Role of glycosylation in hypoxia-driven cell migration and invasion

Arriagada, Cecilia

Silva, Patricio

Torres, Vicente A.

Hypoxia, a common condition of the tumor microenvironment, induces changes in the proteome of cancer cells, mainly via HIF-1, a transcription factor conformed by a constitutively expressed ?-subunit and an oxygen-regulated ?-subunit. In hypoxia, HIF-1? stabilizes, forms the heterodimeric complex with HIF-1?, and binds to Hypoxia Response Elements (HRE), activating gene expression to promote metabolic adaptation, cell invasion and metastasis. Furthermore, the focal adhesion kinase, FAK, is activated in hypoxia, promoting cell migration by mechanisms that remain unclear. In this context, integrins, which are glycoproteins required for cell migration, are possibly involved in hypoxia-induced FAK activation. Evidence suggests that cancer cells have an altered glycosylation metabolism, mostly by the expression of glycosyltransferases, however the relevance of glycosylation is poorly explored in the context of hypoxia. Here, we discuss the role of hypoxia in cancer, and its effects on protein glycosylation, with emphasis on integrins and cell migration.