Representation of the Liver Immune Response

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Immunology Ontologies and Their Applications in Processing Clinical Data
Buffalo 2012
Metabolic functions

Synthesis and secretion of protein

Purification, transformation, and clearance of toxins

Storage
Clinical relevance of Liver diseases

Local immune response plays a key role in the pathogenesis of the majority of liver diseases.

Changes in mortality

- Liver
- Hearth
- Respiratory
- Diabetes

Major Liver Diseases

- Metabolic: Alcohol abuse; obesity;
- Infectious: HBV, HCV, HIV and Plasmodium;
- Drug toxicity (DILI)

Immune response is context dependent

The Curious Case of Tumor Necrosis Factor (TNF)

\[
\text{induction of apoptosis} \quad \text{GO:0006917} \quad \text{IsA} \quad \text{negative regulation of apoptosis} \quad \text{GO:0043066}
\]

\[
\text{positive regulation of apoptosis} \quad \text{GO:0043065}
\]

still got doubts?

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The Curious Case of TNF and Cell Death: part II
The CD40 conundrum

GO:2000353: Positive regulation of endothelial cell apoptotic process

In Liver context

• Positive regulation of hepatocyte Fas-induced apoptosis
• Positive regulation of cholangiocyte Fas induced apoptosis
• Positive regulation of liver endothelial cell proliferation

Evidence for HCAECs PMID: 12885753
Liver functional unit
Liver immune response

Immune cells

Relations

Parenchimal cell
Liver Immunology Ontology

Liver tissue

Liver cell type

part_of

part_of

Macromolecule

Liver Biological Process

occurs_in

has_participant

has_participant

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LiverSinusoidalEndothelialCellCytokineSecretion

Cytokine secretion

LiverSinusoidalEndothelialCell

PlatetDerivedGrowthFactorBB
TumorGrowthFactorBeta

hepatic sinusoid

hasQuality
damaged

FMA:17543
PATO:0001167
GO:0050663
PATO:000012491
PR:000000046
CL:1000398

occursIn

hasParticipant

resultsInReleaseOf
connective tissue replacement involved in inflammatory response wound healing

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Liver Acute Tissue Injury

Liver Inflammation
Liver Fibrogenesis

Liver Chronic Tissue Damage
Liver Tissue Remodeling
Liver Vascular Remodeling
Liver Vascular Injury

- Injured liver platelet aggregation
- Injured liver platelet degranulation
- Injured liver blood clotting
- Injured liver cytokine secretion
- Injured liver positive regulation of vascular permeability
- Injured liver neutrophil cellular extravasation
- Injured liver neutrophil cell degranulation
LIO has the ability to capture differences between physiological and pathological responses.
Bridging biological ontologies

LIO

- Anatomical entity (FMA)
- Biological process (GO BP)
- Cellular component (GO CC)
- Macromolecule (PRO, SO, CheBi)
- Other ontologies
- Cell type (CL)
- Molecular function (GO MF)
**PROS**

Loss of the capacity to connect with other domains
Specific representation of Liver immune response
Loss of interoperability within other ontologies
Maintaining formal structure
Generation of a complex network of knowledge by bridging multiple ontologies
Future plans

Liver immune response in

• Infectious diseases
• Metabolic disorders
• Drug cytotoxicity
Aknowledgement and ongoing collaborations

Research Computing Center, University of North Carolina, Jeffrey Roach

European Molecular Biology Laboratory, European Bioinformatics Institute, UK Bernard de Bono Pierre Grenon

Department of Gastroenterology, Duke University Anna Mae Diehl

UT Southwestern Medical Center Lindsay Cowell
EVERYTHING SHOULD BE MADE AS SIMPLE AS POSSIBLE, BUT NOT SIMPLER

A. EINSTEIN