Fluorescent activatable peptides for first in-human imaging studies

Fluorescent peptides are valuable tools for live cell imaging because of their tunability and specificity.[1] Our group has designed fluorescent amino acids to label peptides and proteins without affecting their functionality and biological activity. Our fluorescent amino acids are designed to: 1) be compatible with solid-phase peptide synthesis, 2) maintain the recognition features of native peptides and 3) emit fluorescence preferentially after target binding, improving signal-to-noise ratios for imaging. We have successfully prepared fluorescent antimicrobial peptides including the Trp-BODIPY amino acid to detect pathogens in *ex vivo* human lung tissue under multi-photon microscopy.[2] We have also extended the toolbox with the first Trp-based red fluorogenic amino acid and used it to prepare cyclic peptides for imaging of aggressive cancer cells in tumors.[3] Recently, our developments include the incorporation of these technologies into proteins, and we have generated the fluorescent activatable chemokine PhagoGreen-CCL2 as the first probe for imaging of metastasis-associated macrophages in mouse models of lung metastasis.[4] The preparation of new amino acids based on smaller fluorophores[5,6] with additional optical properties and alternative connecting groups[7] will allow us to expand the building blocks to generate peptide-based fluorescent probes. Furthermore, we have established a translational pipeline to manufacture these probes as clinical grade reagents and to use them in pioneering first-in-human imaging studies.

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[6] Mendive-Tapia, L. et. al. *Angew. Chem. Int. Ed*. **2022,** e202117218.

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