What the Body’s Most Regenerative Organ Has to Teach Us

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Your liver has a unique ability to heal itself. New science is working to apply that power elsewhere.

People often talk about aging as an irreversible process of breakdown over time, but that's **not entirely true**. Some systems and organs in the body have **the ability to regenerate**, and the liver is a standout example.

Crucial for longevity and healthspan, it can rebuild up to **100% of its own mass and function after injury**. It also responds well to specific therapies designed to keep it working into older age.

In most cases, maintaining liver health is simple. It typically begins with liver function testing and lifestyle interventions you're already well aware of: good nutrition (fewer sugary drinks and fatty meals), curbing alcohol, exercising regularly, and managing your medications and supplements.

What's far more interesting is what our most regenerative organ, the liver, *could* teach us about the rest of the body's regenerative capacity. In cutting-edge research, scientists now are working to apply what we know about the liver to the heart, kidneys, lungs, and more.

Your Aging (and Age-Reversing) Liver

It's a good thing your liver is so capable of regeneration, given its status as a central hub for keeping the rest of your body healthy. It controls more than **500 vital functions** — most notably, filtering the blood, regulating the metabolism, and aiding

in digestion by producing bile, proteins, and enzymes.

“The liver is a major metabolic organ doing multiple functions,” says Dr. Gayatri Ramakrishna, a researcher at the Institute of Liver and Biliary Sciences in New Delhi.

Several of its functions, he says, have an impact on **blood glucose levels**, which broadly affect every other organ. The liver is also “the major detox organ” of the body, connecting the gut to the rest of your organs through portal circulation.

As with other organs, your liver typically becomes less effective with age. **Studies show** that over time, DNA and gene-control changes disrupt how liver cells manage energy and sense nutrients, causing cells to get “stuck” in a non-functioning state and driving low-level, chronic inflammation. This affects every cell type in the liver and gradually impairs how well it works overall. In particular, age-related changes in the liver’s blood vessel lining cells can quietly raise the risk of heart problems and metabolic disease elsewhere in the body.

What Makes Liver Regeneration Possible?

If it seems that the liver declines steadily with age just as other organs do, keep in mind that it has a few secret weapons that allow it to reverse the effects of aging and injury. This list isn’t exhaustive, but it gives you an idea of some of the overlapping systems and pathways that make liver regeneration possible.

HGF (Hepatocyte Growth Factor)

HGF is often called the liver’s primary regenerative signal. Within minutes of liver injury, levels of this protein surge in the bloodstream, traveling directly to liver cells

and instructing them to divide (a process known as mitosis). What makes HGF particularly remarkable is that much of it is produced not by the liver itself, but by **surrounding organs** — the lungs, kidneys, and spleen — which essentially send emergency reinforcements through the bloodstream. The liver, in this sense, is never regenerating alone. Worth noting: EGF (epidermal growth factor) consistently appears alongside HGF as another important mitogenic signal.

Cytokines IL-6 and TNF

Before liver cells can respond to growth signals, they need to be woken up. That's the job of cytokines, particularly **interleukin-6 (IL-6) and tumor necrosis factor (TNF)**, which are released by immune cells residing in the liver almost immediately after injury. These molecules don't directly cause cell division. Instead, they shift hepatocytes (the liver's primary cells, which make up 80% of its mass) from a dormant state into a growth-ready one, priming them to respond to the proliferative signals that follow. Think of them as the alarm that gets the crew out of bed before the real work begins.

The Wnt/?-catenin Pathway

The **Wnt/?-catenin pathway** is one of the liver's fundamental organizational systems, governing not just regeneration, but also dictating which cells do which jobs. During regeneration, Wnt signals help coordinate which hepatocytes divide, in what order, and how the liver's complex functional zones are restored as new tissue grows in. It works in close conversation with other regenerative signals, including HGF, and is particularly important for restoring not just the liver's mass, but its full functional structure.

The Hippo Pathway

More a regulator of regeneration than a primary driver, the **Hippo pathway's** main job is controlling when cells stop dividing, making it a critical safeguard against uncontrolled growth and cancer. When it's switched off, cells are freed to proliferate and rebuild damaged tissue. In the liver, this brake releases naturally after injury. Damage triggers a cascade of signals that suppress Hippo pathway activity, allowing a protein called YAP to move into cell nuclei and switch on the genes responsible for regeneration. Once the liver has rebuilt itself to its original size, Hippo signaling switches back on and growth stops.

