

# FULL SPEAKER BIOGRAPHY and ABSTRACT

**Kevin Eggan, PhD**  
Harvard University

Kevin Eggan is a developmental biologist at the forefront of addressing fundamental questions about cellular differentiation and plasticity; in addition to their importance to basic biology, these questions hold essential implications for developing therapeutic stem cell lines from adult cell nuclei. His research explores the mechanisms by which somatic cell nuclear transfer (cloning) can reverse the differentiation of a cell by “reprogramming” its nucleus to the totipotent state. His accomplishments place him at the forefront of a most exciting new branch of biology: the use of nuclear transfer and stem cell technologies to explore mammalian development, i.e., how a single cell grows into a complex organism. In an important study of X chromosome inactivation in cloned mouse embryos, Eggan demonstrated that the nuclear transfer procedure leads to epigenetic reprogramming of the donor genome. More recently, he showed that nuclei of even highly specialized cells, such as olfactory neurons which express only a single odorant receptor, retain full developmental potential. After careful review by independent human subjects and ethics panels, Eggan received permission in June 2006 to initiate efforts at Harvard to create embryonic stem cell lines from skin cells of patients suffering from several debilitating or terminal diseases. By exploring the possibilities of redirecting stem cells from adult tissue or differentiated tissue, Eggan is moving us an important step closer to developing therapeutic applications for diseases such as Amyotrophic Lateral Sclerosis and insulin-dependent diabetes, as well as providing an experimental platform for investigating the genetic and environmental factors that give rise to such diseases.

Kevin Eggan received a B.S. (1996) in microbiology from the University of Illinois, Urbana-Champaign, and a Ph.D. (2003) in biology from the Massachusetts Institute of Technology. He was a postdoctoral fellow at the Whitehead Institute for Biomedical Research (2002-2003) and a Junior Fellow in the Harvard Society of Fellows beginning 2003, prior to joining Harvard University's Department of Molecular and Cellular Biology as an assistant professor in 2005, then the newly developed Department of Stem Cell and Regenerative Biology. In 2006, he was also named an assistant investigator of the Stowers Medical Institute.

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## Using stem cells and reprogramming to understand neural degeneration

The combined activity of three transcription factors can reprogram adult cells into induced pluripotent stem (iPS) cells. However, the transgenic methods used to deliver reprogramming factors have raised concerns regarding the future utility of the resulting stem cells. These uncertainties could be overcome if each transgenic factor were replaced with a small molecule that either directly activated its expression from the somatic genome or in some way compensated for its activity. To this end, we have used high-content chemical screening to identify small molecules that can replace Sox2 in reprogramming. We show that one of these molecules functions in reprogramming by inhibiting Tgf- $\beta$  signaling in a stable and trapped intermediate cell type that forms during the process. We find that this inhibition promotes the completion of reprogramming through induction of the transcription factor Nanog.

### What is the central hypothesis of your presentation?

That adult somatic cells can be reprogrammed to pluripotency by the activity of small molecule compounds

### What is the most important observation you will discuss?

Most important observation: Will discuss the discovery of small molecules that replace reprogramming transgenes

### What is the translational significance?

That ultimately small reprogramming molecules will allow efficient and reliable production of safe pluripotent somatic cells