Pyruvate Kinase type M2 (PKM2) Promotes Cancer Cell Metastasis Through Interacting with TWIST-1

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Abstract

Tumor growth and metastasis are key processes in understanding tumor progression and cancer fatality. Pyruvate Kinase type M2 (PKM2) is a key enzyme that regulates glucose metabolism in cells in a biochemical pathway known as glycolysis. Glycolysis provides cells with energy (ATP) and building blocks (nucleic acids, amino acids and lipids) that are critical for cell survival and proliferation. Therefore, cancer cells rely heavily on this metabolic process to survive and thrive. PKM2 is overexpressed in most cancers, and is highly involved with cancer cell growth. Several recent studies have further revealed a potential role of PKM2 in regulating epithelial-mesenchymal transition (EMT[PTT1]) and cancer cell metastasis. The aim of this study is to study the mechanisms by which PKM2 regulates EMT and promotes cancer metastasis.

In our previous studies, we identified a potential Pkm2 protein interacting partner - Twist1 protein. Twist1 is a key transcription factor that regulates EMT and cancer metastasis. It has been reported that the nuclear translocation of PKM2 can regulate transcriptional activity of several other transcription factors. Therefore, the interaction between Pkm2 and Twist1 can potentially enhance Twist1 transcriptional activity in EMT and metastasis.

In the current study, we are knocking out the *PKM2* gene in cancer and immortalized primary cell lines by using the CRISPR-Cas9 system. We will study the changes in cell proliferation and migration after knocking out *PKM2*. Later, we will overexpress TWIST1 in these cells by using plasmid transfection or viral infection and study whether TWIST1 can restore the cells to their original phenotype.

Keywords

Metastasis; EMT

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Tumor growth and metastasis are key processes in understanding tumor progression and cancer fatality. Pyruvate Kinase type M2 (PKM2) is a key enzyme that regulates glucose metabolism in cells in a biochemical pathway known as glycolysis. Glycolysis provides cells with energy (ATP) and building blocks (nucleic acids, amino acids and lipids) that are critical for cell survival and proliferation. Therefore, cancer cells rely heavily on this metabolic process to survive and thrive. PKM2 is overexpressed in most cancers, and is highly involved with cancer cell growth. Several recent studies have further revealed a potential role of PKM2 in regulating epithelial-mesenchymal transition (EMT[PTT1]) and cancer cell metastasis. The aim of this study is to study the mechanisms by which PKM2 regulates EMT and promotes cancer metastasis.

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