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TISSUE REPLACEMENT TO CURE HUMAN DISEASE

Chronic disease states such as Type 1 Diabetes, Parkinson's Disease, and Spinal Cord Injury result from the destruction of specific cells. Replacement of these tissues may provide immense relief, and possibly cure, of the disease.

One approach to replace these tissues is to find acceptable transplantation sources and implant donor cells into a patient. If these cells are derived from a source other than the patient, there will be problems with rejecting the "foreign" transplant material. Cloned patient cells (cells that are induced to replicate with the same DNA template as the patient) do not have foreign markers and theoretically would not be rejected. However, cloned cells as well as other cells still must overcome the problem of appropriate integration into the transplant site in order to replace the function of the destroyed tissue.

Shortly after conception, a human being has a unique DNA template from which *all* other cells (except some germ cells) are generated. A differentiated heart cell has the same DNA template as a differentiated skin cell, and they both have the same DNA template as the undifferentiated cells early in embryogenesis. Different areas of the DNA template are promoted and repressed, resulting in different cell functions. What areas of the DNA template are promoted and repressed are largely determined by environmental factors outside the cell. Thus, it is hypothetically possible to induce *any* cell to become any other kind of cell, if the right environment were provided.

The developing embryo is surrounded by different proteins and factors than later in development, but the DNA template remains the same throughout a person's life. One hypothesis is that if the correct embryonic environment could be duplicated, a patient-s cells might be induced to regenerate in a given site, as they rapidly do during embryogenesis. This would result in totally compatible, integrated replacement tissue for the disease being treated.

This concept was tested in an FDA monitored feasibility study in which patients with chronic diabetic foot ulcers were injected with an artificially made embryonic matrix at the ulcer site. Within days, all the patients experienced rapid diminution of ulcer size, with apparent regeneration of skin, blood vessels, and surrounding structures. In animal studies, the new tissue resulting from exposure to the embryonic-like matrix was determined to be structurally identical to non-wounded areas, without the usual scarring that is normally seen with healing lesions. Since the new tissue derived from the patient-s own tissue, there was seamless integration with no evidence of rejection.

Transplantation strategies, whether derived from foreign donors or cloned cells from patients themselves, are clearly not the only approach to replace damaged tissues. Other avenues are much further along in clinical trials, and should be considered as a first approach for study. Claims that only embryonic stem cells, or cloned tissues, can overcome problems of rejection are false. Indeed, the patient's existing cells provide the most rational source for fully integrating replacement tissues, as occurred during embryogenesis.

REFERENCES

Usala AL. Methods for increasing vascularization and promoting wound healing. US Patent #6,261,387; issued July 17, 2001.

Usala AL, Klann R, Bradfield J, Ray S et al: Rapid Induction of Vasculogenesis and Wound Healing Using a Novel Injectable Connective Tissue Matrix. Diabetes 49 (Supplement 1): Abstract 1664 PO, 2000.

Usala AL, Dudek R, Lacy S, Olson J, Penland S, Sutton J, Ziats NP, Hill RS: Induction of Fetal-Like Wound Repair Mechanisms *In Vivo* with a Novel Matrix Scaffolding. Diabetes 50:(Supplement 2)A488, #2048-PO, 2001.

Hill RS, Klann RC, Lloyd WH, Lacy SA, Pitts JD, Penland SL, Dudek R, Marston W, Usala AL: Improved wound healing of diabetic foot ulcers following treatment with a novel biopolymer. Abstract submitted to the ADA Annual Meeting, 2002.

Usala AL. On the Horizon: Current Research into Advanced Therapies for the Diabetic Foot Ulcer. Wound Management Symposium 2000, UNC Chapel Hill School of Medicine, Chapel Hill, NC, September 22, 2000.

lUsala AL. Current Research and Future Products. Wound Management Symposium 2001, UNC Chapel Hill School of Medicine, Chapel Hill, NC, September 29, 2001.