COULD STEM CELL THERAPY RENEW YOUR BODY CELLS?

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An intriguing, novel phenomenon with possible therapeutic dividends has begun to emerge from our observations of the behavior of neural stem cells (NSCs) in various mouse models of CNS injury & degeneration. During phases of active neurodegeneration, factors seem to be transiently elaborated to which NSCs may respond by migrating (even long distances) to degenerating regions & differentiating specifically towards replacement of dying neural cells. In other words, NSCs may "attempt" to emulate in the brain what hematopoietic stem cells do in the periphery: repopulate & reconstitute ablated regions. These "repair mechanism" may actually reflect the re-expression of basic developmental principles (particularly during particular temporal "windows" following injury) that may be harnessed for therapeutic ends. In addition, NSCs may serve as vehicles for gene delivery and appear capable of simultaneous neural cell replacement & gene therapy (e.g., with factors that might enhance neuronal differentiation, neurite outgrowth, proper connectivity, and/or neuroprotection). Intriguingly, many of these factors are produced spontaneously by the stem cells based on their state of differentiation and do not require ex vivo genetic engineering (though that technique can be used to enhance the expression of certain molecules). When combined with certain synthetic biomaterials, NSCs may be even more effective in "engineering" the damaged CNS towards reconstitution.

An intricate meshwork of many highly-arborized neurites of both host- and donor-derived neurons emerges, and some anatomical connections appear to be reconstituted. The NSCs nestled within damaged brain, altered the trajectory and complexity of *host* neural connections. In a reciprocal manner, donor-derived neurons extended processes into host brain material as far as the opposite hemisphere. Of interest is the degree to which these neurons are capable of seemingly directed, target-appropriate outgrowth without specific external instructive guidance cues, induction, or genetic manipulation of host brain or donor cells. NSCs appear to unveil and/or augment a constitutive reparative response by facilitating a series of reciprocal interactions between NSCs and host CNS tissue (both injured and intact) including promoting neuronal differentiation, enhancing the ingrowth/outgrowth of neural processes, fostering the reformation of cortical tissue, and promoting connectivity following brain injury. Inflammation and scarring are also reduced, perhaps facilitating reconstitution. Interestingly, it is to areas of inflammation that NSCs are most drawn. Furthermore, not only gene expression programs, but also an epigenetic programs seem critical for dictating plasticity and potency.