

**Title**

MicroRNA Drivers for Regenerative Capacity in Liver Transplantation

**Authors**

Ankita Srivastava, Benjamin K. Barnhart, Alexandra Manchel, Jan B. Hoek, Rajanikanth Vadigepalli

**Affiliation**

Daniel Baugh Institute for Functional Genomics/Computational Biology, Department of Pathology, Anatomy, and Cell Biology, Thomas Jefferson University, Philadelphia, PA.

**Introduction:** Liver diseases, including alcoholic liver disease, nonalcoholic fatty liver disease, hepatitis, hepatocellular carcinoma, and other end-stage chronic liver disease complications, often require liver transplantation. There is an unmet demand for liver transplantation due to the limited availability of deceased-donor livers with adequate regenerative capacity. Current efforts to address this need involve treatments to improve transplant outcomes and utilize livers with diminished regenerative potential. Hence it is imperative to characterize the regenerative potential of donor livers for maximizing the utilization of available organs. We aim to characterize the microRNA profiles of deceased donor livers selected for transplant to those deemed non-transplantable. Further, the study aims to identify microRNAs that can serve as potential markers of the regeneration potential of the deceased donor livers. **Method:** For this study, flash-frozen wedge-biopsy samples were received from the Thomas Jefferson surgical team collected under the approved consent to research authorization obtained by the Gift of Life Donor Program. We collected NanoString microRNA profiling data from 798 human microRNAs from each sample and analyzed for differential expression between transplant-accepted and deemed non-transplantable liver biopsies. **Results:** Our results show that the accepted and rejected samples did not form distinct sample groups according to microRNA expression, suggesting that some of the samples at the “borderline” may have similar molecular features between accepted and rejected livers. We predicted a microRNA signature that is likely representative of the regenerative potential of the liver, based on similarities of microRNA expression between donor liver samples and regenerating livers in laboratory animal experiments. **Conclusion:** These results suggest a path towards a molecular biomarker to augment the current evaluation for transplantability and thus increase the potential pool of transplantable livers.

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