# Integrative network-based analysis for subtyping and cancer driver identification

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Inter-cellular communication is critical to coordinate cellular function in tissue during steady state and inflammation. Few efforts have been done to reconstruct cell communication networks. In addition, the molecular events shaping communication and connectivity within inter-cellular networks are not known. This question is particularly relevant to immune cells during controlled and dysregulated inflammation. We have developed an original systems biology framework to reconstruct cell connectivity networks based on transcriptomics data of purified cell types. In cultured human dendritic cells (DC), we could show that LPS activation promotes an increased cell connectivity, which is controlled by an IL-10 auto-regulatory loop. Blocking endogenous IL-10 increased communication of DC with 12 distinct cell types. Experimental validation was obtained for four communication channels. Results show that a single molecule can control communication of one cell with multiple other cell types. We are now applying this and other strategies to the tumour microenvironment, in order to attempt deciphering the complex cellular networks engaged during tumour inflammation. A combination of molecular and cellular data can be used to infer intercellular communication paths, with the ultimate perspective of reconstructing and modelling complex cell networks. These should be valuable tools to better understand the organisation of anti-tumour immune responses and guide therapeutic manipulations.