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Two Ph.D.-Students Wanted

(3 years DFG-funded)

Project: **Impact of Tumor-associated Glycosylation on the Multi-Functionality of TIMP-1 (Tissue Inhibitor of Metalloproteinases-1)**

Expression of the multi-functional protein TIMP-1, which can act as a protease-inhibitor as well as a cytokine, positively correlates with progression of virtually all immune-associated diseases, including inflammation and cancer. Recently, we have discovered that N-glycosylation fine-tunes whether TIMP-1 functions as protease-inhibitor or as a cytokine (*Häußler et al. J Biol Chem 301:110211, 2025*). With your help, we would like to investigate the in vivo-impact of circulating recombinant murine TIMP-1 glycosylation variants by sn/scRNA-seq and subsequent construction of gene regulatory networks (GRN) in liver and bone marrow cells from female and male individuals, as we had found that biological sex makes a difference (*Hermann et al. J Exp Med 218 :* e20210911, 2021*)*.

We employ a wide spectrum of technologies encompassing all aspects of molecular cloning/genetic engineering, expression-vector design, biochemistry, cell culture including functional cell-assays, metabolic assays, protein-design and purification, flow-cytometry, histology, *in silico*-modeling, TIMSTOF, statistical analyses, bioinformatics etc. in order to explore the biology of TIMP-1.

Through cooperation with colleagues in the clinic we constantly validate our data with material from the clinic towards a transfer of new knowledge from bench to the bedside.

If you have completed or are about to complete your Master's in areas of biochemistry, molecular biology, molecular biotechnology or other pertinent areas, and if you would like to work in an excellent technical and scientific environment at the TUM (Tech Univ Munich)…

…please contact me at: **achim.krueger@tum.de**

Examples of more recent **publications** from our group (**our PhD students underlined**):

Häußler, D., D. Manevski, J. Frädrich, V. Brunner, O. Prokopchuk, A. Sommer, B. Toledo, P. Knolle, M.E. Martignoni, H. Friess, P. Waterhouse, A. Krüger. Extent of N-glycosylation of the metalloproteinase inhibitor and cytokine TIMP-1 determines pancreatic cancer cell proliferation and survival via CD63. J Biol Chem 301 : 110211, 2025.

Lambert, J., S. Oc, M.D. Worssam, D. Häußler, C.U. Solomon, N.L. Figg, R. Baxter, M. Imaz, J.C.K. Taylor, K. Foote, A. Finigan, K.T.Mahbubani, T.R. Webb, S. Ye, M.R. Bennett, A. Krüger, M. Spivakov, H.F. Jorgensen. Network-based prioritisation and validation of novel regulators of vascular smooth muscle cell proliferation in disease. Nat Cardiovasc Res 3 : 714-733, 2024.

Eckfeld, C., B. Schoeps, D. Häußler, J. Frädrich, F. Bayerl, J.P. Böttcher, P. Knolle, S. Heisz, O. Prokopchuk, H. Hauner, E. Munkhbaatar, I.E. Demir, C.D. Hermann, Achim Krüger. TIMP-1 is a novel ligand of Amyloid Precursor Protein and triggers a pro-inflammatory phenotype in human monocytes. J Cell Biol *222* : e202206095, 2023.

Schoeps, B., J. Frädrich, A. Krüger. Cut loose TIMP-1: an emerging cytokine in inflammation. Trends Cell Biol *S0962-8924(22)00207*, 2022.

Hermann, C.D., B. Schoeps, C. Eckfeld, E. Munkhbaatar, L. Kniep, O. Prokopchuk, N. Wirges, K. Steiger, D. Häußler, P. Knolle, E. Poulton, R. Khokha, B.T. Grünwald, I.E. Demir, A. Krüger. TIMP1 expression underlies sex-disparity in liver metastasis and survival in pancreatic cancer. J Exp Med *218* : e20210911, 2021.

Schoeps, B., C. Eckfeld, L. Flüter, S. Keppler, R. Mishra, P. Knolle, F. Bayerl, J. Böttcher, C.D. Hermann, D. Häußler, A. Krüger. Identification of invariant chain CD74 as a functional receptor of tissue inhibitor of metalloproteinases-1 (TIMP-1). J Biol Chem *297* : 101072, 2021.

Schoeps, B., C. Eckfeld, O. Prokopchuk, J.P. Böttcher, D. Häußler, K. Steiger, I.E. Demir, P. Knolle, O. Soehnlein, D.E. Jenne, C.D. Hermann, A. Krüger. TIMP1 triggers neutrophil extracellular trap formation in pancreatic cancer. Cancer Res *81* : 3568-3579, 2021.