The Integrative Liver Cell Core

Our purpose

THE INTEGRATIVE LIVER CELL CORE (ILCC)...

- **Strives** to serve the scientific community of alcoholic liver disease (ALD) and cirrhosis via specialized services involving isolation of different liver cell types from normal rodents and rodent models of ALD and liver fibrosis.

- **Provides** primary or stored hepatocytes (HC), hepatic macrophages/Kupffer cells (HM), hepatic stellate cells (HSC), liver sinusoidal endothelial cells (LSEC), liver mesothelial cells (MC), CD133+ liver tumor-initiating stem cell-like cells (TICs), and CD133+ liver progenitor cells, each isolated from mice or rats.

- **Supports specialized analysis** such as cell lineage and fate tracing using Rosa-reporter mice; FACS-based isolation of quiescent vs. activated HSCs from Col1α1-GFP mice; infiltrating vs. resident HM and tracking on blood monocytes.

- **Offers Cell Bank**, a collection of small aliquots of isolated cells or RNA from normal and diseased rodent livers for nominal fees – ideal for pilot analysis.

Did you know? During the last funding period, the ILCC served 39 investigators from 16 institutions by performing 2,388 isolation preparations.

The ILCC provides unique services involving isolation of different liver cell types. The most powerful outcome ensues when our services are applied to the rodent models of ALD or liver fibrosis, allowing direct analysis of specific cellular changes in the evolution of the diseases. This approach is achieved by the ILCC’s close collaboration with the Animal Core of the NIAAA P50-funded Southern California Research Center for ALPD and Cirrhosis and allows isolation of the different cell types from diverse pathologic spectra. These models include the intragastric ethanol infusion (IG) models now...
reproducing the clinically relevant pathologic spectra of ALD, such as mild or severe chronic alcoholic steatohepatitis (ASH), with liver fibrosis and alcoholic neutrophilic hepatitis (AH). The services are rendered on a chargeback basis to recover the costs of supplies which are not supported by the Center and resource grants from NIAAA. See the chargeback fees below for commonly performed services, and visit www.usc.edu/alpd for further details:

<table>
<thead>
<tr>
<th>Cell Isolation Services</th>
<th>Rat</th>
<th>Mouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatic Macrophages (HM)</td>
<td>$200</td>
<td>$150</td>
</tr>
<tr>
<td>Hepatic Stellate Cells (HSC)</td>
<td>$200</td>
<td>$150</td>
</tr>
<tr>
<td>HM &amp; HSC (from the same rodent)</td>
<td>$300</td>
<td>$250</td>
</tr>
<tr>
<td>Liver Sinusoidal Endothelial Cells (LSEC)</td>
<td>$200</td>
<td>$150</td>
</tr>
<tr>
<td>Hepatocytes (HC)</td>
<td>$150</td>
<td>$100</td>
</tr>
<tr>
<td>LSEC &amp; HC (from the same rodent)</td>
<td>$300</td>
<td>$200</td>
</tr>
<tr>
<td>HM &amp; Hepatocytes (from the same rodent)</td>
<td>N/A</td>
<td>$200</td>
</tr>
</tbody>
</table>

50% discount for "F" & "K" awardees

In addition to the routine and customized cell isolation services, the ILCC has recently established a Cell Bank that utilizes the ILCC’s resources and provides a variety of low-cost cells. The Cell Bank is based on collected and stored fresh or cultured primary cells isolated by the core from the livers of normal or diseased rodent models of liver injury. The Cell Bank charges a flat rate of $30/vial of cells which contains a minimum of 5x10^6 freshly isolated or 1x10^6 cultured cells.

ILCC Cell Bank also has limited RNA extracts from the fresh isolated or cultured primary cells from normal or diseased mouse/rat models of liver injury. In general, we will provide a small quantity of the RNA (200-500 ng) free of charge for the purpose of a pilot or feasibility study. If larger quantity is needed, we recommend the investigators to request for the frozen cells through the Cell Bank.

The cells currently available through the Cell Bank include mouse or rat HC, HM, HSC, and LSEC as snap-frozen cell pellets stored at -80°C. Disease models include IG alcohol control mice, CCl4 or BDL mice or rats. The lists of cells and RNA samples available from the Cell Bank are available at www.usc.edu/alpd.

The ILCC also provides or assists in specialized services as described below:

1. Genetic cell lineage and fate tracing: The ILCC now performs cell lineage and cell tracing with collaboration with the Animal Core of the NIAAA P50-funded Southern California Research Center for ALPD and Cirrhosis by using a variety of Rosa26mTmGflox reporter crossed mice. For biochemical characterization, culture experiments, or cell fate analysis via transplantation.

2. FACS isolation of activated HSC from Col1a1-GFP transgenic mice developing alcoholic liver fibrosis: The ILCC now applies a FACS-based isolation technique to Col1a1-GFP mice to separate HSC based on their UV fluorescence for vitamin A content and the activation marker of type I collagen promoter activity as detected by GFP. Using this method, a pure population of UV+ and GFP+ cells is isolated as activated HSC.

3. CD133+ liver progenitor isolation: The ILCC has developed an isolation method of CD133+ liver progenitors.

4. Assessment of infiltrating vs. resident HM and tracking on blood monocytes: This method allows investigation into how these 2 populations contribute to inflammation in ASH and the role of a particular gene of interest in monocyte transmigration into ASH livers by using donor monocytes with ablation of the gene as used to demonstrate the important role of Notch1.

5. Hypoxia system: The ILCC utilizes a complete hypoxia system from BioSpherix, NY which allows culture and manipulations of the cells under a constant hypoxic condition. This system has allowed a demonstration of cooperative actions of HIF-1 and NICD1 in Nos2 gene activation under hypoxia.

6. Mesothelial cell (MC) isolation and culture: Isolation and culture of mouse liver MC has recently been accomplished by the ILCC. Details at www.usc.com/alpd.

Did you know? The ILCC has served as a national resource by providing its services to 12 out-of-region investigators from 11 institutions across the nation and supporting grant acquisition and application by 6 of these investigators.

The ILCC (formerly known as the Non-Parenchymal Liver Cell Core) functions within the Southern California Research Center for ALPD and Cirrhosis, and is responsible for numerous liver cell isolation preparations for researchers across the country.

Cross-talk among parenchymal and non-parenchymal liver cell types, along with genetic and environmental effects on these communications, are critical components of the cellular and molecular mechanisms of alcohol liver disease (ALD), cirrhosis and liver cancer. The ILCC’s services are intended to lead to novel therapeutic targets for these diseases.

The ILCC is funded by an NIAAA R24 grant, and it was concurrent with the third renewal application for this grant that the ILCC underwent its extensive makeover, expanding existing services to include new, cutting edge procedures. Investigators across the nation will benefit from these changes!