the consortium members, the recruited ESRs, the Advisory Board and the management team gathered last November 2016 in Paris. This meeting helped to settle the scientific objectives of each PhD fellowship and strengthen the collaboration between academic/non-academic supervisors and co-supervisors and share convivial moments.

Almost all ESRs were recruited only few months before the meeting. Therefore, during these 2-day symposium, they mainly presented their scientific background and the objectives of their PhD project.

“I was really curious to hear about the projects of all the other ESRs, and I found their presentations very inspiring. At first sight the chemistry we are developing might seem different, but the objective we are pursuing is the same and this makes me feeling of being part of a big team. Some of our projects are already connected, as it was evident from the presentations themselves, and I hope this networking would strengthen in the future, because this is a key aspect in science development.”  
ESR6 - Anna Chiara VICINI (UOXF)

“Despite the recent start, my co-ESRs were able to explain their projects in high accuracy and all have excellent presentation skills. We got valuable ideas for our own work as well. During the meeting and social events we also practiced networking skills as we met the other participants of the project.”  
ESR9 - Kaisa HORKKA (KI)

An invited speaker, Prof. Tobias RITTER (Max Planck Institute, Germany), gave an outstanding conference about “Late-Stage Fluorination for PET Imaging”. Prof. RITTER frequently involved the ESRs during the conference by questioning them. This first class research presentation was inspirational for the fellows.

“We were pleased to have a conference of such as Tobias RITTER, to give us an introduction on late stage fluorination. His conference was really interesting, complementary to the course of Véronique GOVERNEUR and interactive with a lot of questions to make us think about Fluorine-18 problematics.”  
ESR13 - Laura TRUMP (UCB)

“The advisory board gave us many very useful advices and not only about chemistry. Of course we are lucky to participate to this PhD program and we enjoy to do chemistry everyday. But they also told us that we have to be aware of discussion with people that we will meet during this 3 next years. At work with our supervisor and other colleagues but also during the meetings, the trainings and in each new opportunity that we have to seize because ISOTOPICS is not only a chemistry adventure, it is also a human adventure!”  
ESR15 - Mégane VALERO (Sanofi)

“The Advisory Board provided us with helpful advice on how we should tackle our PhD. I have found them really useful so far and I am convinced this and future Meetings would help me to successfully guide me through my research project.”  
ESR7 - Mateusz IMIOLEK (UOXF)

To conclude the meeting, the members of the Advisory Board provided helpful advices and recommendations to the ESRs for the implementation of their PhD project.

“This meeting allowed all ISOTOPICS members to have a quick integration and better understanding of the project. It helped us to better identify and understand all project specifications thanks to the precious advices from the supervisors and the active participation of the trainers”  
ESR11 - Donia BOUZOUITA (CNRS/INSA Toulouse)
Interview of the ESRs

ESR 14 – Malvika SARDANA (AstraZeneca), group of Dr. Charles ELMORE

Could you tell us about your background?

I am a synthetic organic chemist from the Netherlands. I received both my BSc in Pharmaceutical Sciences and MSc in Medicinal Chemistry from VU University Amsterdam. During my academic career I had the opportunity to do an internship in both the academic setting as well as an industry within Medicinal Chemistry. My internship at the VU University was a project supervised by Dr Maikel Wijtmans, targeting G-Protein Coupled Receptors, with small molecules. At Boehringer Ingelheim in Vienna I gained more insight on an oncology related target by synthesizing small horsfiline-like molecules.

After graduating from VU University Amsterdam, I worked at a contract research organization, Mercachem in Nijmegen. Here I was an integral part of the library synthesis team within the department of Parallel Chemistry.

What is your PhD project about?

The PhD project has been divided in four aims. First aim is to develop novel methods to apply carbonylation with unlabelled CO, $^{13}$CO and $^{14}$CO. Followed by streamlining this method with $^{11}$CO, and utilizing this method on useful PET ligands. Finally, developing a novel method for the application of $^{18}$F in PET ligands.

