

Scarless wound healing in the liver: Role of the extracellular matrix carbohydrate, hyaluronan.

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Two kinds of wound healing exist: regenerative wound repair which occurs without the formation of a scar, and imperfect, scar-forming, wound repair. Skin wound healing exemplifies these two types of wound repair: fetal skin wounds heal perfectly and without a scar, while adult skin wounds heal with formation of a scar. One molecule, hyaluronan (HA), plays a particularly large role in regenerative wound repair in the skin. Another organ which is capable of regenerative wound repair is the liver. Therefore, we asked the question: What role does hyaluronan play in regenerative repair of the liver? In parallel to what is observed in fetal skin wound repair, we recently discovered that the scarless wound repair which occurs in the liver after acute liver injury is associated with robust HA accumulation. HA accumulation occurs in damaged areas of the liver prior to infiltration of non-parenchymal cells recruited for wound repair. Further, we have also discovered that Rhamm (*Hmmr* gene product, CD168), an HA binding receptor which plays roles in skin wound healing, is robustly induced, concurrent with cell migration into necrotic areas of the liver. Using pharmacologic strategies to inhibit HA synthesis and genetic studies to prevent Rhamm expression, we are beginning to appreciate that regenerative repair in the liver requires dynamic regulation of both of these molecules. Future work will explore the role of HA and Rhamm in the liver after chronic, fibrosis-inducing, liver injury. We hope to leverage what we know about regenerative hepatic repair after acute liver injury to prevent fibrosis or hasten fibrosis removal after chronic liver injury.