Comparative analysis of the frequency and distribution of stem and progenitor cells in the adult mouse brain.

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Abstract

The neurosphere assay can detect and expand neural stem cells (NSCs) and progenitor cells, but it cannot discriminate between these two populations. Given two assays have purported to overcome this shortfall, we performed a comparative analysis of the distribution and frequency of NSCs and progenitor cells detected in 400 mum coronal segments along the ventricular neuraxis of the adult mouse brain using the neurosphere assay, the neural colony forming cell assay (N-CFCA), and label-retaining cell (LRC) approach. We observed a large variation in the number of progenitor/stem cells detected in serial sections along the neuraxis, with the number of neurosphere-forming cells detected in individual 400 mum sections varying from a minimum of eight to a maximum of 891 depending upon the rostral-caudal coordinate assayed. Moreover, the greatest variability occurred in the rostral portion of the lateral ventricles, thereby explaining the large variation in neurosphere frequency previously reported. Whereas the overall number of neurospheres (3730 +/- 276) or colonies (4275 +/- 124) we detected along the neuraxis did not differ significantly, LRC numbers were significantly reduced (1186 +/- 188, 7 month chase) in comparison to both total colonies and neurospheres. Moreover, approximately two orders of magnitude fewer NSC-derived colonies (50 +/- 10) were detected using the N-CFCA as compared to LRCs. Given only 5% of the LRCs are cycling (BrdU+/Ki-67+) or competent to divide (BrdU+/Mcm-2+), and proliferate upon transfer to culture, it is unclear whether this technique selectively detects endogenous NSCs. Overall, caution should be taken with the interpretation and employment of all these techniques.

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