Expression of Notch Proteins in Pyramidal Neurons in Vivo

In their recent study, Zheng et al. (1) concluded that Notch1 and Notch2 are not expressed in pyramidal neurons in the postnatal mouse forebrain. This conclusion was based upon an inability to detect expression changes in vivo after presumptive deletion using their CaMKII-Cre line (2, 3). Unfortunately, the authors provided no direct evidence that they efficiently deleted Notch1 or Notch2 in pyramidal neurons in vivo. They infer such deletion because (a) their Cre driver deleted other loci in pyramidal neurons, (b) they detected recombined Notch1 and Notch2 alleles in brain tissue by PCR, and (c) Cre-expressing retrovirus could delete both alleles in vitro. However, (a) recombination efficiency varies at different loci (4), (b) PCR detection of deleted alleles in tissue is uninformative regarding recombination efficiency and which cell type(s) harbor the deletion, and (c) confirming that these alleles are capable of being recombined (which was already known) does not prove that Notch1 and Notch2 were efficiently deleted in vivo using their Cre driver. Even if Zheng et al. had deleted Notch1 and Notch2 in neurons in vivo, the Northern and Western blots they employed to detect reduced expression would be inadequate if neuronal expression represents a modest fraction of the total Notch1 and Notch2 expression in the brain. In short, the authors have presented a collection of negative data, which are insufficiently compelling to contradict previous studies (including our own) indicating not only that Notch proteins are expressed in pyramidal neurons but that they serve essential functions in that context (5).

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