Biomateriales, Scaffolds, y Descelularización

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Widening gap between available organs and patients waiting for liver transplant

- Waiting List Candidates 123,514 as of today 1:07am
- Liver Waiting List Candidates 15,690 as of today 1:07am

Source: The Organ Procurement and Transplantation Network
Regenerative Medicine: Strategy

Biopsy → Cells → Scaffold → Tissue

Clinical Translation
Using this strategy, we have been able to bioengineer and transplant multiple tissues.
The last decades were quite successful making this transition, however...
Whole Organ Decellularization

Surgery and organ retrieval

Detergent perfusion
## Preservation of ECM Protein Localization

<table>
<thead>
<tr>
<th></th>
<th>Collagen I</th>
<th>Collagen III</th>
<th>Collagen IV</th>
<th>Laminin</th>
<th>Fibronectin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staining Control</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
<td><img src="image5.png" alt="Image" /></td>
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<tr>
<td>Acellular Liver</td>
<td><img src="image6.png" alt="Image" /></td>
<td><img src="image7.png" alt="Image" /></td>
<td><img src="image8.png" alt="Image" /></td>
<td><img src="image9.png" alt="Image" /></td>
<td><img src="image10.png" alt="Image" /></td>
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<tr>
<td>Fresh Liver</td>
<td><img src="image11.png" alt="Image" /></td>
<td><img src="image12.png" alt="Image" /></td>
<td><img src="image13.png" alt="Image" /></td>
<td><img src="image14.png" alt="Image" /></td>
<td><img src="image15.png" alt="Image" /></td>
</tr>
</tbody>
</table>

- Preservation of matrix components in their original localization
Decellularized Liver

Injection of trypan blue dye in the portal vein
Decellularized Organs

Lungs
Pancreas
Kidney
Intestine
Liver

Human fetal liver progenitor cells

Wang et al, Hepatology, 2010
Re-Cellularization of the Bioscaffold

Cell perfusion seeding preserves bioscaffold integrity
Perfusion Seeding Bioreactor

Method Used:

• Perfusion seeding of a total of 70 million human fetal liver cells and 30 million human umbilical vein endothelial cells per bioscaffold.
• Continuous flow of culture medium with nutrients and oxygen.
• Pre-conditioning period after seeding of 1 week in the bioreactor.
Liver Bioengineering with hFetal Liver Cells

Unseeded Bioscaffold

Baptista et al. Hepatology, 2011
hFLC Maintain Their Phenotype and Differentiate in the Liver Bioscaffold
Urea and Albumin Secretion and Drug Metabolism from Cells Seeded in the Bioscaffold

Urea Secretion

Albumin Secretion

Bioengineered Liver

Phase I Metabolism

Phase II Metabolism

MRM of 7 Channels ES+
191 > 163
1.2485

MRM of 6 Channels ES+
163 > 107
1.2763

MRM of 7 Channels ES+
339 > 163
5.084