

2015-2016 Faculty Grant for International Connections
Developing Strong Ties Between Lehigh University and the University of Toulouse

Damien Thévenin, Department of Chemistry, Lehigh University

Professional and personal goals for the visit: The goal of the proposed visit is two-fold: (1) To develop new collaborative research ideas with the research group of Dr. Marie-Pierre Rols at the Institute of Pharmacology and Structural Biology (IPBS) in Toulouse, France, and (2) to develop strong educational ties with the University of Toulouse III, with which the IPBS is affiliated. The University of Toulouse III encompasses 5 disciplines of study and research (health, sciences, sport, engineering and technologies) and has over 32,000 students and 2,600 faculty.

My group focuses, in part, on the development and validation of the pH (Low) Insertion Peptide (pHLIP), as a versatile and effective targeting and delivery platform to improve the treatment modality of cancer, while sparing healthy tissues and limiting the development of drug resistance. We have shown that pHLIP and one of its variants can kill cervical and triple-negative breast cancer cells in a pH-dependent manner via translocation of a highly potent and clinically validated anticancer agent, and that one of these conjugates can selectively target tumors in mice. We have also obtained recently very exciting therapeutic data, showing that mice treated with our conjugate exhibited significant tumor size reduction when compared to non-treated animals. While these results are extremely encouraging, a better understanding of pHLIP targeting properties in vivo at the molecular level is essential to move our pHLIP conjugates towards the clinics.

I met Dr. Rols during my one-day visit at the IPBS in 2015 at the invitation of Prof. Alain Milon (head of the Integrative Biological NMR group). We realized very quickly that our respective expertise were perfectly complementary, and that, if combined, would allow us to answer unmet needs in the field of drug delivery. Indeed, the group of Dr. Rols focuses on defining the mechanisms of drug delivery to cells and to tumor at the molecular level. Their approach is to use various imaging tools to visualize and define these phenomena on models of increasing complexity: giant vesicles, cells in culture, multicellular spheroids, and small animal. They are also developing new targeting and diagnostic strategies.

The collaboration is thus important to us, as it will allow us to develop our pHLIP delivery platform further and acquired new expertise. It will also provide critical contact with a great community of researcher and scholars (see below).

Expected outcomes: We will first identify collaborative projects with the Rols group, and disseminate to the IPBS and the surrounding institutions the research conducted at Lehigh. We hope to also establish a long-term collaboration with the Rols group such that we could publish research articles and apply to external funding together. This visit may also provide an opportunity to seek external funding to support a possible future sabbatical leave. Indeed, a sabbatical leave at the IPBS would allow myself and thus my group to acquire crucial expertise in cell and animal biophysics (Dr. Rols group) or/and in nuclear magnetic resonance (NMR; Dr. Milon group), areas that are not only essential to the research conducted in my lab but also in which Lehigh University is growing infrastructures and competencies. The visit will also initiate strong ties between our two universities, with the hope of future exchanges (e.g., internships, study abroad) of undergraduate and graduate students not only in chemistry and biomedical disciplines, but also in all fields encompassed by our two institutions.

Nature of interaction: The visit will provide for an opportunity to have extended brainstorming sessions with the Rols group that phone conversations do not allow. I plan to give a seminar at the beginning of my stay so everyone in her group and institute is aware of the research conducted at Lehigh. I will also attend her group meetings so I can see the entire scope of her research and identify the areas where my group could be of any help (and vice versa). Dr. Rols group, in addition to be affiliated to the University of Toulouse, is part of the Oncopole, a unique campus gathering public and private researchers, academics, healthcare professionals and entrepreneurs involved in the fight against cancer. I anticipate that I will give a seminar at the Oncopole and at the University of Toulouse III (see letter of support from Dr. Fabrice Dumas), which would undoubtedly provide opportunities for collaborations not only for my research group, but also for Lehigh University. In addition to Dr. Rols' laboratory, many other research groups at the IPBS have overlap with my group, as one of the institute's primary objectives is the identification and characterization of novel pharmacological targets in the fields of cancer. For example, collaborations with the groups of Drs. Milon, Muller (Microenvironment and Cancer), Girard (Vasculature biology), and Zajac (Molecular and functional pharmacology of membrane receptors) are also possible.

