S009 Large-scale detection of low-affinity extracellular protein interactions

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Extracellular protein interactions are essential to initiate signalling pathways that orchestrate individual cellular behaviours within a multicellular organism. Despite their importance, an overall view of extracellular protein interaction networks is still lacking because existing high throughput protein interaction assays are not generally suitable to detect this class of interactions. To address this, we have developed AVEXIS (AVidity-based EXtracellular Interaction Screen), a high throughput assay that can detect direct physical interactions between recombinant soluble ectodomain fragments expressed in mammalian cells. Using this assay and a large protein library consisting of the ectodomain fragments of zebrafish immunoglobulin superfamily and leucine-rich repeat receptor proteins, we have compiled the first extracellular protein interaction network. I will present a comparative analysis with other protein interaction networks and show how we are using the experimental advantages of the zebrafish model organism to functionally analyse some of these interactions *in vivo.* I will also show how we are developing this technology to identify novel cell surface receptor-ligand pairs in other biological settings.