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Role of bromodomain extra terminal proteins in cellular reprogramming

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Pluripotent stem cells (PSCs) have differentiation potentials into any type of cells in our bodies and therefore hold great promise for regenerative medicine. The conventional PSCs are embryonic stem cells (ESCs) derived from the inner cell mass (ICM) of a pre-implantation embryo. The clinical application of ESCs is hampered by issues of ethical concern, technical limitation, a limited supply of human embryos, and non-autologous nature. PSCs can be induced from fibroblasts or other somatic cells by ectopic expression of a few transgenes, e.g. OCT4, SOX2, KLF4, and C-MYC. Induced pluripotent stem cells (iPSCs) have removed many problems associated with the use of ESCs. However, iPSC reprogramming still has problems of low efficiency, incomplete reprogramming, epigenetic memory of the starting cells, stochastic nature, immunogenicity, and reprogramming-associated mutagenesis. The molecular mechanisms of iPSC reprogramming remain poorly understood. My lab found that proteins of bromodomain extra-terminal (BET) family play different roles in iPSC reprogramming process. By screening a human cDNA library, we discovered that a short isoform of human BRD3, BRD3R, displayed reprogramming activity while other BET proteins lack reprogramming activity. BRD3R also gains mitotic activities, which may be partially responsible for its gained reprogramming activity. Interestingly, our further detailed study showed that chemical inhibition of BET proteins at low concentration enhanced iPSC reprogramming by three distinct BET inhibitors, while a high concentration of these BET inhibitors impairs iPSC reprogramming. At the same time, our RNA-seq data showed that such mild chemical inhibition of BET proteins erased fibroblast transcriptional program. Our published and unpublished data indicate sophisticated roles of BET protein in cellular reprogramming.

Biography

Kejin Hu received his PhD degree in animal molecular biology in 2003 from Hong Kong University. He received postdoctoral training in human pluripotent stem cell biology at University of Wisconsin – Madison. He has more than 12 years of experience in pluripotent stem cells and cellular reprogramming. He has established his own laboratory at the Department of Biochemistry and Molecular Genetics, University of Alabama at Birmingham (UAB). He is currently an Assistant Professor in stem cell biology and cellular reprogramming at UAB. He has been involved in the improvement of iPSC technology. His method of iPSC reprogramming is widely used, and human iPSC lines he generated are also widely used. He has authored more than 20 scientific articles. His lab is deciphering the molecular regulation of pluripotency, and dissecting the molecular mechanisms of cellular reprogramming. The works from his laboratory enhance our understanding of iPSC reprogramming process. His research is supported by Alabama Institute of Medicine, American Heart Association, and NIH.

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