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# Re-Programming or Selecting Adult Stem Cells?

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A Challenge to the "Re-Programming" Hypothesis of the Somatic Cell Nuclear Transfer Experiments. The recent observations that embryonic stemness associated genes could assist in the "de-differentiation" of adult skin fibroblast cells to "embryonic-like stem cells", using the "somatic cell nuclear transfer" techniques, have been interpreted as indicating a "re-programming" of genes. These reports have demonstrated a "proof of principle" approach to by-pass many, but not all, of the ethical, scientific and medical limitations of the "therapeutic cloning" of embryonic stem cells from embryos. However, while the interpretation that real "re-programming" of all those somatic fibroblastic differentiation genes might be correct, there does exists an alternative hypothesis of these exciting results. Based on the fact that multipotent adult stem cells exist in most, if not all, adult organs, the possibility exists that all these recent "re-programming" results, using the somatic nuclear transfer techniques, actually were the results of transferred rare nuclear material from the adult stem cells residing in the skin of the mouse, monkey and human samples. An examination of the rationale for this challenging hypothesis has been drawn from the hypothesis of the "stem cell theory of cancer", as well as from the field of human adult stem cells research. In view of the major paradigm- altering effects of the discovery of DNA as the molecular entity behind genetics, development of molecular biological techniques, and, more recently, the completion of the "Human Genome" project, the fact that one could take the molecular genetic information from a somatic differentiated tissue of an adult animal and re-program its genetic expression to clone an genetically identical individual has dramatically influence the thinking in many biological/medical fields, as well shifted the focus of research in these fields. Together with this discovery of cloning animals, the reports of isolating human embryonic stem cells have stimulated the field of "regenerative therapy" with embryonic stem cells, as well as with the use of stem cells for drug development and safety assessment, as well as for basic biology of gene regulation during development and differentiation. Even in the field of cancer research, while the concept of stem cells as targets for cancer has existed for a long time the introduction of the "cancer stem cell" has dramatically altered new research approaches to the understanding the origins of cancer and cancer therapy. The recent excitement over the discovery of the "relatively simple" approach, converting an adult somatic differentiated rodent, monkey, and human skin cells to an embryonic-like stem cells (albeit, at low frequencies and via different techniques), that could, in the case of the mouse, give raise to clone mice, has really opened new research potentials for the unique generation of embryonic-like stem cells .The emerging term in the fields of stem cell and molecular biology of gene expression is that of "re-programming". However, in these reports, none of the investigators seriously considered an alternative explanation of these results. This is illustrated by this statement: "The work of Park and colleagues, together with the related studies, proves beyond doubt that direct reprogramming is an efficient way of generating human pluripotent stem cells from adult cells." If the weight of the evidence, so far presented by these skilful and creative experiments, ultimately turn out to be correctly interpreted, many of the legal/ethical limitations might be overcome by the use of various nuclear somatic transfer techniques. Yet, as has been pointed out by all these investigators, these new observations, although pointing out a "proof of principle" approach, still pose major therapeutic problems, including, but not limited to, the potential formation of teratomas.