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**The death receptor CD95 activates adult neural stem cells for working memory formation and brain repair.**

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[**Author information**](http://www.ncbi.nlm.nih.gov/pubmed/19664992)

**Abstract**

Adult neurogenesis persists in the subventricular zone and the dentate gyrus and can be induced upon central nervous system injury. However, the final contribution of newborn neurons to neuronal networks is limited. Here we show that in neural stem cells, stimulation of the "death receptor" CD95 does not trigger apoptosis but unexpectedly leads to increased stem cell survival and neuronal specification. These effects are mediated via activation of the Src/PI3K/AKT/mTOR signaling pathway, ultimately leading to a global increase in protein translation. Induction of neurogenesis by CD95 was further confirmed in the ischemic CA1 region, in the naive dentate gyrus, and after forced expression of CD95L in the adult subventricular zone. Lack of hippocampal CD95 resulted in a reduction in neurogenesis and working memory deficits. Following global ischemia, CD95-mediated brain repair rescued behavioral impairment. Thus, we identify the CD95/CD95L system as an instructive signal for ongoing and injury-induced neurogenesis.