

Viable interspecies chimeras created by injection of *Apodemus* embryonic stem cells into *Mus* blastocysts

Andy Peng Xiang^{1,*}, Frank Fuxiang Mao^{1,2,*}, Donghyun Park², Bao-Feng Ma¹, Wei-Qiang Li¹, Tao Wang¹, Tammy W Vallender², Eric J Vallender², Li Zhang², Jaehyun Lee², John A Waters³, Xiu-Ming Zhang¹, Xin-Bing Yu¹, Shu-Nong Li¹, Bruce T Lahn^{1,2}

¹Center for Stem Cell Biology and Tissue Engineering, Sun Yat-sen University, Guangzhou 510080, China; ²Howard Hughes Medical Institute, Department of Human Genetics, University of Chicago, Chicago, IL 60637, USA; ³Department of Veterinary Clinical Sciences, University of Liverpool, UK

Embryonic stem (ES) cells can differentiate into a variety of specialized cell types when introduced into early embryos (i.e., morulas or blastocysts) of the same species. A question of medical and basic biological importance is whether ES cells of one species can differentiate properly and contribute significantly to chimerism when placed within early embryos of another distantly related species. Here, we address this question using two divergent mammalian model organisms, *Apodemus sylvaticus* and *Mus musculus*, whose genomes differ by about 15%. Despite this considerable evolutionary distance, injection of *Apodemus* ES cells into *Mus* blastocysts led to viable chimeras bearing extensive *Apodemus* contributions in all the major organs. Immunostaining showed that *Apodemus* ES cells had differentiated into a wide range of cell types in the chimeras. These results support the feasibility of deriving a variety of specialized cells or perhaps even complex tissues from ES cells of one species by placing them in the blastocysts of another divergent species. Our data also highlight the remarkable evolutionary conservation of developmental signaling by revealing its compatibility between two rather distantly related organisms.

Keywords: interspecies, chimera, *Apodemus sylvaticus*, *Mus musculus*, embryonic stem cells, blastocyst, microinjection
Cell Research (2008) 18:s32. doi: 10.1038/cr.2008.122; published online 4 August 2008

*These two authors contributed equally to this work.

Correspondence: Andy Peng Xiang^a, Bruce T Lahn^b

^aE-mail: xiangp@mail.sysu.edu.cn

^bE-mail: blahn@bsd.uchicago.edu

Andy Peng Xiang, PhD, Dr Xiang received a PhD in biochemistry and molecular biology from West China University of Medical Sciences and took postdoctoral training in Department of Human Genetics, University of Chicago. He is current Associate Professor in Sun Yat-sen University,

Director of Center for Stem Cell Biology and Tissue Engineering, SYSU. He has received funding from National Natural Science Foundation of China, the Key Scientific and Technological Projects of Guangdong Province, etc. He has published more than 30 papers in peer-reviewed journals, such as *Human Molecular Genetics*, *Rejuvenation Research*. Dr Xiang research focused on the molecular mechanisms of stem cells self-renewal and multi-differentiation. Please visit his website for more details. [http:// www.stemcells.cn](http://www.stemcells.cn)