Tumor imaging with bicyclic peptides as affinity reagent

V. Baeriswyl[1], P. Diderich[1] and C. Heinis[1]

1 Institute of Chemical Sciences and Engineering (ISIC), EPFL

Recent technology developments had facilitated the generation of ligands with significantly different size and properties than antibodies (150 kDa), such as small organic molecules (0.3-0.5 kDa)(1) or bicyclic peptides (2 kDa)(2). In our work, we aim at comparing the performance of the different molecule families in targeted molecular imaging of cancer. Towards this end, we are currently developing bicyclic peptide ligands to a range of cancer-associated proteins. The bicyclic peptides are generated with a phage display-based methodology that had recently been developed by Heinis, C. and Winter, G. (2). Ligands will be labelled with fluorophores and radionuclides and their performance assessed in targeting and imaging experiments in tumour-bearing mice and compared with the performance of the other two ligand families. With this work, we hope to develop optimal affinity reagents for the molecular imaging of tumours using cancer-associated proteins as markers. Furthermore, information gained in this study about the targeting efficiencies of the three molecule families should help our and other groups to choose optimal molecule formats in the future development of imaging reagents.

(1) S. Melkko, J. Scheuermann, C. E. Dumelin and D. Neri, *Nat Biotechnol*, 2004, **22**, 568-574.
(2) C. Heinis, T. Rutherford, S. Freund and G. Winter, *Nat Chem Biol*, 2009, **5**, 502-507.

Structures of a small immunoprotein (SIP) antibody (left), bicyclic peptide (middle; specific for plasma kallikrein developed by Heinis, C. and Winter, D.) and small organic ligand (right; specific for albumin; developed by Neri, D. and co-workers). The regions of the antibody fragment and bicyclic peptide that potentially interact with the targets are highlighted in colour.