Role of macrophages in growth and progression of breast cancer

Macrophages and tumor cells mutually influence each other’s behaviour in majority of cancers, with the tumor cell attracting macrophages and sustaining their survival and they, in turn, producing a myriad of factors to promote or regulate tumor growth and angiogenesis. The pro-inflammatory cytokine cocktail of TNF-α, IL-1β and IL-6 secreted by macrophages (Mϕ) induce secretion of TGF-β1 in MCF7 cells. This results in dichotomy of responses with apoptosis in a fraction of cells and activation of MAPK pathway, increase in redox signalling and DNA damage response in the remaining cells. All these events triggered CREB mediated survival signalling inducing EMT responses. Blocking of all the upstream events resulted in abrogation of MϕCM induced pCREB expression and migration. The effect of these macrophages seems to be differential since the highly invasive MDA-MB-231 cells already having a high basal level of ROS/ATM/CREB signaling axis seems to be tolerant to further induction. Many other crucial players present in macrophage secretome were identified apart from the proinflammatory cytokines. All these proteins play a functional role in tissue remodelling, breakdown of extracellular matrix, membrane trafficking and cell migration. The crucial players of this macrophage –tumor cell interaction identified from the in vitro study were also subjected to validation in clinical benign and invasive ductal carcinoma (IDC) samples. A statistically significant higher expression of iNOS and CREB was observed in IDC samples as compared to the benign fibroadenoma samples. High coincidental expression of iNOS and p53 protein accumulation was observed. Expression of pCREB was significantly but inversely associated with the staging of the IDC samples and p53 expression was significantly associated with expression of hormone receptors in IDC samples.
List of Publications arising from the thesis

Journal


Conferences
