Novel MRI/Optical imaging agents for targeted diagnosis and treatment of diseases

Amerigo Pagoto Department of Molecular Biotechnology and Health Sciences University of Torino amerigo.pagoto@unito.it

Tutors: Prof. Enzo Terreno

Prof. Silvio Aime

Targeted molecular imaging offers the possibility to widely improve the quality of diagnosis and treatment for different pathological conditions. My PhD project has been mainly focused into the design, development and test of novel molecular probes for MRI targeted diagnosis and Optical imaging intraoperative applications. Despite the superb spatial resolution of MRI, the lack of sensitivity still remains one of the main drawbacks of this technique in molecular imaging. The use of highly efficient contrast agents conceived to specifically reach the target, it is an established way to overcome this obstacle. For these reasons, two targeted peptide-based probes were synthesized and tested in vivo on tumor and inflammation mouse models. The former is the molecular tetramer CREKA-dL-(AAZTA-Gd³⁺)₄ that, using the innovative Gd-AAZTA ligand and the small peptide vector CREKA, can interact with the tumor extracellular microenvironment and give a localized in vivo contrast on MRI images of prostate cancer. The latter is a micellar nanosystems bearing anti-VCAM-1 peptide, a powerful tool to visualize both peripherical that brain inflammation. As mentioned above, the molecular imaging turned out to be an interesting and useful instrument in tumor treatment. In particular, Imaging Guided Surgery (IGS) is an emerging field that exploits the properties of optical fluorescent dyes to precisely localize the malignant tissue, thus allowing surgeons to remove the tumor mass with the minimum impact on healthy tissues. The near infrared fluorescent dye BBN-Cy5.5 is a peptide-based probe, designed and tested in vivo on a mouse model of prostate cancer, where it showed a high potential for real-time intraoperative intervention. Finally, considering the high translational applications of this method, I spent the last part of my PhD in Rotterdam (The Netherlands), deepening the potential of novel molecular dyes on spontaneously developed dog tumors.

