Galectin-3 as a potential biomarker for liver regeneration and transplant outcomes

Ivana Vasic[1], Nathaly Limon-de la Rosa[2], Eduardo Cervantes[2],Nalu Navarro-Alvarez[1,2], Christene A. Huang[1]

[1]University of Colorado Anschutz Medical Campus, Department of Surgery, Division of Plastic & Reconstructive Surgery and Division of Transplant Surgery, Aurora, Colorado

2 Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico.

Background

Galectin-3 is an endogenous β-galactoside binding lectin released into the extracellular space mainly by macrophages and fibroblasts under hypoxic conditions. Increased extracellular galectin-3 levels have been associated with chronic inflammatory disorders (1). Moderate activation of inflammatory factors such as IL-6 have been shown to mediate liver regeneration after injuries or partial liver resection (2). An excess of cytokines in liver recipients is known to induce cytotoxic T-lymphocytes and lead to a graft rejection. Our research has two primary goals. First, we want to understand the relationship between the level of galectin-3 in liver donors and the post-transplant outcomes in the recipients, including 5-year survival and graft rejection. Second, we want to understand the role of galectin-3 in liver regeneration in patients with chronic liver diseases.

Objectives

- Compare plasma Galectin-3 levels between deceased liver donors and healthy subjects
- Investigate co-expression of Galectin-3 and cell cycle markers in liver tissues from patients with liver cirrhosis

Methods

1) Invitrogen Human Galectin-3 ELISA kit was used to analyze circulating levels of Galectin-3 in sera of healthy donors (n = 10) and deceased liver donors (n = 64) collected immediately prior to graft procurement. Unpaired t-test was performed and a p-value <0.05 was considered to be of statistical significance.
2) Liver tissue samples from patients with liver cirrhosis were stained for DAPI, Galectin3,Ki67 CyclinD1,EPCAM, p21, and p53 and analyzed using inForm® software.

Results

1) Deceased donors had significantly higher levels of serum Galectin-3 (mean 17.1659 ng/ml, standard deviation 7.525991) in comparison to healthy controls (mean 11.4919 ng/ml, standard deviation 4.480911) (Figure 1).
2) Preliminary data shows that in a cirrhotic liver galectin 3 co-localizes with known cell cycle suppressors including p53 and p21 (Figure2). At the same time, regenerative nodules that express EPCAM, a marker of pluripotency, show low levels of Galectin-3 (Figure 3).

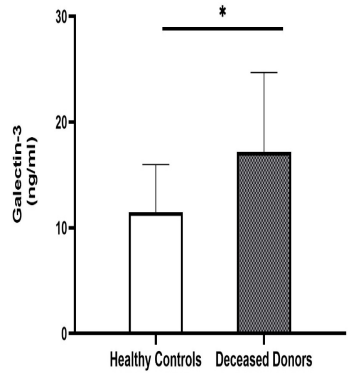

Figure 1 Comparison of serum Galectin-3 levels between healthy volunteers (n=10) and deceased donors (n=64).

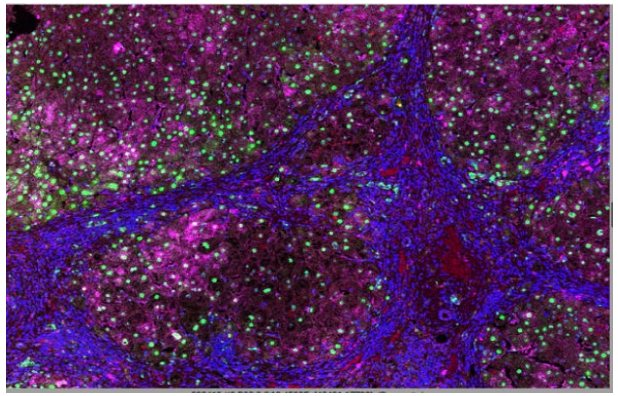

Figure 2. Galectin-3 (magenta) is co-expressed with p53 (green) in regenerative nodule of a cirrhotic liver. Fibrotic bridges (blue) show minimal expression of both markers.

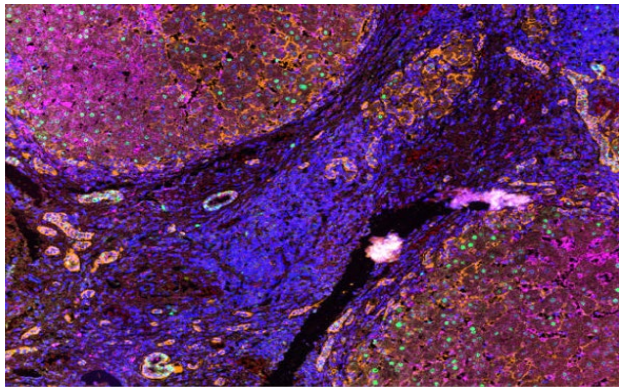

Figure 2. Galectin-3 (magenta) is expressed in one half of a regenerative nodule. The other half stains positive for EPCAM but is negative for Galectin-3.

Conclusion and Next Steps

Galectin-3 is a known inflammatory marker. Here, we are showing that it could also be involved in the regulation of cell cycle in the regenerative liver nodules. This, along with its pro-inflammatory effects could significantly contribute to the outcomes in liver transplant recipients and liver regeneration in patients with chronic diseases. We have shown that deceased liver donors show an increase in circulating, extracellular Galectin-3 as compared to healthy controls immediately prior to organ procurement. Future studies will characterize the relationship between Galectin-3 levels in the donors and post-transplantation outcomes in the recipients.

References

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