Synthetic small molecules interfering with oncogenic microRNAs for the induction of glioblastoma initiating cells differentiation: new perspectives in cancer chemotherapies

Job offer: PhD
Employer: Laboratoires Servier/Université Nice Sophia Antipolis
Discipline: Organic Chemistry
Start date: October 1st or November 1st 2017

The Institute of Chemistry of Nice belongs to Université Côte d'Azur and is located in Valrose Campus in the center of Nice. The lab is organized in three main scientific axes:
- Bioactive Molecules
- Fragrances: synthesis, analysis and molecular modeling
- Radiochemistry

The group coordinated by Dr. Duca belongs to the Bioactive Molecule axes and focuses its researches on the design and synthesis of new RNA ligands as potential anticancer and antibacterial agents.

This PhD project is conducted in collaboration with Laboratoires Servier who financially support the PhD grant as well as the entire research project.

Glioblastomas (GBM) are the most common form of primary brain tumors afflicting adult patients of all ages. These highly vascularized and infiltrating tumors are resistant to current therapies and inevitably lead to a fatal outcome in less than 18 months. The current treatment associates surgery, when possible, radiotherapy and the use of Temozolomide. However, the efficiency of this treatment of reference, even associated to anti-angiogenic molecules (bevacizumab), is limited and this cancer remains incurable. The aggressive behavior of GBM, including resistance to current treatments and tumor recurrences, has been attributed to the presence of GBM stem-like or progenitor cells (GSCs), which remain persistent and even more aggressive following conventional cytotoxic treatments (radio-chemotherapy).
Recently, out of a collection of small-molecule RNA binders that we previously synthesized, we identified original compounds that are able to induce GSCs differentiation, inhibit clonal proliferation and strongly increase the sensitivity of these cells to temozolomide. The purpose of this research project is to develop new drug candidates starting from these hits able to induce GSCs differentiation and to increase their sensitivity to current chemotherapies by interfering with GSCs miRNAs network. The three main goals of this project are:
From the achievement of this project, we expect the identification of drugable compounds for anti-GSC strategies bearing an extremely original mechanism of action and directed toward a particular cancer (GBM) against which no efficient therapy exists. The interest of using compounds interfering with one or more miRNAs is to restrain the adaptive capacities of the cells to bypass the tumor suppressor activity. The synthesis of new compounds targeting the production of miRNAs involved in the differentiation of cancer stem cells would represent a major breakthrough in anticancer therapy, thus constituting an innovative and attractive approach for clinicians, compatible with industrial pipelines. In the future, this kind of

therapeutic approach could be applied to other cancers whose persistence of CSCs population is related with miRNAs networks.

Applicants should have an excellent background in organic chemistry as well as a predisposition for research projects at the interface of chemistry and biology. We seek for highly motivated PhD candidates with the capability to integrate in a research group and to participate to all lab activities. Master grades as well as one or more reference letters are required for application. A global grade of 12/20 for Master 2 and/or a ranking in the first third of final students' ranking are required for the position, applications that do not respect these requirements will not be taken into account.

Deadline for application is September 15th 2017. Please send your cover letter, Master grades and CV to maria.duca@unice.fr