

Post-doctoral position in Targeted Nanotherapy for cancer

A post-doctoral position is now opened in the INSERM ERL1226 Team of Receptology and Therapeutic Targeting in Cancerology of the Laboratory of Physics and Chemistry of Nano-Objects (LPCNO-CNRS UMR5215-INSa), in Toulouse (France). This position is funded by the Labex NEXT.

Scientific context: Endocrine tumors are usually diagnosed by an imaging technique using a radio-labeled peptide (somatostatin or Osteoscan), the receptor of which is present in 80% of the tumors. Overexpression of the CCK2R cholecystokinin receptor belonging to the transmembrane domain (R7TM) family has also been demonstrated in a collection of human endocrine tumors. Moreover, the studies carried out in our team show that this receptor is massively internalized and is directed with its ligand towards the lysosomes.

Our team established *in vitro* proof of concept that overexpression of CCK2R in endocrine tumors compared to healthy tissues and its capacity for massive internalization could be used to develop a new therapeutic approach. This strategy is based on the use of magnetic nanoparticles functionalized with the CCK2R selective agonist, gastrin. Our results show that the nanoparticles thus vectorized are massively and specifically internalized in cancer cells expressing the CCK2R, and then accumulated in the lysosomes, according to a mechanism identical to the free ligand. The application of an alternating magnetic field induces the death of 25 to 50% of the tumor cells, depending on the cell model. We have called this mechanism: magnetic intra-lysosomal hyperthermia because it occurs without detectable temperature increase. Recent results show that this new approach activates a particular death pathway that could be an alternative to cancer treatments, especially on resistant cancer cells.

Objectives of the project: The project developed by the candidate will be integrated into the research axis "Targeted nanotherapy of cancers by magnetic intra-lysosomal hyperthermia". The objectives will consist, on one hand, in continuing the study of the mechanisms involved in the death of cancer cells and, on the other hand, in increasing the effectiveness of this strategy by optimizing several parameters (Heating of nanoparticles, use of pharmacological agents, etc.). *In vivo* studies may also be considered on the murine transgenic MEN1 knockout model representative of human MEN1 syndrome, developing multiple endocrine tumors. The efficacy of therapeutic targeting and the magnetic intra-lysosomal hyperthermia nanotherapy to inhibit tumor growth or induce tumor regression will be evaluated.

Profile: We are looking for a candidate with a PhD in life sciences and a strong background and expertise in cellular biology and/or physiology. He (She) must possess:

- Knowledge in: cell biology, physiology and pathophysiology applied to cancer, pharmacology, receptors.
- Expertise in: animal experiments, cell culture, histology, immunohistochemistry, microscopy, flow cytometry, transfection.
- Abilities: good communication in the context of teamwork, coaching of students

Administrative aspects: The post-doctoral position is funded for 12 months. The position will be open in September 2017. The post-doctoral position may be extended depending on the acceptance of additional funding requests.

Applicants should submit curriculum vitae, a list of publications, a brief description of their research and the career goals to Véronique GIGOUX (veronique.gigoux@inserm.fr).

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