Differences and similarities among phenotypes of mesenchymal and neural stem cells

Do stem cells in adult tissue retain some degree of plasticity? Is differentiation of their progeny dependent on the microenvironment rather than on their previous ontogenetic history? These are major issues common to hematology and neuroscience.

Despite controversial results, there is some evidence that at least a subpopulation of mesenchymal stem cells (MSC) derived from the bone marrow may differentiate into neural cells if challenged by the appropriate environmental cues.[1-4]

Conversely, freshly isolated fetal neural cells, a population enriched in neural stem cells (NSC), seem unable to repopulate the hematopoietic system of sublethally irradiated mice.[5] Moreover, under similar experimental conditions NSC expanded *in vitro* for many passages, contrary to what was initially shown,[6-7] are extremely inefficient in turning into blood cells.[8]

In this issue of Haematologica Vogel *et al.*[9] describe a systematic study of immunological markers present in mesenchymal stem cells and neural progenitor cells of human origin. This study contains three main indications of general interest:

- few antigens (CD90, CD164 and CD172a) are shared by cells of mesenchymal and neural origin, moreover, none of these antigens is limited to these two populations of cells or even to stem cells in general. CD90 is also expressed in endothelial cells, CD164 and CD172a are also expressed by other cell types, such as epithelial cells (CD164) and macrophages (CD164, CD 172a). Interestingly, nestin, an intermediate filament protein expressed by the majority of neural precursor cells, and by immature muscle and myocardial cells, is also expressed by some MSC;
- many antigens found on/in MSC are not detectable on/in NSC and *vice versa*;
- subpopulations of MSC and NSC were identified by morphologic criteria and the use of some antibodies, which reacted only with a subpopulation of MSC (e.g. W8B2) or NSC (e.g. CD33 and W8C3).

These results could improve our ability to identify these cells in a complex cellular mixture by vital methods such FACS and/or immuno-panning.

Neural cells freshly dissociated either from the developing brain or from neurospheres grown *in vitro* under the influence of basic fibroblast growth factor and epidermal growth factor do not represent a pure preparation of stem cells. Moreover the efficacy of methods proposed for neural stem cell purification[10-11] is still not validated by independent laboratories. Similar considerations can be made for MSC purification.

Further studies are necessary to determine whether positive and negative immunoselection using the panel of the markers described by Vogel and colleagues could increase our ability to purify MSC and NSC from complex cellular mixtures.

The results of the study by Vogel *et al.* indicating which antigens, from a large list of antibodies tested, are detectable by immunological techniques in MSC and NSC that have not been submitted to specific differentiation treatments are also helpful for a better understanding of the results of previous experiments on transdifferentiation. These experiments have been largely, if not exclusively, based on immunological techniques. Very recently Sanchez-Ramnos and collegues used nestin as a marker of transdifferentiation of MSC into neural-like cells after *in vitro* treatment. Interestingly, Vogel *et al.* now show that nestin is already expressed by a subpopulation of MSC even before applying specific treatments that should induce transdifferentiation.

In conclusion, stem cells purified from hematopoietic tissues may develop into a valuable resource for treating non-hematologic diseases; nevertheless, further studies on their biological properties are necessary before their non-controversial use could be justified in other fields such as neurology.

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