

## Adult Stem Cells: Plasticity, Trafficking and Therapeutic Placement

N. D. Theise<sup>1</sup>

<sup>1</sup>Beth Israel Medical Center, New York City, New York, United States

In the last half decade there has been ample demonstration that adult cells have the capacity to display multi- or totipotency that cross organ and developmental lineage boundaries which had previously been thought inviolate. These phenomena are referred to as “plasticity”; four different pathways of plasticity, perhaps better termed “differentiative potential” have now been described: 1. traditionally conceived stem/progenitor cell hierarchical lineage systems; 2. dedifferentiation of mature cells to a stem/progenitor cell phenotype with subsequent differentiation along a different lineage pathway; 3. direct differentiation of cells from one lineage to another without intervening dedifferentiation; 4. fusion of cells of different lineages (sometimes followed by nuclear fusion) leading to alterations in gene expression of one of the cells to the differentiation state of the other. Experiments to test the latter two of these pathways generally involve transplantation of cytogenetically or transgenically marked donor cells into recipient animals. Sites of cell delivery may be important in determining outcome and include placement of donor cells into the vascular tree (systemically or locally into a target organ), the bone marrow, intrasplenically, or directly into the parenchyma of a target organ. Many of these experiments are done in coordination with a selected organ injury model which appears to stimulate the process to detectable and sometimes to robust levels. Such experimental models are simultaneously early attempts at determining possible routes of delivery for therapeutic cell transplantation. In this regard, tracking of cells from point of delivery to final engraftment or demise would be extremely useful both theoretically and practically. MRI detection of labeled cells could therefore be an extremely useful adjunct to work in this field and, potentially, in the assessment of therapeutic outcomes if/when clinical trials become possible. Examples of experimental designs and of the first clinical trials to make use of plasticity effects will be highlighted.