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Abstract

Selective Activity-Based Probes Targeting Fibroblast Activation Protein (FAP) †

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Abstract: Fibroblast activation protein (FAP) is a type II transmembrane serine protease that belongs to the dipeptidyl peptidase (DPP) family. Although FAP expression is practically non-existent in the majority of healthy adult tissues, it is clearly upregulated in tissue remodeling processes associated with several diseases. These include cancer, atherosclerosis, arthritis, hepatic, and pulmonary fibrosis. This finding has recently sparked intensive research aiming at the clinical implementation of FAP as a diagnostic and/or prognostic biomarker for the aforementioned diseases. Several immunochemical approaches have been reported that can quantify FAP expression. The main drawback of these approaches, however, lies in the fact that some of the commercially available FAP antibodies have been reported to lack specificity. On the other hand, an orthogonal line of research focuses on the quantification of the enzymatically active fraction of FAP, generally relying on peptidic activity-based probes. Developing a selective activity-based assay for FAP has proven to be challenging, owing to the frequently encountered lack of probe selectivity towards prolyl oligopeptidase (PREP, PO). In response, we report a novel series of activity-based FAP probes, based on our potent and selective inhibitor UAMC-1110.

Keywords: FAP; Fibroblast activation protein; ABP; fluorophore; fluorescent inhibitor derivative