

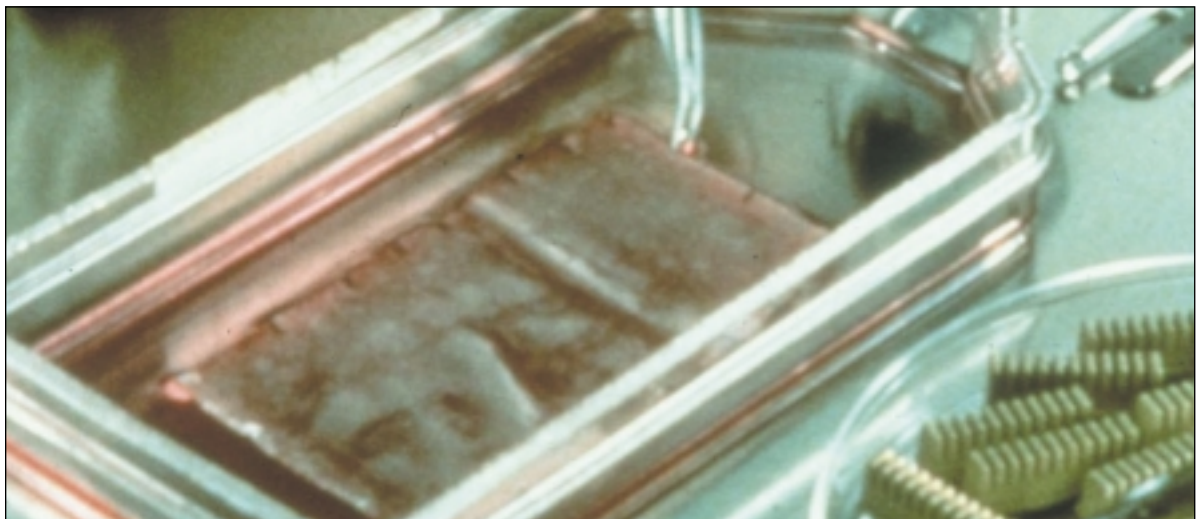
"Healthcare biotech is a fast growing field within modern medicine. It can play a vital role in tailoring healthcare to the individual as well as providing treatments for hitherto incurable diseases." The story below is one example.

Human Cell and Tissue Based Products

Human cell and tissue-based products offer quality treatments for many patients suffering from life threatening or seriously debilitating conditions. Currently these products are classified as medicinal products, while others are not yet categorised. The market for these products is very diverse, highly segmented and still not often recognised as a high technology sector. The field is undergoing radical changes, not least due to the use of new biotechnology-derived solutions within existing applications, as well as the creation of new treatment concepts for major human health problems.

An increasing number of innovative human tissue products are being developed with a variety of health care applications, from prosthetic and restorative to therapeutic or even cosmetic in nature. However, the introduction of this new class of products into the marketplace has been complicated by the lack of harmonized regulations, even within Europe.

Over the next decade, we can expect increasingly dramatic advances in medical technology, and as it expands the industry will develop more cell and tissue-based products. The availability of these innovations to patients, and their potential to provide advantages over currently available treatments, will depend not only on researchers and industry, but also on a regulatory framework that offers a favourable legal environment for research and innovation and in particular takes into account the boundary-crossing nature of many of these new products.



Human cell and tissue therapies and products

Human cell and tissue-based product categories contain only cells or tissues of human origin and include non-viable or viable tissue transplants; unmanipulated or manipulated autologous (a patient's own cells); and/or allogeneic cells (originating from another person than the patient); fusions of those cells; modified cells with factors or genes; and human stem cells.

It is important to know that the field is complex and that some (e.g. surgical) procedures and/or services may overlap with the products based on human cell and tissues. In this section we want to highlight some of the areas developing by using cell and tissues from human origin, in addition to those already on the market.



Skin repair

Most victims of severe burns are treated with a procedure known as autografting, in which a surgeon replaces a patient's damaged skin with a thin layer of healthy skin from another part of the body. In the case of burns over a relatively large part of the body, however, a surgeon may determine that there is not enough healthy skin available to cover the affected area. A severe burn can destroy both the epidermis and dermis, leaving the skin unable to regenerate on its own to cover the wound and protect the underlying muscle and organs. Such patients often die within days after sustaining the injury.

When treating these severe burn patients, doctors must cover the injured area with a permanent skin replacement to retain the body's fluids and prevent infection. Cultured dermal and epidermal grafts are grown from a patient's own skin cells and are therefore not rejected by the patient's immune system.

Also allogeneic epithelial cells can be cultured and grafted. They stimulate the healing in the same way as autologous cells. They can also be applied on chronic skin ulcers to initiate the healing process.

Application of autologous keratinocytes and fibroblasts proved to be effective also in the treatment of chronic wounds, such as diabetic foot ulcers, reducing healing time and improving the quality of the new tissue.

Orthopedics

Once damaged, joint cartilage does not normally regenerate in the body. In addition to causing pain and restricted mobility, chronic injuries to joint cartilage may over time lead to further deterioration of the joint surface. This can severely diminish a person's quality of life. For several years now, cell therapy for restoring defects to knee cartilage has been available, based on expanded autologous cultured cartilage cells. This method employs a commercial process to grow a patient's own cartilage cells, known as chondrocytes, for use in the repair of symptomatic cartilage defects. Tissue engineered products composed of autologous chondrocytes cultured on a resorbable biomaterial (scaffold) are currently available.

