

The international debate on Role of the proinflammatory cytokine IL-1 β in breast cancer progression to malignancy

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In the tumor inflammatory microenvironment, interleukin-1 β (IL-1 β) has been associated with tumor development, invasiveness, metastasis and initiation of the epithelial to mesenchymal transition (EMT). Using a model of breast cancer non-invasive cells, we have recently demonstrated that IL-1 β triggers the activation of a signaling pattern, not previously described, named as IL-1 β /IL-1RI/ β -catenin that induces accumulation of β -catenin in the nucleus and GSK1 inactivation by AKT phosphorylation. Translocation of β -catenin to the nucleus and formation of the TCF/Lef/ β -catenin complex causes sequential expression of genes that leads to up-regulation of cell proliferation, migration and invasion. By the activation of these processes, the IL-1 β -stimulated cells enter the transition program, from a non-invading to an invading phenotype, known as EMT. Initial results on a selected MCF-7 cell clone (6D) highly sensitive to IL-1 β showed that IL-1 β up-regulated SNAIL, c-MYC and MMP2, genes involved in replication and invasion. Subsequent RNA-seq showed direct correlation

between upregulation of cell survival and drug resistance genes such as BIRC3, CDKN1A, TP63 and BCL2. Our results with this 6D cell model, in which EMT has been induced by IL-1 β , showed that methylation of the ESR1 promoter occurred as consequence of the up-regulation of TWIST1 through the cytokine activated pathway, leading to decreased levels of the oestrogen receptor ER α , as observed in aggressive breast cancer tumors classified as triple negative. We hope that our results showing some of the mechanisms by which an inflammatory environment influences malignancy will draw attention to this aspect of cancer pathology and the possibility for using new therapeutic schemes in its treatment.

Biography

Isaura Meza graduated from the University of California, Berkeley and has always been interested in cell motility mechanisms. She has done her Post-doctoral studies from the University of Geneva. She works as a Professor at CINVESTAV in Mexico City.