Pre-trip planning and preparation: Dr. Rols and Dr. Dumas (director of the Master Program in Structural Biology, and vice-President of International Relations) will be my hosts at the IPBS and the University of Toulouse III, respectively. Their letters of support are provided with this application. I will arrange to stay at a hotel close to the institute, and I will also contact neighboring institutions to explore the possibility of giving seminars in their departments. These universities include the University of Bordeaux, the Université of Montpellier and the Université of Nice Sophia Antipolis.

Expected follow-up steps upon return to Lehigh: I will first direct my research group to perform the studies on which Dr. Rols and I agreed. Obtaining results and publications from this joint effort will be essential in exploring sources of funding (not only in US but also in France and Europe) to support future studies and exchanges. I will also explore the possibility of inviting scientists for France to give talks at Lehigh University. Moreover, I will put in contact our respective Offices of International Affairs to initiate and facilitate exchanges between our institutions. As required, I will also write up a summary of my visit in France for Lehigh University.

Proposed budget:

Air-fare to Toulouse (Kayak):	\$1,200
Housing and meals (US State Department per diem) for Toulouse:	\$4,788
Internal travel in France and Europe:	\$700
Total:	\$6,688



Institut de Pharmacologie et de Biologie Structurale

Toulouse, January 18th 2016

Faculty Grants for International Connections Committee
Office of International Affairs
Lehigh University

Re: Prof. Damien Thévenin's Application

To Whom It May Concern:

I am writing to support Professor Thévenin's application for funds to visit the Institute of Pharmacology and Structural Biology (IPBS), which is a joint institute of the French National Centre for Scientific Research (CNRS) and the Paul Sabatier University (University of Toulouse). One of the main objectives of the Institute is to characterize and validate new pharmacological targets for cancer therapy, through the analysis of the influence of tumor microenvironment, for example. As so, the IPBS is also part of the Oncopole, a unique campus gathering public and private researchers, academics, healthcare professionals and entrepreneurs involved in the fight against cancer.

Professor Thévenin and I met for the first time when he was invited by one of my colleagues to give a seminar at our Institute in 2015. During this brief visit, we recognized that our complementary skill sets could be combined for a mutually beneficial collaboration. Indeed, my research group focuses, in part, on the development of new tools for delivery, targeting and diagnostic. To do so, and define the mechanisms of drug delivery to cells and to tumor at the molecular level, we use sophisticated and unique imaging tools on models of increasing complexity: giant vesicles, cells in culture, multicellular spheroids, and small animal.

The proposed two-week visit would allow us to develop new ideas and discuss on how our expertise could be combined to tackle unmet needs in the field of drug delivery. In addition, Professor Thévenin would have an opportunity to present a lecture at the Paul Sabatier University (and/or at the Oncopole), which always has the potential to stimulate interest from other researchers.

Please, do not hesitate to contact me if you require more information regarding this letter.

Yours sincerely,

Dr Marie-Pierre Rols, PhD

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Toulouse, 21/01/2016

TO WHOM IT MAY CONCERN

Dear Sir or Madam,

I am director of the Master 2 “Biologie Structurale et Fonctionnelle” of the University of Toulouse (France). This master aims to produce 15 to 20 graduate students per year with detailed knowledge of molecular mechanisms in biology applied to pharmacology, structural biology, cellular biophysics or biotechnology.

Within the year, our students have to follow 3 months of lectures before working into a research lab. The formation also involves participation to seminar and discussion with the speakers. In this frame, we would be very happy to welcome Damien Thevenin. We can propose him to give a seminar to present his research and spend one afternoon to discuss and answer to student’s questions.

Furthermore, as vice president in charge of International Relation of Toulouse University, I would be happy to take this opportunity to talk with Damien about the possibility to exchange students for studies or lab placements.

Please do not hesitate to contact me if I can be of further assistance.

Yours sincerely,

Fabrice Dumas
Director of Master 2
Vice President International Relations
University Toulouse III

A handwritten signature in black ink, appearing to read 'Fabrice Dumas', with a long horizontal line extending to the right.