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Mir-302 contributes to tumorigenicity through promoting G1 to S transition and maintaining OCT4 overexpression by inhibiting AKT1

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Abstract

The tumorigenicity of human pluripotent stem cells (hPSCs) has been considered to be a major hurdle for their clinical applications. Here, we found that downregulation of miR-302 suppresses the tumorigenicity of hNT-2 cells (a human embryonal carcinoma pluripotent stem cell line). By gain- and loss-of-function approaches, we demonstrated that miR-302 promotes the proliferation and tumorigenicity of hPSCs through the dominant regulation of a set of cell cycle inhibitors and subsequent acceleration of the G1 to S transition. Importantly, we also found that downregulation of miR-302 damages the self-renewal and pluripotency, and promotes differentiation of hPSCs. The underlying mechanism is that high endogenous expression of miR-302 suppresses the expression of Akt1 by directly targeting its 3'UTR, and subsequently maintains pluripotent factor OCT4 at high level in hPSCs. However, overexpression of miR-302 in human mesenchymal stem/stromal cells (hMSCs) dose not leads to tumor formation in vitro or in vivo. These findings indicated that in human pluripotent stem cells miR-302 is not a causal factor, but just a contributing factor for the tumorigenicity through promoting G1 to S transition and maintaining OCT4 at high level by directly inhibiting AKT1.

Biography

Robert Chunhua Zhao, M.D., Ph.D is Cheung Kong Professor, Director of Center for Stem Cell and TE at CAMA& PUMC, the chief scientist of National 973 Basic Research Program of China and a Regional Editor of the Journal of Stem Cells and Development. His research is directed at studying the fundamental properties of stem cells and translating their unique biological properties into clinical application. In 2004 his group won the first official approval of “mesenchymal stem cell” from SFDA as to start clinical trials in China. Dr. Zhao has published 212 papers in international and domestic journals.