HAIR TRANSPLANT forum INTERNATIONAL

Volume 23, Number 1 • January/February 2013

Inside this issue

A review of cellular biopreservation considerations during hair transplantation

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Introduction

Appropriate clinical biopreservation of cells and tissues is a critical factor in hair transplantation procedures, as well as in regenerative medicine (cell therapies and tissue engineering) and organ preservation. During the course of a hair transplantation procedure, the cells and/or tissues experience multiple forms of stresses related to the procedure from before the donor strip and/or follicular units are extracted, through the dissection and graft holding stages, and past the point of re-implantation. There are certain cellular and biochemical aspects of the hair transplant model that are unique to the specific types of cells and tissues involved. However, there is also much that can be taken into consideration from other *in vitro* and clinical cell models relevant to regenerative medicine, as well as from existing organ/tissue preservation knowledge.

Under normal conditions, the environment of human cells and tissues consists of an isotonic osmotic balance of ions that is maintained by ATP-driven cell membrane pumps. Major ionic constituents include sodium, potassium, calcium, and magnesium—each regulated by membrane pumps/channels that, along with chloride, are actively pumped inside or outside the cell to counterbalance the osmotic pressure of non-permeable fixed molecules inside the cell and subsequently regulate the passive flow of water into and out of the cells. In this manner, although highly simplified, there is an intracellular milieu and an extracellular milieu that are distinctly different from one another. Under normothermic conditions (37°C, appropriate balance of oxygen/carbon dioxide, exchange of nutrients/wastes, etc.), the fluid bathing the cells and tissues is isotonic, or also referred to as extracellular-like. The normothermic flow of nutrients through the cellular metabolic pathways fuels the production of ATP (adenosine triphosphate) that, in turn, drives the membrane ion pumps to maintain the osmotic balance. Cellular waste products are expunged from the cells, and free radicals generated by normal metabolism are removed from potential negative impact by the cell's antioxidant mechanisms. Only once these basic cell processes for maintaining "life" are in working order can the cell's energies be directed to further functional cellular processes specific to that cell's "job."

When cells, tissues, and organs are disconnected from this "normal" set of conditions even for a short time, there are many potential unbalanced states leading to detrimental consequences. Absence of nutrients (glucose, oxygen, etc.) deprives the cells of the raw fuel components needed to generate the cell's refined fuel, ATP. Short-term interruptions to the cell energy cycle can be compensated with derivation of cellular energy via the lactic acid cycle but cannot be maintained indefinitely. However, it is important to appreciate that the overall cell machinery is a highly complex engine of parts and pathways that generates intermediate compounds from specialized reactions at specific steps, and that there are aspects of this cellular engineering that cannot currently be artificially replicated in the laboratory or by cell culture media. Furthermore, it is also important to remember the critical functions of waste removal and gas exchange, which often require specialized laboratory equipment to effectively compensate in the absence of the natural cellular mechanisms. Therefore, current attempts to replicate out-of-body normothermic conditions have the potential to be incomplete and suboptimal.

Cellular and Molecular Considerations for Biopreservation

Biopreservation can be described as processes that suppress degradation of biologics for the post-preservation recovery of structure, viability, and function.[1,2] Hypothermic storage (primarily 2°-8°C) has been the preferred practical mechanism for storing cells, tissues, and organs for short periods of time (such as applicable in typical hair transplantation procedures). The ability of hypothermia to suppress metabolism is the key to maintaining cells, tissues, and organs under ischemic conditions.[3] The beneficial properties of hypothermia have been appreciated for a number of years. For example, in 1939, surface cooling of ischemic limbs was found to confer preservation ability for rat limb survival.[4] In the 1950s, hypothermia played an important role in the development of cardiopulmonary bypass surgery,[5,6] and in 1969 the demonstration that cold storage was an effective means of kidney preservation[7] stimulated the development of cold storage solutions for the purpose of organ preservation. Ambient

⇨ page 7