Microencapsulated Non-Autologous Cells

The Benevolent Trojan Horse

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A single substitution of one base pair out of billions in our DNA can lead to horrific diseases. Millions of people afflicted with genetic disorders as a result of point mutations can attest to this fact. Over the past few decades much research has been geared towards finding treatments or cures for such diseases.

Diseases involving genetic mutations may fail to produce necessary proteins. Intially, to treat these conditions, scientists administered the necessary recombinaint proteins to patients through injections. The problem with this, however, was that these proteins were rapidly eliminated from the bloodstream. Also, this would entail the need for costly regular injections of high dosages, which may have toxic effects. Gene therapy may provide the solution by targeting the root of this problem: genetic mutation.

Gene therapy methods can vary drastically. One method involves the use of viruses, such as an adenovirus, to insert a correct copy of the specific gene into the genome of a sample of proliferating cells, like bone marrow, from the patient. These "infected" cells are inserted back into the patient where they would produce the required protein in physiologically acceptable quantities. While this appears to be an ideal treatment, there is one drawback: the patient's own cells must be used in order to eliminate the need for immuno-suppressant drugs, rendering this type of gene therapy extremely costly (Campbell, 2001). The work of McMaster University's Microencapsulation Gene Therapy Group focuses on a promising technique that bypasses the need to use autologous cells, which are from the recipient.

Recent technological advances have made microencapsulation a plausible protein delivery system. The technique is elegant in its simplicity. Cells from healthy individuals, or even those of another species, are encased in a polymeric matrix that allows diffusion of nutrients, wastes, and protein products while acting as a barrier to the conduits of the immune system once the cells are implanted into the patient (Fig. 1).

The polymeric matrix usually consists of alginate, a substance extracted from seaweed and chosen for its low toxicity and its ability to maintain cell viability (Dhoot, 2002). The process of microencapsulation involves

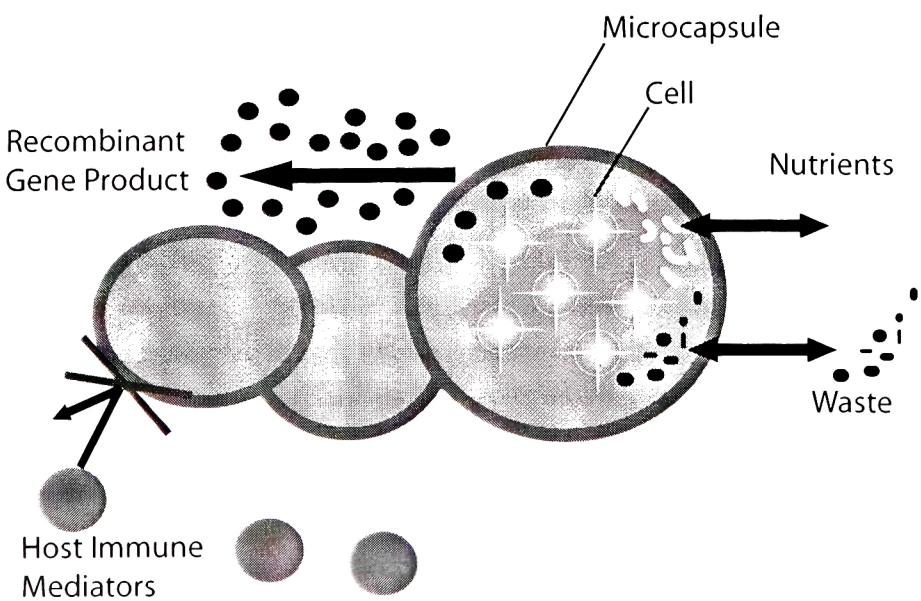

Figure 1
Cells from healthy individuals or even from other species can be encased in a polymeric matrix that allows diffusion of nutrients, wastes and protein products while acting as a barrier to the conduits of the immune system once the cells are implanted into a patient. <Source: http://www.fhs.mcmaster.ca/gene/overview.htm>

dispensing tiny droplets of cell-alginate suspension into a solution of $CaCl_2$, which provides crosslinking ions that trap the cells inside tiny beads. The entire process takes about an hour, and the product can be stored for extensive periods of time (Microencapsulation Gene Therapy Group Homepage, 1997).

The process has a myriad of advantages. Since the microcapsules act as a barrier between the graft and the immune system, doctors can implant foreign cells into a patient without the use of immuno-suppressant drugs (Orive, 2003). The fact that the same cell-lines can be used for different recipients eliminates the need for customized genetic engineering of the patients' own cells using viruses. In addition, by changing the properties of the capsules, doctors can alter the rate at which the patient receives the protein products of the implanted cells (Dhoot, 2002).

That is not to say that microencapsulation techniques have been perfected. Much more research is needed to make the capsules biocompatible and stable *in vivo* (Orive, 2003). This necessitates collaboration with researchers from various disciplines to find novel substances from which to build the casing for the cells. Such substances may have new properties that give doctors more control over the way in which the protein products are released. In clinical trials involving diabetes patients, the capsules were found to be too large to use in the amount necessary to completely eliminate the need for insulin injections; therefore, there is an emphasis towards further miniaturization before microcapsules can be used to treat diseases.

Despite the many obstacles that researchers must still overcome, microencapsulation of non-autologous cells has the potential to become synonymous with hope for many patients afflicted with genetic disorder. M

LDL, HDL, and the Battle Against Heart Disease

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As North Americans progress into the 21st century, life has become increasingly chaotic and fast paced. The average North American lives in such a high-speed society that it is almost impossible to avoid fast food chains and express lines in the grocery markets. People now have no time to slow down their lives and adopt or maintain a healthy lifestyle. Consequently, heart disease, in particular atherosclerosis, has become the leading cause of death in North America (Ezekowitz et al., 2003). Atherosclerosis is a condition where deposits of fatty substances, cholesterol, cellular waste products, calcium, and other substances accumulate on the inner lining of an artery and form build-ups called plaque. If a clot forms and blocks a narrowed artery, it can result in a heart attack or stroke. Recently, there have been a number of breakthroughs in the fight against atherosclerosis, which have linked high-density lipoprotein (HDL) to antiatherogenic effects. The latest studies have linked HDL to the reversal of cholesterol transport, a process that removes excess cholesterol from the body.

Cholesterol is a normal constituent of most body tissues, especially vital in the brain, nervous system, liver, and blood system. Cholesterol is also needed to form the sex and adrenal hormones, bile in the liver, and vitamin D (Kumar et al., 2001). Unfortunately, high blood cholesterol levels increase the risk of developing health problems such as heart disease and atherosclerosis (Kumar, 2001).

The first major type of cholesterol is low-density lipoprotein (LDL) cholesterol; this form is often referred to as the "bad" cholesterol. LDL is a type of lipoprotein, which acts as a carrier for cholesterol and fats in the bloodstream. When too much LDL cholesterol circulates in the blood, it can slowly amass on the inner walls of arteries that supply the heart and brain. Together with other substances, plaque is formed. Evidence from observational studies suggests that higher total LDL cholesterol levels are associated with an increased risk of a variety of cardiovascular diseases, such as atherosclerosis (Anderson et al., 1994).