Extracellular glycosaminoglycan-binding proteins: from structure to interactions

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We study the structure - interaction - function relationships of the extracellular matrix (ECM) using biochemistry, biophysics, bioinformatics, structural biology, and systems biology with a focus on multimolecular complexes and interaction networks formed in the pericellular and extracellular matrix and their rewiring in pathological contexts such as Alzheimer's disease[1] and host-pathogen interactions[2]. We have identified new binding partners and build the interaction networks of several glycosaminoglycan (GAG)-binding proteins including the ECM anti-angiogenic fragments, endostatin[3] and the propeptide of lysyl oxidase[4], lysyl oxidases, which initiate ECM cross-linking, procollagen C-proteinase enhancer-1[5,6], membrane collagens, and integrins[7], which are ECM receptors. This allowed us to find new biological functions of these proteins. We have also created an interaction database, called MatrixDB (http://matrixdb.univ-lyon1.fr/, a member of the International Molecular Exchange consortium) to store interaction data[8], and build interaction networks specific of a protein, a GAG, a tissue, a biological process or a disease thanks to the advanced query interface we have developed[8]. We have designed a pipeline to translate the GAG sequences binding to proteins in a computer-readable format and into 3D models for docking with proteins[9], and we have built the comprehensive interaction networks of the six mammalian GAGs (841 partners), and of the four membrane proteoglycan syndecans[10] (351 partners).

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