Conception et synthèse de vecteurs peptidiques pour le ciblage de la périphérie tumorale - outil d'imagerie pour la chirurgie

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Surgery is one of the most efficient treatment of cancer if it can be performed completely without leaving infected tissues on the tumor bed. This implies that the surgeon can discriminate tumor tissues from the healthy ones. To this end, various imaging techniques exist such as X-rays, echography, MRI SPECT or PET. Optical imaging is currently emerging as a new method in the clinics in particular because it can be used easily in real-time during surgery (intra-operative imaging). This requires combining an optical instrumentation that work in the near-infrared spectrum (NIR), and tumor specific fluorescent contrast agents.

In this context, the aim of our project is to design macromolecules that would permit a very accurate and specific labeling of the tumor borders. Our strategy is to selectively target receptors that are overexpressed in the tumor margins and area where tissue remodeling is extremely rapid and cross-talks between the tumor and stroma cells are of the outmost importance.

We chose two receptors that are overexpressed in the tumor periphery – αvβ3 integrin and neuropilin 1 (NRP1). They are expressed at the surface of different cell types in the tumor periphery (endothelial cells, tumor cells, tumor-activated macrophages…) and are especially involved in neoangiogenesis, cell migration, differentiation and survival. For targeting these 2 receptors, we used the well known -cRGD- and the ATWLPPR peptides that target respectively the αvβ3 integrin and NRP1 receptors. We constructed sophisticated macromolecules encompassing both ligands along with a NIR Cy5.5 dye. This was accomplished via the use of a peptidic scaffold displaying orthogonal functions allowing chemoselective reactions, such as the Huisgen cycloaddition and the oxime ligation. We then prepared different molecules combining both ligands. The biological tests of those macromolecules are in progress.