"Small Molecule Therapeutics as an alternative to Peptide Therapeutics: a clean strategy to delivery bioactive payloads to tumors"

Philochem AG, R&D department, CH-8112 Otelfingen, Switzerland
Samuele Cazzamalli, Andrea Galbiati, Aureliano Zana, Matilde Bocci, Dario Neri

samuele.cazzamalli@philochem.ch

Tumor-targeting peptides have been used with the aim to target bioactive payloads, including drugs and radionuclides, to tumors [1, 2]. While tumor-targeting peptide with high affinity and target specificity can be obtained, these agents typically suffer from high and prolonged accumulation in the kidney [2] and from possible degradation in circulation by enymatic activity of serum proteases [3]. Small organic ligands targeting tumor-associated antigens have been proposed as valuable alternatives to peptides for the delivery of cytotoxic drugs and radioactive payloads to solid tumors [4]. Small molecules benefit from a rapid extravasation, high stability in blood, efficient penetration of solid malignancies, low cost-of-goods and minimal immunogenicity potential [5]. We have recently described the discovery of OncoFAP, a novel ultra-high affinity ligand of FAP which has been already validated for PET imaging applications in more than twenty patients with solid tumors [6]. In this presentation, we describe the development of small molecule therapeutics targeting FAP and based on OncoFAP and derivatives with longer tumor residence time [7, 8].

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