

## "First evidence of Cancer-Immune System crosstalk in a Microfluidic Device"

**Abstract:** The reconstitution of a complex microenvironment on microfluidic chips is one of the cornerstones to demonstrate the improved flexibility of these devices with respect to macroscale in vitro approaches. In this work, we realised an on-chip model to investigate the interactions between cancer and immune system. B16 cells (melanoma) and immune cells isolated from the spleen of wild type (WT) and IRF-8 KO mice (deficient, KO, for interferon regulatory factor 8) were co-cultured for one week in a PDMS platform and monitored by fluorescence microscopy and time-lapse recordings. In vivo, IRF-8 KO mice are highly permissive to B16 melanoma growth due to failure of immune cells to properly exert immunosurveillance. We observed that WT spleen cells migrated through microchannels connecting the culturing chambers towards B16 cells and tightly interacted with tumor cells, forming clusters of activation. In contrast, IRF-8 KO immune cells poorly interacted with melanoma cells. In parallel, B16 cells were more attracted towards microchannels acquiring a more invasive behaviour in the presence of IRF-8 KO spleen cells, with respect to WT cells. Our results strongly confirm the in vivo observations and highlight the value of on chip co-culture systems as a useful in vitro tool to elucidate the reciprocal interactions between cancer cells and host immune system