A new quantitative approach for the study of polyvalent CD44-HA interactions - nanoscale model surfaces of HA-rich films

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The hyaluronan (HA) rich pericellular coat that surrounds many cells has been linked to a variety of vital cellular functions[1-3], but the regulatory mechanisms at the cell-HA matrix interface remain poorly understood. For the thorough investigation of specific interactions between the cell surface receptors and HA as well as the structural properties of this supra-molecular matrix, it is desirable to switch from the complex cellular environment to simplified and well-controlled *in-vitro* model systems. Our approach relies on the stable and oriented immobilization of ectodomains of the HA cell surface receptor, CD44[4,5], on supported lipid membranes (SLBs). The confinement of the model systems to solid supports enables the in-depth characterization by complementary surface sensitive techniques. Here, quartz crystal microbalance with dissipation monitoring (QCM-D), ellipsometry and microinterferometry provide detailed insight into the formation, stability and morphology of the model surfaces and the HA films, and involved molecular interactions.

The physico-chemical properties of the created HA films reveal many similarities between the binding behavior of HA chains and flexible polymer chains adsorbing to a homogeneously attractive surface. The new model surfaces with tunable receptor density are exploited to qualitatively and quantitatively investigate the polyvalent interaction between HA and CD44 as a function of HA molecular weight and receptor surface density. Quantifying the number of receptors that are available per HA chain provides insight into the importance of polyvalent interactions and how they stabilize HA binding on receptor covered surfaces. We find that HA binding is regulated by both polyvalency and the intrinsic affinity of individual receptors.

The developed model systems represent a novel, well-controlled and tunable experimental platform for the investigation of the interactions between proteins and HA in a supra-molecular context, and between cells and HA matrices.

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