

Title: Development of miniaturized technologies for the development and electrophysiological validation of novel molecules on ion channels and transporters involved in orphan cancer or neurodevelopmental disorders.

PI and name of the lab: Marco Lolicato and *Elements S.r.l.*

Research Theme/Topic: Biophysics, Engineering, Chemical and Molecular Biology.

Main Abstract:

The doctoral student will acquire, through laboratory activities, *ad hoc* seminars and participation in congresses, skills in complementary fields of translational medicine with particular attention to the molecular and functional aspects of transmembrane therapeutic targets such as ion channels and transporters.

Through the collaboration with the company *Elements S.r.l.*, the student will also develop in-depth knowledge of microelectronics and electrophysiology that will make him competitive in the job market both in industries and in the academic field.

The laboratory mainly works on the biophysics of ion channels and transporters involved both in neoplastic pathologies and in the neurodevelopment process. The goal of the laboratory is the identification (1) of the role of the Hv1 channel in breast cancer metastases; (2) of the molecular mechanisms of the interactome of the KCC2 channel; (3) of the molecular structure of the divalent VDAC1-Hexokinase complex. In the laboratory we are able to purify sufficient quantities of protein targets for structural and functional studies and we are actively collaborating with international companies for the development of new anticancer molecules. The PhD student will enter this context by learning both the molecular biology and biochemical techniques that will allow him to produce the proteins of interest and by acquiring the necessary skills to perform independently and unsupervised electrophysiology measurements to evaluate the effects of molecules on purified proteins. The PhD student will learn to evaluate the quality of a protein preparation and to analyze and interpret electrophysiology data. The student's progress will be constantly monitored by the laboratory manager and the industrial tutor. Laboratory progress reports will be organized weekly and a virtual meeting with company managers will be held on a monthly basis.

The PhD student will also acquire experience in "troubleshooting" both in the laboratory and in the electronics of the components of the high-throughput electrophysiology system.

The project is highly innovative and competitive because it combines laboratory research with the development of microelectronic components for electrophysiology measurements. The goal, in fact, is to identify antitumor and neurodevelopmental molecules by means of a thorough screening of both commercial molecular libraries and libraries of compounds already available but approved for the treatment of different pathologies (drug repurposing / repositioning). These types of screening require numerous experiments and electrophysiology measurements. However, thanks to the tools developed by the *Elements* company and optimized / developed by the doctoral student, it will be possible to quickly test dozens of molecules per day. The development of this methodological approach will be useful not only for the laboratory and for the University of Pavia in general, but above all for the national and international scientific community through the export of the technology.

Techniques: Electrophysiology, protein expression and purification, cell biology assays, computational methods (docking, molecular dynamics, protein engineering).

