WWTF Project LS19-035

Combined optical single molecule and atomic force microscopy to elucidate enzyme-induced collagen degradation kinetics

Abstract

We propose to combine atomic force microscopy (AFM) and single molecule fluorescence microscopy (SMFM) to study the spatiotemporal mechanisms of collagen degradation by matrix metalloproteinases (MMPs). MMPs play a pivotal role in both physiological and pathological processes, such as wound healing, tissue remodelling, fibrosis, and cancer. MMPs can degrade collagen fibrils in the extracellular matrix (ECM), affecting mechanical stiffness of tissues and organs. Binding and diffusion of MMPs on the surface of collagen fibrils have been measured using SMFM. However, specific mechanisms of collagen degradation via MMPs are far from being understood: for example, is MMP activity altered due to mechanical load and local damage and is pathological cross-linking hindering such degradation? Such structure-function relationships can only be determined by combining imaging modalities that provide access to information on the kinetics of MMP (un-)binding and the mechanical/structural properties of the collagen fibril. We hence aim at using AFM - as the perfect tool for imaging mechanics and structures at nanometer resolution - together with SMFM - as the ideal method or quantifying binding kinetics. Combining the two modalities in the same instrument for simultaneous operation will enable for the first time the direct correlation between MMP binding with the consequence on collagen structure and mechanics at the degradation locus.

Scientific disciplines:
106006 - Biophysics (35%) | 211904 - Biomechanics (30%) | 104025 - Single-molecule chemistry (35%)

Keywords:
single-molecule tracking, atomic force microscopy, matrix metalloproteinases, degradation kinetics, collagen fibril

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Status: Ongoing (01.04.2020 - 30.04.2024) 49 months

Funding volume: EUR 591,120

Further links about the involved persons and regarding the project you can find at
https://archiv.wwtf.at/programmes/life_sciences/LS19-035