Affibodies for PET imaging of active fibrosis

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Affibody molecules are three-helix bundle proteins consisting of 58 amino acids from the immunoglobulin-binding domain of staphyloccocal protein A (Figure 1). Affibody molecules are an excellent platform for radiopharmaceuticals due to their e.g. capacity for high affinity binding, relatively small size, thermal stability and ease of functionalization and production [1]. We are using the Affibody molecule platform to develop Positron Emission Tomography (PET) imaging technologies to assess tissue inflammation and fibrosis, for use in drug development, diagnostics and therapy. Activated hepatic stellate cells (HSCs) are the main culprit in fibrotic collagen deposition in the liver [2]. PDGFRβ is strongly upregulated on activated HSCs but shows low background expression in healthy liver and is undetectable on quiescent HSCs [3]. Similarly, PDGFRβ is a surface marker of fibrogenic myofibroblasts in many other tissues such as lung, heart and tumor stroma. PDGFRβ is therefore a potential general imaging target for detection of active fibrosis in tissue.

We are developing Affibody molecule ATH001 as an imaging agent for detection of PDGFRβ in fibrotic disease. ATH001, radiolabeled with Gallium-68 or Fluorine-18, demonstrated increased binding in fibrotic lesions in preclinical models of tissue fibrosis, including CCl4 induced liver fibrosis, bleomycin induced lung fibrosis and infarct induced heart fibrosis. These findings were corroborated by in vitro binding studies using human biopsies, e.g. liver biopsies with different stages of fibrosis.

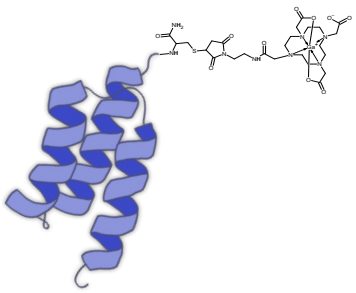

Fig. 1. Schematic structure of Affibody molecule ATH001

[1] Ståhl S, Graslund T, Eriksson Karlstrom A, Frejd FY, Nygren PA, Löfblom J, *Trends Biotechnol.,* **2017**, 35, 691-712.
[2] Friedman SL, Pinzani M., *Hepatology*, **2022**, 75, 473-488.
[3] Pinzani M, Milani S, Herbst H et al., *Am J Pathol.*, **1996**, 148, 785-800.