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Hypoxia promotes satellite cell self-renewal and enhances the efficiency of myoblast transplantation

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Microenvironmental oxygen level is a critical regulator of stem cell activity, and a hypoxic niche has been reported in multiple stem cell types to regulate their stemness. Satellite cells are muscle resident stem cells that maintain the homeostasis and mediate the regeneration of skeletal muscles. We demonstrate here that hypoxic culture conditions favor the quiescence by promoting asymmetric self-renewal divisions and inhibiting the asymmetric differentiation divisions without affecting the proliferation of satellite cell-derived primary myoblasts. Mechanistic studies reveal that hypoxia upregulates Pax7, a key regulator of satellite cell self-renewal, via downregulating miR-1 and miR-206. Gain- and loss-of-function studies show that the Notch signaling pathway, activated by hypoxia, represses expression of both miR-1 and miR-206. More importantly, hypoxia conditioning enhances the efficiency of myoblast transplantation and the self-renewal of implanted cells. Given the robust effects of hypoxia on maintaining the quiescence and promoting the self-renewal of cultured myoblasts, we predict that oxygen levels in the satellite cell niche play a central role to precisely balance the quiescence versus activation, and self-renewal versus differentiation, of muscle stem cells in vivo.

Biography

Shihuan Kuang received his Ph.D from University of Alberta and postdoctoral studies from Washington University School of Medicine and Sprott Center for Stem Cell Research, Ottawa Hospital Research Institute. He is currently an assistant professor at Purdue University and his research concerns stem cell-based therapies to treat degenerative muscle diseases such as Duchenne Muscular Dystrophy. Dr. Kuang has published more than 40 papers in reputed journals and serving as an editorial board member of Cloning & Transgenesis.

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