Active research, involving human cell-and tissue-based products, is currently also conducted in the regeneration and repair of bones, tendons, nerves and ligaments.

Cardiac cells

Several research groups, both academic and commercial, are developing a cellular therapy to treat heart tissue damaged by myocardial infarction (MI).

Although there are many well-established treatments for MI patients, no therapy exists for restoring function to a heart damaged by large myocardial infarct. According to the British Heart Foundation, there are more than one and a half million people who die each year from Cardiovascular disease in the European Union.

Many patients surviving an acute MI will require prolonged medical therapy. By restoring function and/or arresting the subsequent decline in heart functions, this new cellular therapy could delay or prevent the onset of congestive heart failure among these patients.

Some promising results have been obtained in this field by injecting autologous stem cells into the heart to heal the damaged organ.

Cell-based Cancer Immunotherapy.

For decades doctors and scientists have sought to harness the body's immune system to fight cancer.

Success has been sporadic and unpredictable, though reproducible results against specific diseases such as advanced renal cell carcinoma have served as proof of principle for the entire field of cancer immunotherapy.

More recently, advances in the understanding of basic immunobiology (e.g. isolation and characterisation of dendritic cells, the critical antigen presenting cell), combined with

preliminary but compelling cell-based tumour vaccine human data, have created renewed interest in a variety of cellular immunotherapies.

The shared goal of these cell-based approaches is the induction of non-toxic, specific, cellular immune responses in order to break tumour tolerance. Clinical progress is being made in this field along several fronts. Broadly, efforts in cell-based tumour vaccine approaches have consisted of either administering autologous or allogeneic tumour cells which have been manipulated *ex vivo* in various ways, or expanding dendritic cell populations *ex vivo* followed by alteration of this expanded cell population to present specific tumour antigens upon reintroduction to the patient. Each of these approaches comes with its own set of advantages and particular challenges. A third cellular vaccine approach consists of the *ex vivo* fusion of tumour cells and dendritic cells followed by re-administration of the fused hybridoma as a vaccine.

Stem Cell Therapies for Neurodegenerative Diseases

Stem cell-based therapies may provide hope for treating several neurodegenerative diseases and conditions. Small molecule and protein therapies have historically failed to treat neurological disorders due to the brain's multiple physical barriers and complex biology. Stem cells, however, exhibit unique characteristics that are critical to treating these neurological diseases such as the ability to regenerate tissue, rejoin neural connections, secrete proteins, adapt to their environment, grow after injection, migrate throughout the brain and/or produce needed neurotransmitters. As a result, stem cells are being investigated for an equally long list of diseases, including Parkinson's Disease, Multiple Sclerosis, Huntington's

Disease, Alzheimer's Disease, cancer of the central nervous system, spinal cord injury, retinal degenerative disorders, stroke and trauma.

In general, scientists work with three kinds of stem cells: embryonic, adult or foetal stem cells. These can be harvested from a myriad of sources. Embryonic stem cells are believed to have the highest potential for research and future medical applications. However, adult stem cells have been successfully isolated from adult tissue such as the brain, bone marrow, muscle, skin, and blood.

There's only one certainty in the future of stem cell therapy – that no single cell type will be effective for all diseases.

Conclusions

With the clinical promise of novel therapeutic strategies, comes new challenges.

Products manufactured from or composed of human tissue have many unique features, which must be considered over and above those typically covered by traditional medicinal product or medical device regulation. Regulatory authorities have a responsibility to ensure the safe administration of treatments. While future regulation should be proportionate and not stifle the development of these potentially less toxic, more effective and targeted treatments, must take into account ethical considerations as well as issues potentially related to ownership and confidentiality. Authorities need to then ensure appropriate application of such regulations.

Worldwide harmonisation of regulations is particularly important where potential safety issues are concerned such as



the safe administration of treatments and the prevention of the transmission of infectious agents that have no national or international borders. In addition, companies need to operate on a global basis, and all players should be subject to the same regulations for the safety of the patients being treated.

Even within countries where a well-developed regulatory pathway for cellular therapies exists, there is often inconsistent application of regulation. This is a barrier to the development and commercialisation of cell and tissue-based products and ultimately means many patients will miss out on potential new therapies. This by itself is becoming an ethical issue.

Harmonised regulations for tissue-engineered products would also provide a basis for regulating the next generation of cell and tissue products, and could subsequently be extended to

xenografts and embryonic or foetal stem cell-based therapies. Product development is generating a body of clinical and scientific evidence to support its potential at a rate that is running faster than regulations can be drawn up to cover them. Industry therefore has an important role in working with the regulatory authorities to ensure that new developments are covered appropriately. Industry is advocating the generation of new, specific legislation to regulate the increasing number of products being developed in this area, and applauds the current global International Conference on Harmonisation (ICH) and EU legislative initiatives. It also recognizes that potential ethical issues, related to the application of new technologies, need to continue to be discussed and resolved within society in an open and transparent way. The social debate about the ethical issues surrounding the many applications of these cells in human therapy has only just begun.

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