Asymmetric cell division and stem-cell homeostasis

Weimin Zhong¹

¹Department of Molecular, Cellular and Developmental Biology, Yale University, New Haven, Connecticut, USA

Asymmetric cell division is a process by which a cell divides to produce two different daughter cells. Conceptually, such divisions are an attractive means for stem cells to balance the needs of self-renewal and differentiation during organogenesis and tissue maintenance, by producing one daughter cell that self-renews and another that differentiates. Studies using invertebrates show that intrinsically asymmetric cell divisions are made possible by a complex, but evolutionarily conserved, molecular machinery that polarizes cells and subsequently enables cell fate determinants to be differentially inherited by the two daughter cells, thereby allowing them to adopt different fates. A key determinant of asymmetric cell fates in *Drosophila* is Numb, a cytoplasmic signaling protein. To examine the importance of asymmetric cell division in mammalian development, we used molecular and genetic approaches to examine the roles played by the mammalian Numb homologues during mouse neurogenesis. Our findings show that the two mouse *numb* genes, *m-numb* (*Numb*) and *numbl* (*Numbl*), are functionally redundant and that asymmetric segregation of the Numb proteins and, therefore, asymmetric cell division are essential for stem/progenitor cells to balance self-renewal and differentiation. We further show that stem-cell numbers are strictly controlled *in vivo* and that tumor suppressors likely play a key role in maintaining stem-cell homeostasis. We also provide evidence that Golgi fragmentation and reconstitution during cell cycle dynamically regulate Numb signaling and represent a novel mechanism for coupling cell-fate determination and cell-cycle progression. We propose that Numb-mediated asymmetric cell division is a mechanism shared by stem cells in many tissues for their progeny to choose between self-renewal and differentiation.

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Correspondence: Weimin Zhong
E-mail: weimin.zhong@yale.edu

Weimin Zhong is an Associate Professor of Molecular, Cellular and Developmental Biology at Yale University. He received his PhD at Rockefeller University in 1993, after studying at Peking University (1981-1984) and Peking Union Medical College (1984-1988). He was a postdoctoral fellow at the Howard Hughes Medical Institute and Department of Physiology at the University of California, San Francisco,

before joining Yale faculty in 1999. Research in his laboratory focuses on the fundamental biology of stem cells and currently investigates how neural stem cells are maintained and neuronal diversity is generated in the mammalian nervous system. He has served on expert panels at the National Institutes of Health, American Cancer Society, and National Natural Science Foundation of China. He is also a section editor for *Neuroscience*, the official journal of the International Brain Research Organization (IBRO).