Grenoble Alliance for Integrated Structural & Cell Biology

GRAL MASTER 2 RESEARCH SCHOLARSHIP - Program 2018 - 2019

CALL FOR RESEARCH INTERNSHIP TOPICS

Deadline for proposal submission: **DECEMBER 15th, 2017**

Please fill in the template in English and send it back to manel.boumegoura@cea.fr

MASTER II University programs compatible with the scholarship program:

Master in biology: *Specialty biochemistry and structural Biology / Specialty cell Biology, Physiology and development / Specialty neurobiology and neurosciences / Specialty immunology, microbiology, infectiology/ Master Biology, Ecology, Environment*

Master in physics: *Specialty « Complex matter, living matter » (MCMV)*

Master in Nanosciences, nanotechnologies: ***S****pecialty Nanochemistry-Nano-objects / Specialty Nanobiology-Nanobiotechnology / Specialty Nanophysics – Nanostructures*

INTERNSHIP PROPOSAL

Institute and Group: BIG/ Biology of Cancer and Infection/ Invasion Mecanism in Angiogenesis and Cancer

Supervisor: Odile FILHOL **Phone:** +33 4 38 78 56 45

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Research project title: Organotypic tissue slide culture to monitor anti-tumor drug therapy

5 Keywords to describe the project:

Renal Cancer, Prognostic, tissue slice culture, protein-kinase inhibitors, Fluorescence imaging

Description of the project (aims, experimental techniques, recommended background): 10 to 15 lines:

Renal cell carcinoma (RCC) is the 8th leading malignancy in the world. Approximately 50% of RCC patients present or will develop metastasis. Several available kinase-targeted agents have shown beneficial effects for the treatment of patients with metastatic renal cell carcinoma, but some patients experience disease progression. Thus, the lack of long-term efficacy of current treatments reveals the urgent need to find other therapies. Using a high-throughput chemo-genomic screening, we have identified several new drug combinations active on renal carcinoma cells. Among them, a synthetic-lethal interaction between CK2 and ATM kinase inhibitors was highly efficient on the aggressive 786-O VHL null cell line (PCT/EP2016/072458). Validation of this combination was performed using 2D and 3D cell cultures as well as organotypic tissue slice culture and mouse models (cell line xenografts and PDX).

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The objectives of the current project are first to validate this combination on kidney tumours provided by the Grenoble Alpes University Hospital using the tissue slice culture approach and second to make the proof of concept that the technology can accurately predict clinical responses to targeted therapies. A special focus that need to be improved is the quantification of the cell viability in the tissue slices after drug treatment using fluorescence imaging.

Justification that the internship's subject fits with the general theme of GRAL (3 lines):
Thanks' to the support of Vallogral, we successfully characterized this drug combination in *in vitro* models. Now, through the collaboration with the Grenoble Alpes University Hospital we are in a position to test the ability of patient-derived tissue slice cultures to predict patient responses to targeted therapies.

Relevant publications of the team (3 max):

Roelants, C., Giacosa, S., Bastien, O., Guyon, L., Descotes, J-L., Bussat, R., Cochet, C., Filhol, O., Vulnerability of clear-cell renal carcinoma cells to combined PI3K and SRC inhibition. Oncotarget, 2017 submitted.

Roelants, C., Giacosa, S., Duchemin-Pelletier, E., McLeer-Florin, A., Tisseyre, C., Aubert, C., Champelovier, P., Boutonnat, J., Descotes, J-L., s Rambeaud, J-J., Arnoux, V.,Long, J-A., Pasquier, D., Laramas, M., Kassem, M.,David-Boudet L., Schoutteten, L., Bestgen, B., Pillet, C.,Cochet, C., and Filhol O, Dysregulated Expression of Protein Kinase CK2 in Renal Cancer. Advances in Biochemistry in Health and Disease ed. Protein Kinase CK2 Cellular function in Normal and Disease States, ed. A.i.B.i.H.a. Disease. 2015: Springer.

PCT/EP2016/072458 : A synthetic lethal drug combination for treating renal cell carcinoma. Filhol O Cochet C Giacosa S, Pillet C, Barette C, Soleilhac E.