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Neural stem cells and neurospheres—re-evaluating the relationship

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For most of the past century, the prospect of replacing lost or damaged cells in the central nervous system (CNS) was hampered by the opinion that the adult mammalian CNS was incapable of generating new nerve cells. This belief, like most dogmas, was essentially founded on a lack of experimental evidence to the contrary. The overturning of this 'no new neuron' hypothesis began midway through the twentieth century with a series of reports documenting neurogenesis in the postnatal and adult brain¹, continued with the isolation and *in vitro* culture of neurogenic cells from the adult mammalian brain^{2, 3}, and culminated in the discovery of a population of multipotent, self-renewing cells in the adult CNS (that is, *bona fide* neural stem cells)^{3, 4, 5}. Although a variety of techniques were initially used, the neurosphere assay (NSA)^{3, 6} rapidly emerged as the assay of choice and has since become a valuable tool for isolating, and understanding the biology of, embryonic and adult CNS stem cells. Like all technologies, it is not without its limitations. In this article we will highlight several shortcomings of the assay related to its application and interpretation that we believe have led to a significant body of research whose conclusions may well be misleading.

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