# Targeted Radiotherapy using CLIPS™ Macrocyclic Peptides

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In the past decade, the fusion of therapy and diagnostics has surged, giving rise to a distinct field known as theranostic. This approach relies on a ligand that precisely targets solid tumors, typically attached to a radioactive isotope for detection via PET scan or SPECT imaging. By employing the same ligand and linker molecule combined with another radionuclide could selectively kills cells in tumor micro-environment.

In this lecture, we present our collaboration work with Perspective Therapeutics for the discovery and pre-clinical development of [212Pb]-PSV359, a macrocyclic CLIPS$^{TM}$ peptide with high binding affinity and specificity against the Fibroblast Activation Protein Alpha (FAP$\alpha$).

FAP$\alpha$ is a 170 kDa homodimeric serine protease that is highly expressed in activated stromal fibroblasts of more than 90% of all human carcinomas [1,2]. These stromal fibroblasts are crucial for cell progression, including development, proliferation, and metastasis. However, under normal physiological conditions, FAP$\alpha$ expression remains minimal in most adult tissues.

[1] Puré & Blomberg, "Pro-tumorigenic roles of fibroblast activation protein in cancer: back to the basics", *Oncogene* **2018**, *37 (32),* 4343-57 (doi:10.1038/s41388-018-0275-3).
[2] Busek et al., "Targeting fibroblast activation protein in cancer - Prospects and caveats", *Front. Biosci.* **2018**, 23(10), 1933-68 (doi:10.2741/4682).