

FULL SPEAKER BIOGRAPHY and ABSTRACT

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Susan McConnell received her A.B. degree in Biology from Harvard and Radcliffe Colleges in 1980 and her Ph.D. in Neurobiology from Harvard University in 1987. She joined the Stanford faculty in 1989 and is currently the Susan B. Ford Professor of Humanities and Sciences. McConnell is interested in how neural circuits are established during mammalian brain development. She studies the mechanisms by which young neurons are generated, acquire an identity, and establish specific connections in the developing cerebral cortex. McConnell is a member of the American Academy of Arts and Sciences and has received the Society for Neuroscience Young Investigator Award.

Building the cerebral cortex: neuronal fate determination

During the development of the mammalian cerebral cortex, progenitor cells produce neurons that migrate into specific laminar positions, adopt discrete neuronal identities, and form appropriate local and long-distance axonal connections. An essential step in the creation of neural circuits is the specification of neurons that form local connections within the cerebral cortex, and of those that extend axons to subcortical targets such as the spinal cord. We have identified two opposing genetic pathways that confer a cortico-cortical vs. subcortical projection neuron identity onto differentiating neurons. *Fezf2*, a putative zinc-finger transcriptional repressor, is required for the differentiation of subcortical projection neurons in cortical layer 5. The disruption of *Fezf2* (or its downstream target, *Ctip2*) leads to molecular, physiological, and axonal targeting defects in these neurons, which fail to form normal projections into the corticospinal tract and instead project axons to the contralateral cerebral hemisphere. Mutant neurons also adopt the electrophysiological properties and patterns of gene expression typical of callosal projection neurons. A complementary pathway is required for the differentiation of callosal (cortico-cortical) projection neurons, which normally express the chromatin remodeling protein *Satb2*. In *Satb2* mutant mice, neurons that normally extend axons across the corpus callosum to the contralateral cerebral hemisphere instead form subcortical projections along the corticospinal tract. These cells also acquire the expression of *Ctip2*. *Satb2* binds directly to the *Ctip2* locus, where it confers repressive modifications to histone H3. Collectively our data suggest that the choice by an individual neuron to express either *Fezf2* or *Satb2* constitutes an essential step in the elaboration of a subcortical or cortico-cortical projection neuron identity

What is the central hypothesis of my presentation?

The fates of cortical projection neurons are determined by the expression of the DNA binding proteins *Fezf2* and *Satb2*.

What is the most important observation I will discuss?

Most important observation: Mutation of *Fezf2* or *Satb2* results in fate shifts by cortical neurons, revealing a bistable switch between subcortical and corticocortical projection neuron identity.

What is the translational significance?

Understanding the transcriptional control of fate determination offers insights into methods by which to direct the fates of multipotent stem cells into cortical neurons with specific patterns of axonal projections.