

# Journal of Liver: Disease & Transplantation

### Commentary

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# Liver Regeneration: Factors Influencing Efficiency, and its Potential Implications

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#### Description

The liver is a distinctive organ identified for its exceptional ability to regenerate. Liver regeneration is a complex and highly orchestrated process that enables the liver to recover from various forms of damage, including injuries, infections, and partial surgical removal. This regenerative capacity ensures the maintenance of significant liver functions, in addition to the presence of significant challenges.

Liver regeneration is the process by which the liver restores its tissue mass and function after injury or partial removal. In opposition to many other organs in the human body, which have limited regenerating capacity, the liver is an accurate regenerative power. It can regenerate up to 70%-80% of its lost tissue within weeks as a result; it is one of the most regenerating organs in animals. The process of liver regeneration primarily involves hepatocytes, the main functional cells of the liver. While injury or loss of liver tissue, quiescent hepatocytes are stimulated to re-enter the cell cycle and undergo rapid increase to replace the damaged or lost cells. Additionally, non-parenchymal cells, such as Kupffer cells, hepatic stellate cells, and liver sinusoidal endothelial cells, also play essential roles in the regeneration process by creating a supportive microenvironment and releasing various growth factors.

#### Mechanisms of liver regeneration

Liver regeneration is a highly complex process by various signaling pathways and molecular factors. The following are some important mechanisms involved in the liver's regenerative capacity: **Cytokines and growth factors:** After liver injury, cytokines and growth factors are released, triggering a cascade of cellular responses. Prominent among these factors is Hepatocyte Growth Factor (HGF), which connects to its receptor c-Met on hepatocytes, promoting cell proliferation and survival.

**Wnt/\beta-catenin pathway:** The Wnt/ $\beta$ -catenin pathway plays a significant role in liver regeneration. While injury, the pathway is activated, leading to the accumulation of  $\beta$ -catenin in the nucleus, where it regulates the expression of genes involved in cell cycle progression.

Epidermal Growth Factor (EGF) and Transforming Growth Factor- $\alpha$  (TGF- $\alpha$ ): EGF and TGF- $\alpha$  are growth factors that promote hepatocyte proliferation by binding to the EGF receptor (EGFR) on hepatocyte membranes.

**Signal Transducer and Activator of Transcription 3** (STAT3): STAT3 activation is essential for liver regeneration. It promotes the expression of various genes involved in cell survival and proliferation.

**Immune response:** The immune system plays an important role in the regeneration process. Kupffer cells and other immune cells release various cytokines that influence hepatocyte proliferation and tissue repair.

#### Factors influencing liver regeneration efficiency

Several factors can influence the efficiency of liver regeneration, including:

**Age:** Liver regeneration is more efficient in younger individuals compared to older ones. With age, the regenerative capacity of the liver decreases, as a result, regeneration is slower and less effective.

**Pre-existing liver conditions:** Liver diseases, such as chronic hepatitis or cirrhosis, can impair the regenerative capacity of the liver. In advanced liver diseases, scarring and fibrosis can hinder the restoration of functional liver tissue.

**Nutrition:** Adequate nutrition is important for supporting liver regeneration. Malnutrition or deficiencies in essential nutrients can hamper the regenerative process.

**Underlying medical conditions:** Certain medical conditions, such as diabetes and metabolic syndrome, may negatively impact liver regeneration due to their effects on cellular signaling and metabolism.

**Lifestyle factors:** Alcohol abuse and excessive drug use can impair liver regeneration and lead to irreversible damage.

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