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EXTRACELLULAR PKM2 FACILITATES WOUND HEALING BY PROMOTING MYOFIBROBLAST DIFFERENTIATION

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Injury induced tissue regeneration often starts with inflammation responses. The infiltrated neutrophils and/or macrophages release various different cytokines and growth factors that promotes myofibroblast differentiation. Myofibroblast plays a key role in tissue regeneration and reconstruction. However, sustained myofibroblast differentiation and survival lead to fibrosis. We report here that infiltration neutrophils at the wound site release PKM2, a glycolytic enzyme, by its secretive mechanisms during early stages of regeneration. The extracellular PKM2 facilitates wound healing by promoting early granulation and angiogenesis. PKM2 facilitates formation of early granulates by promoting fibroblast migration and myofibroblast differentiation. Extracellular PKM2 also protects myofibroblasts from apoptosis. We demonstrated that extracellular PKM2 promotes myofibroblast differentiation by a TGF β independent pathway via activation of integrin α v β 3 signaling. Our studies uncovered a novel mechanism of integrin activation. Extracellular PKM2 activates integrin α v β 3 by binding to head open integrin and facilitating a “leg” separation conformation. Our studies reveal a new molecular linker between the early inflammation response and proliferation phase in tissue regeneration process. Our studies also uncover a novel mechanism of promoting myofibroblast differentiation.

Biography

Zhi-Ren Liu is a Professor in Department of Biology, Georgia State University, Atlanta, USA. He completed his Ph.D in Biochemistry from Florida State University in 1994. The goal of our research is to understand the molecular mechanism of cell abnormality, especially the conditions that are associated with many human diseases. We hope that our understanding will ultimately be converted to the development of new diagnostic and therapeutic strategies. Currently, we are focus on following two separate research projects: Function of p68 RNA helicase in cell developmental program and tumor progression. His research area of interest is Molecular Biology & Cancer Biology.

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