

Research on the Role of Platelet Derived Growth Factor Receptor Beta in Promoting Dedifferentiation and Pulmonary Metastasis of Osteosarcoma Under Hypoxic Microenvironment

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Abstract : Abstract: Hypoxia and dedifferentiation of osteosarcoma (OS) cells leads to poor prognosis. We plan to identify the role of hypoxia on dedifferentiation and the associated signaling pathways. We performed a sphere formation assay and determined spheroid cells as dedifferentiated cells by detecting stem cell-like markers. RNAi assay was used to explore the expression relationship between hypoxia inducible factor 1 subunit alpha (HIF1A) and platelet derived growth factor receptor beta (PDGFRB). We obtained PDGFRB knockdown and overexpression cells through lentiviral infection experiments and the effects of PDGFRB on cytoskeleton rearrangement and cell adhesion were explored by immunocytochemistry. Wound-healing experiments, transwell assays, and animal trials were employed to investigate the effect of PDGFRB on OS metastasis. Dedifferentiated OS cells were found to exhibit high expression of HIF1A and PDGFRB, and HIF1A promoted the expression of PDGFRB, subsequently activated ras homolog family member A (RhoA), and increased the phosphorylation of myosin light chain (MLC). PDGFRB also enhanced the phosphorylation of focal adhesion kinase (FAK). The OS cell morphology and vinculin distribution were altered by PDGFRB. PDGFRB also promoted cell dedifferentiation and had a significant impact on the metastasis of OS cells both in vitro and in vivo. Our results demonstrated that HIF1A up-regulated PDGFRB under hypoxic conditions, and PDGFRB regulated the actin cytoskeleton by activating RhoA and subsequently phosphorylating MLC, thereby promoting OS dedifferentiation and pulmonary metastasis.

Keywords : osteosarcoma, dedifferentiation, metastasis, cytoskeleton rearrangement, PDGFRB, hypoxia

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