Telomere reprogramming early in development and cloning

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Stem cells and cancer cells maintain telomere length mostly through telomerase. Telomerase activity is high in male germ line and stem cells, but low or absent in mature oocytes and cleavage stage embryos, and high again in blastocysts. How early embryos reset telomere length remains poorly understood. We show that oocytes actually have shorter telomeres than somatic cells, but their telomeres lengthen remarkably during early cleavage development. We further suggest that telomeres lengthen during the early cleavage cycles following fertilization through a recombination-based mechanism, and that from the blastocyst stage onward telomerase only maintains the telomere length established by this alternative mechanism. It is also interesting to note that telomeres are reprogrammed in cloned calves following nuclear transfer and that telomeres are lengthened in cloned mice with each generation. Yet, when and how telomere length is regulated in cloned embryos remains poorly understood. Interestingly, our work shows that telomere reprogramming might be length dependent. We also found that appropriate telomerase activity is required for differentiation of stem cells. Our findings that telomeres lengthen considerably during early cleavages may help clarifying the basic questions of how telomeres reset during development, and have implications for the study of stem cell and regenerative biology, aging and cancer biology.

Keywords: telomere, telomerase, embryo, stem cells

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Lin Liu, received Doctorate degree in Reproductive Biology and Biotechnology from Beijing Agricultural University. He was a visiting scholar at the BBSRC Babraham Institute, Cambridge, UK, and then had two year post-doctorate training in Cornell University and University of Connecticut, USA. He worked as an Investigator and Assistant Professor (Research) at Women & Infants Hospital/Brown Medical School. He is Professor in Nankai University, Adjunct Assistant Scientist at Marine Biological Laboratory, Visiting Assistant Professor at the University of

South Florida College of Medicine, and Member of H Lee Moffitt Cancer Center & Research Institute. He has been a member of American Association for the Advancement of Science (AAAS), Society for the Study of Reproduction (SSR), International Embryo Transfer Society (IETS), New York Academy of Sciences (NYAS), and council member of Reproductive Biology under Zoological Society China. Dr Liu's research focuses on reproductive aging and egg senescence, molecular mechanisms underlying early embryo development and differentiation, and differentiation of adult stem cells. He is also interested in derivation and understanding of patient-specific stem cells that can be effectively used for regenerative medicine, particularly for treatment of reproductive aging and associated diseases.