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# *In vivo* Human Cell Regeneration: Current Perspectives

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## Introduction

Regeneration of cells for repair of damaged tissue is indeed a very wide topic of research and is emerging as one of the most sought branches of medicine. Human cell regeneration can change the course of disease prognosis in case of chronic diseases and aid in tissue repair in case of other factors such as age, disease, injury, or genetic defects. In this report, some of the most recent scholarly information on human cell regeneration in different tissues and organs has been highlighted while presenting an overview of cell regeneration science and its potential therapeutic applications.

## Peripheral nerve cell regeneration

Injury to the peripheral nerves causes denervation, loss of motor functions, sensory and other autonomic functions. Reinnervation with neuron regeneration can take place after peripheral axotomy. By exploring the regeneration mechanisms of axons and the various environmental factors that affect their regeneration it will be possible to regrow the nerves and direct their development for conferring functional status to the regions affected by nerved lesions. Schwann cells are identified as crucial for the regeneration of motor and sensory axons and could contribute substantially to the reinnervations. L2/HNK-1 carbohydrate is identified as a molecular marker that is expressed in motor and sensory Schwann cells after denervation. Additionally, several molecular factors take part in axon Schwann cell interactions. These intercellular communications take place through the adhesion molecule called polysalicylic acid PSA and HNK-1 aid in guiding the growth of the axons to their targets. Systematic exploration and modulation of these molecular factors could be helpful in the recovery of nerve cells. The target organs and their contact with the axons and several other trophic factors play important role in curtailing the misdirected collaterals and nerve regeneration in the desired direction. Schwann cells are the major source of neurotrophic factors in the nerve and participate in direct communication via adhesion molecules [1].

## Liver cell regeneration

Liver tissue is comprised of hepatocytes and biliary epithelial cells that are differentiated from hepatoblasts during organ development. Hepatocytes detoxify metabolites, regulate glucose and lipid metabolism, synthesize serum proteins, and secrete bile while biliary epithelial cells transport bile from hepatocytes to the gall bladder. The bile released by the gall bladder helps absorb fats from the ingested food. Out of all the organs, the liver is the most regenerative organ and restore its mass after injury. Hepatocyte and liver progenitor cell-based liver regeneration takes place. Biliary epithelial cells can dedifferentiate into liver progenitor cells which later differentiate into hepatocytes. Hepatocytes can also dedifferentiate into liver progenitor cells which form hepatocytes again. Exploration and optimization of enhancing the hepatocyte regeneration from liver progenitor cells would be clinically relevant and beneficial for patients suffering from liver cirrhosis, viral hepatitis, and liver cancer while reducing the release of proinflammatory cytokines and the possibility of liver fibrosis. Identification of the target molecules for differentiation of hepatocytes from liver progenitor cells can be useful for promoting liver regeneration [2]. Reducing oxidative stress and normalizing the fatty acid metabolism help promote liver regeneration. Several other factors are relevant for liver regeneration is platelet count, hormones, and gut microbiota [3].

## Cell regeneration and hematopoiesis

Chemokine receptor called G protein-coupled receptor plays important role in cell movement, tumor metastasis, neurite extension, and axon of neurons. This phenomenon can be exploited for restoration of the injured tissue and cell generation. CXCR4 receptor triggers signaling pathways that cause cell migration, hematopoiesis, cell homing retention in bone marrow, cell proliferation of non-hematopoietic cells. CXCR4 is also an important chemokine receptor that is present in cancer cells at higher levels and they are present on hematopoietic cells, endothelial cells, neurons, embryonic and adult stem cells can be explored for their potential use in tissue repair via cell regeneration. Scientific exploration of the molecules that target CXCR4 receptors may be useful for cell migration and proliferation for organ recovery [4].

## Pancreatic cell regeneration

Beta cells secrete insulin and their failure to secrete insulin causes diabetes. Regeneration of the beta cells can be one of the clinically sustainable solutions. The transcriptional factors in the pancreatic cells for the differentiation of beta cells to produce insulin have been explored. Intrinsic molecular circadian clocks were found to be of immense relevance for the regulation of the beta cells and their regeneration and the enhancing core clock activity was suggested to provide adjuvant for cell replacement therapy [5].

## Regeneration of intestinal epithelium

The intestinal epithelium is the most important surface cell layer that aids in the digestion of food, nutrient extraction, nutrient absorption, hormonal secretion, and protection against pathogens. Enterocytes absorb nutrients, goblet cells secrete mucus, enteroendocytes produce hormones, paneth cells play a defense role while stem cells ns and progenitor cells aid in regeneration. The intestinal epithelium regenerates every four to seven days. Lgr5-marked intestinal stem cells give rise to rapid cellular regeneration via generating progenitor cells that undergo multilineage differentiation. Intestinal stem cells highly express Lgr5, Olfm4, CD133, and Lrig1, and show high clonogenicity and genome stability. Further exploration of the regeneration process can help in developing therapeutic strategies for treating colorectal cancer and inflammatory bowel diseases [6].

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## Inner ear tissue regeneration

Disorder of middle and inner ear causes hearing loss and poses a risk for dementia. Currently, cochlear implants are used as a treatment however, regeneration of the inner ear also possible from inner ear stem cells. These stem cells were discovered in the cochlea and the vestibule can give rise to various cells of the inner ear. Cell therapy based on transplantation of mesenchymal stem cells for regeneration of the inner ear is very promising. Kanzai et al. have demonstrated that spiral ganglion neuron regeneration could potentially improve clinical outcomes among patients with cochlear implants [7].

## Skeletal muscle regeneration

The muscle stem cells mediate the regeneration and development of skeletal muscles. These cells are also termed satellite cells which coordinate to form myofibers. However, it was observed in previous studies that muscle stem cells have to transit through multiple cell states before finally achieving differentiation and myofiber formation. This regeneration happens in response to muscle injury. The muscle stem cell fate is determined by changes in the gene expression pattern and the cell signaling in the muscle environment. Epigenetic mechanisms also contribute to change in gene expression patterns. Post-translational modification of chromatin and nucleosome repositioning renders certain gene loci more or less accessible to transcriptional machinery. Modulation of epigenetic changes has immense potential for restoration of muscle stem cell fate and regeneration to improve muscle repair for treatment of myopathies under disease and advanced age-related conditions [8].

## Conclusion

*In vivo* human cell regeneration is possible with accurate identification of genetic, epigenetic, cellular signaling molecules that participate in cell differentiation from the progenitor or stem cells. Tissue repair has potential for avoiding transplantations and implantations.

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