Objectives: The discovery of extracellular vesicles (EV) as specific communicators between cells has changed our understanding of human physiology and opened up amazing opportunities for drug development and tissue engineering. EV are membrane-derived particles secreted into the extracellular matrix and all body fluids. We are particularly interested in the novel subgroup of EV that carry hyaluronan (HA) on their surface (HA-EV). EVs have a great promise as a solution for drug delivery problems because they are non-toxic and non-immunogenic, the properties that can be further enhanced by HA coating (Rilla et al 2014).

Methods: The purpose of this project is to develop and utilize a unique set of cutting-edge high-resolution bioimaging techniques to study critical questions on basic EV biology, such as mechanisms of biogenesis, access to target cells and interactions with the extracellular matrix (ECM). We aim to analyze HA-EV penetration and interactions with ECM and target cells at a single vesicle-level.

Results: We have shown that the density and length of filopodia associates with the activity of hyaluronan synthesis in tumor cells (Kyykallio et al 2020) and CD44 assembles hyaluronan coat on filopodia and EVs (Härkönen et al 2019). We have developed a novel tumor cell spheroid 3D culture method, based on nanofibrillar cellulose, that allows easy isolation of EV from 3D cultures and imaging analysis of EVs *in situ.* The work with the 3D models and tumor cell lines with manipulated CD44 expression will continue in more detail to solve the mechanisms of EV biogenesis and uptake, and to learn to enhance the therapeutic potential of EVs. As a long-term goal we aim to utilize EVs to deliver therapeutic molecules such as siRNAs to target cells.

References:

Rilla et al. Hyaluronan-coated extracellular vesicles – a novel link between hyaluronan and cancer. Adv Cancer Res. 2014 123:121-48.

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