No. 855

ELAD® Cellular and System Performance Improvements

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Disclosures: J. Brotherton, D. He, & S. Asslani – Employees: Other

Abstract

One of the concerns with immortalized human hepatocytes has been the robustness of the metabolic pathways. As evidence mounted that the pathways expressed were dependant on the conditions the cells were exposed to, effort was placed on optimizing the metabolic function, by modifying the materials and conditions.

Methods

C3A cells were inoculated into improved polysulfone hollow fiber cartridges with 0.2 micron pores and allowed to grow to confluence. Oxygen delivery and culture media were optimized, with pH and temperature maintained at physiologic conditions. Standard metabolic assessments were performed and compared to the cartridges utilized in earlier Phase 1 and 2 clinical trials.

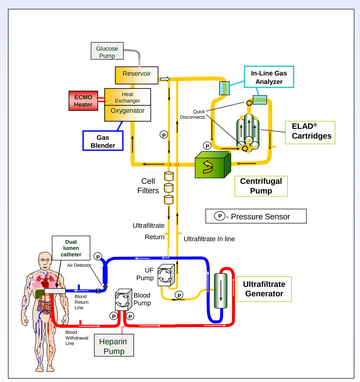
Results

Metabolic Activity of ELAD® Cartridges

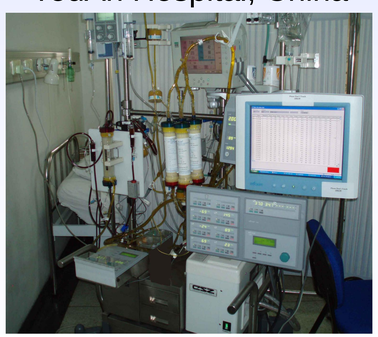
	Phase 1 and 2 Cartridges	New Cartridges and Conditions
Factor V (mg/d/cartridge)	0.056 ± 0.017 (n=25)	1.12 ± 0.83 (n=17)
Glucose Consumption (g/d/cartridge)	13.0 ± 1.8 (n=164)	17.6 ± 2.3 (n=111)
Lactate Production to Glucose Consumption Ratio	0.59 ± 0.04 (n=25)	0.38 ± 0.13 (n=111)
Urea Production (mg/d/cartridge)	N/A	88.5 ± 45.8 (n=89)
Albumin Production (mg/d/cartridge)	264.6 ± 85.3 (n=145)	365.2 ± 87.1 (n=109)
Transferrin Production (mg/d/cartridge)	86.8 ± 29.7 (n=163)	127.5 ± 36.9 (n=171)
Galactose Consumption (µmol/h/cartridge)	28.7 ± 5.1 (n=31)	41.6 ± 9.8 (n=6)
TGF-α Production (ng/d/cartridge)	50.3 ± 18.1 (n = 24)	485.7 ± 407.9 (n=16)

All Differences are statistically significant to the 0.001 level

ELAD System Schematic



ELAD System at Beijing YouAn Hospital, China



Conclusion

The metabolic growth and maintenance conditions that the C3A cells are exposed to and the physical characteristics of the hollow fiber cartridge utilized significantly affect the metabolic repertoire of the cells. The improved metabolic characteristics may have significant affect on the level of metabolic support provided by the ELAD System. The new system with improved metabolic characteristics is currently in a randomized, multi-center clinical trial assessing the safety and efficacy of the ELAD System for acute decompensation of chronic liver disease.

Reference

Acute Liver Failure
Monday, November 5
3:00 - 4:30 PM Hynes, Room 302
MODERATORS: J. Eileen Hay, MD
Andres T. Blei, MD

3:00 PM
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INTERIM RESULTS OF RANDOMIZED CONTROLLED TRIAL OF ELAD® IN ACUTE ON CHRONIC LIVER DISEASE
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