The Hepatostat

Perhaps the most mysterious aspect of liver regeneration is *how it knows* when to stop. The liver has a precise, built-in sense of its own mass — researchers call the mechanism governing this **the hepatostat** — and it ensures that regeneration halts almost exactly when the organ returns to its original size relative to body weight. The signals involved are still being mapped, but bile acids, mechanical pressure, and growth-inhibiting factors all appear to play a role. It's a level of biological self-regulation that no other solid organ has been shown to match — and understanding it may be just as important for regenerative medicine as understanding what starts the process.

What the Liver Has to Teach Us About Our Other Organs

The liver is the only solid organ that reliably regenerates to full function after injury, and for most of medical history, that capacity was treated as a biological curiosity rather than a blueprint. That's changing. Scientists are now systematically studying the molecular signals that make liver regeneration possible and asking a more

ambitious question: can we teach other organs to do the same thing?

The two most advanced pieces of research are on the Hippo pathway and HGF, and both inquiries are moving fast. The Hippo pathway — the molecular brake system that the liver releases to allow cells to proliferate — **turns out to be present** in the heart, lungs, kidneys, and intestine as well. The difference is that those organs don't know how to release the brake.

Take, for example, the heart. When a heart attack **kills cardiomyocytes**, the heart's default response is to fill the gap with scar tissue rather than new muscle cells, because the Hippo pathway remains active and suppresses the regeneration that YAP would otherwise trigger. The heart has the machinery for renewal. It just can't access it.

Another key challenge helps to explain why these insights haven't yet translated into real-world cardiac treatment. YAP activation needs to happen in the right cells at the right time. In **cardiac fibroblasts**, for example, suppressing Hippo appears to promote scarring rather than regeneration (the opposite of what's wanted). So the goal isn't simply to flip the switch, but to flip it selectively in the right cell type, for the right duration. That's the problem the field is currently working to solve.

That said, a **2025 paper** from the Texas Heart Institute is the clearest proof of concept yet: artificially suppressing Hippo signaling in adult heart muscle cells triggers them to divide and rebuild — something the heart can't do on its own after a heart attack.

HGF tells a parallel story. The liver's primary growth signal doesn't stay local. It surges through the bloodstream during injury and has been shown to support repair in the kidneys, lungs, and heart. Early clinical trials are investigating its use in treating **ALS** and **spinal cord injury**, making it one of the first liver-derived regenerative signals actively being tested in humans for conditions that have nothing to do with the liver.

And there’s more coming. A **2025 paper** in *Nature* identified an entirely new regenerative mechanism in the liver — one involving immune cells and glutamate signaling — that researchers are only beginning to understand. **Another paper** published this month in *Science* tackles a question that has puzzled researchers for decades: how does the liver know how much of itself it has lost, and how does it know when to stop rebuilding? The answers to both are likely to have implications far beyond hepatology.

It’s important to be realistic about the current limits of the research and the things that make the liver unique (both its form and function are exceptional in some ways that simply don’t transfer to other organs). But as we begin to decode some of the mechanisms that aid in regeneration, the forward-looking science is still genuinely exciting. Today’s glimpses of insight could someday tell us how to fix a failing heart, a damaged kidney, or a scarred lung.

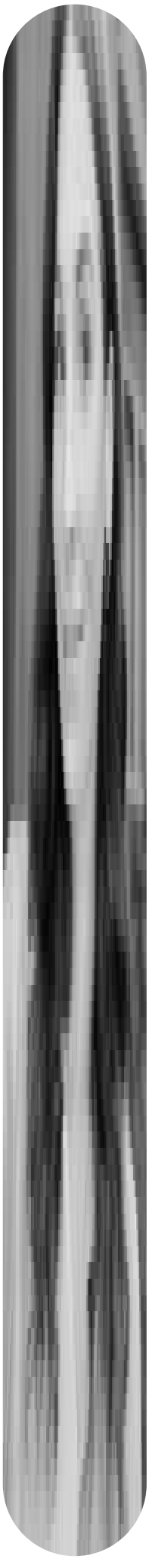
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