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Transcriptional control of stem cell pluripotency and somatic cell reprogramming

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Embryonic stem cells (ESCs) derived from preimplantation blastocysts have unique self-renewal and multilineage differentiation properties that are controlled by key components of a core regulatory network including Oct4, Sox2 and Nanog. Understanding molecular underpinnings of these properties requires identification and characterization of additional factors that act in conjunction with these key factors in ESCs. We have previously identified Zfp281, a Krüppel-like zinc finger transcription factor, as an interaction partner of Nanog. We now present detailed functional analyses of Zfp281 using a genetically ablated null allele in mouse ESCs. Our data show that while Zfp281 is dispensable for establishment and maintenance of ESCs, it is required for their proper differentiation *in vitro*. We performed microarray profiling in combination with previously published datasets of Zfp281 global target gene occupancy, and found that Zfp281 mainly functions as a repressor to restrict expression of many stem cell pluripotency genes. In particular, we demonstrated that deletion of Zfp281 resulted in up-regulation of Nanog at both the transcript and protein levels with concomitant compromised differentiation of ESCs during embryoid body culture. Chromatin immunoprecipitation experiments demonstrated that Zfp281 is required for Nanog binding to its own promoter, suggesting that Nanog-associated repressive complex(es) involving Zfp281 may fine-tune Nanog expression for pluripotency of ESCs. We also presented evidence that Nanog autorepression requires the coordinated action of Zfp281 and other co-repressor complexes associated with the Nanog interactome. Finally, we show that Zfp281-mediated Nanog autorepression may pose a roadblock to efficient iPSC generation during somatic cell reprogramming

Biography

Jianlong Wang has completed his Ph.D in 2000 from University of Massachusetts at Amherst and postdoctoral studies from University of North Carolina at Chapel Hill and Harvard Medical School. He is currently an Assistant Professor at the Department of Developmental and Regenerative Biology, Black Family Stem Cell Institute in the Mount Sinai Medical Center. He has published more than 26 papers in reputed journals and serving as an editorial board member of Journal of Stem Cell Research and Therapy (JSCRT)

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