## DESCRIPTION FOR THE GENERAL PUBLIC

The extracellular matrix (ECM) is the non-cellular component present within all tissue and organs, which provides essential structural scaffold and biochemical support to surrounding cells. It consists of fibrous proteins allowing for stable cell adhesion and migration. An intricate network of macromolecules constitutes the matrix, supplemented by locally secreted proteins and polysaccharides, produced by attached cells. Tissue homeostasis is coordinated between a series of responses particularly by epithelial cells, endothelial cells and fibroblasts mediated *via* proteases. Proteases, the essential enzymes within ECM, are required for activation of ligands for cell surface receptors, providing a necessary step in signal transduction. Extracellular proteases prevalently expressed in the ECM include metallo- and serine- proteases, more specifically matrix metalloproteinases (MMPs) and tissue kallikrein related peptidases (KLKs). Both families play vital roles controlling the assembly and degradation of and within the ECM. MMP activity is low in normal healthy tissue due to their regulation *via* transcriptional activation, posttranscriptional processing and activity control by locally produced tissue inhibitor metalloproteinases (TIMPs). In addition, serum-derived serine proteases inhibitors of the serpin family and tissue-specific Kazal-type serine protease inhibitor (SPINKs) regulate KLK activity. Yet during tissue remodeling and in a diseased or inflamed state, protease expression is elevated and notably detectable. This adds to the importance of proteases and highlights the fact that control of their trafficking and activity is essential for the tissue function. Any dysregulated proteolysis may lead to physiological and pathological states, which impact wound healing, inflammation and cancer progression. A lot is known about the activation cascade within each proteinase family but surprisingly little is known on their crosstalk between these proteolytic systems. Therefore, this project is focused on the elucidation of tissue KLKs role in the regulation of local MMP activity within the ECM.

The project is designed to determine KLK substrate preference amongst all 23 proMMPs as well as their interactions and biochemical function. First, which MMP prosequences can be activated by specific KLKs using a complete fusion protein library will be determined. Next, the results will be verified and confirmed using selected full-length proMMP proteins, allowing detailed analysis of the activation parameters. This is essential to fully comprehend and prove the initial observation as seen in the fusion library. Lastly, a cell model will be used to confirm that KLKs activate proMMPs through the investigation of ECM degradation. Obtained results in the proposed project will significantly broaden our knowledge on KLK interaction with MMPs, two protease families essential for the ECM function. To date, there is not much known on proMMP activation *via* KLKs therefore this project will provide a new and intriguing discovery. Furthermore, it will shed more light on the characterization of cooperation between host-derived KLKs and MMPs in the ECM, which can help understand the switch between physiological and pathological states.