According to you, what are the strengths of the ISOTOPICS project?

The strength of the ISOTOPICS projects is the opportunity to work in an industrial setting along with increasing my personal knowledge in chemistry, radiochemistry and medicinal chemistry.

ESR 4 – Gianluca DESTRO (CEA), group of Dr. Frederic TARAN and Dr. Davide AUDISIO

Could you tell us about your background?

Hi everybody, I’m Gianluca and I came from Italy, more precisely from Torino. In this city I obtained my master degree in Chemistry and Pharmaceutical Technologies under the supervision of Prof. Marco Lolli, in the project titled:” Design and synthesis of flufenamic acid derived bioisosteres as inhibitors of aldo-keto reductase 1C3 (AKR1C3) expressed in prostate cancer”. After that I won a LPP/Erasmus Traineeship fellowship and I worked with Prof. Ulf Nilsson at Lund University, Sweden, on the development of new inhibitors of dihydroorotate dehydrogenase (DHODH), a newly characterized target protein for Malaria. Then I joined the ISOTOPICS Consortium where I began my PhD.

What is your PhD project about?

The PhD project deals with using readily available, radio – labelled sources as $^{14}$CO$_2$ and introduced it in drugs as late step during the synthesis in order to minimize the radioactive wastes. All this work focuses on developing a green chemistry and to expand the knowledge about the drug ADME – Toxicology.

According to you, what are the strengths of the ISOTOPICS project?

In my opinion the strength of this project lies on the multidisciplinary fields developed from the Universities and the Industries together; giving us the opportunity to go deeper in science both from the chemistry and the biological point of view.

ESR 5 – Francesco IBBA (UOXF), group of Prof. Veronique GOUVERNEUR

Could you tell us about your background?

I am an Italian organic chemist currently doing my PhD at the University of Oxford. I studied in Genova, my home town, where I have achieved both my bachelor (with Prof. Fatima Paiva-Martins, University of Porto as Erasmus exchange student) and my master degree (with Prof. Andrea Basso, University of Genova). After my master I moved to Basel to work few months as intern in Novartis. From Switzerland I finally arrived in UK in the group of Professor Gouverneur, and here I am. I would describe myself as a pure synthetic organic chemistry with a passion for drug discovery and medicinal chemistry.

What is your PhD project about?

My PhD is about nucleophilic fluorination with the aim to contribute to $^{18}$F-labeling, more in particular we are developing a new organocatalyzed fluorination that we hope to take into the hot lab. In two words: methodology development.

According to you, what are the strengths of the ISOTOPICS project?

ISOTOPICS project, in my opinion, has its major strength in the possibility to build a network between young and more experienced researchers, industry and academia, this is crucial for science. I am a little worried that things might change, in UK, after Brexit.
Message from the ISOTOPICS Coordinator – Dr. Christophe DUGAVE (CEA)

It was a great pleasure to host the first ISOTOPICS training session at CEA-Saclay at the end of last November. This workshop permitted the 13 ESRs who attended the training to get familiar with isotopic labeling chemistry including deuterium and tritium, carbon-11 and carbon-14 as well as fluorine-18 through first-class taught courses. They also got basic training in transferable skills which should be helpful for their PhD preparation and communication of their results to the broadest possible audience including scientists but also the Public.

The first ISOTOPICS Meeting which has followed the training gathered Partners Representatives and Advisory Board Members. It was a real milestone for the ISOTOPICS scientific kick-off. All participants had the opportunity to meet the ESRs and to discuss informally with them about their projects and their expectations. Our young colleagues delivered their first talk explaining their scientific background and their individual research projects. They benefited from fruitful exchanges between all scientists but also well-informed advices provided by the five Advisory Board Members who shared their dual academic/industrial experiences. Thank you to all of them for their contribution to the success of the meeting! Recently, the two last ESRs have started their contracts.

I am looking forward to welcome them to the second ISOTOPICS meeting and to see you again in Frankfurt!

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