



Representation of the Liver Immune Response

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**Immunology Ontologies and Their Applications in
Processing Clinical Data
Buffalo 2012**



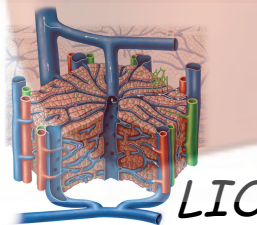
Metabolic functions

**Synthesis and
secretion of protein**

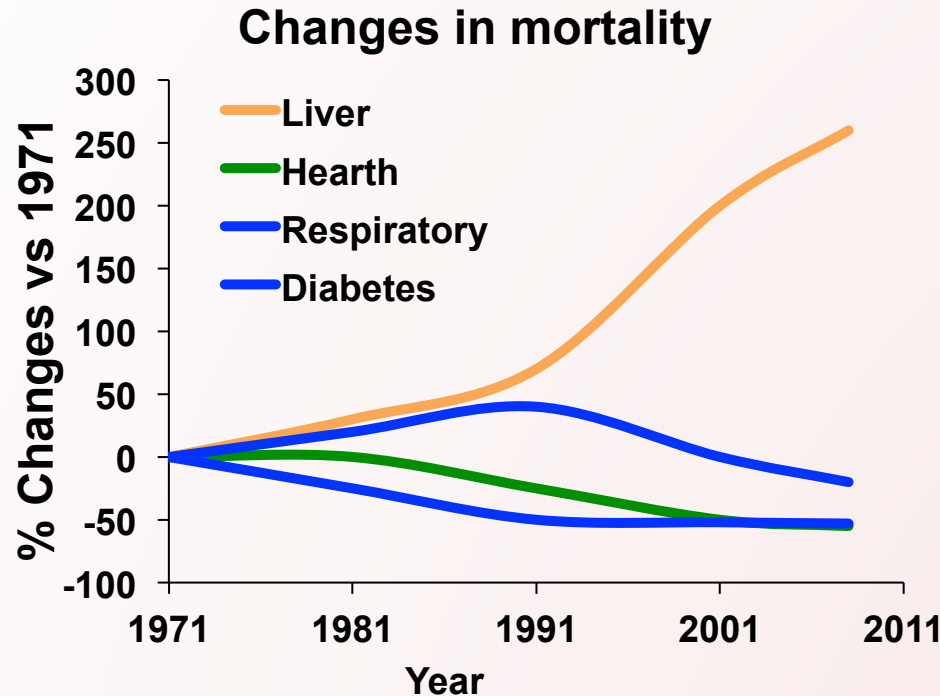
LIVER

**Purification
transformation
and clearance of
toxins**

Storage



Clinical relevance of Liver diseases



Office for National Statistics: Health Service
Quarterly, Winter 2008, No. 40 p59-60

Major Liver Diseases

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

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

Immune response is context dependent

The Curious Case of Tumor Necrosis Factor (TNF)

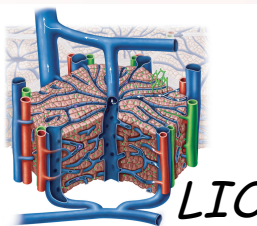
induction of apoptosis
GO:0006917

negative regulation of apoptosis
GO:0043066

IsA

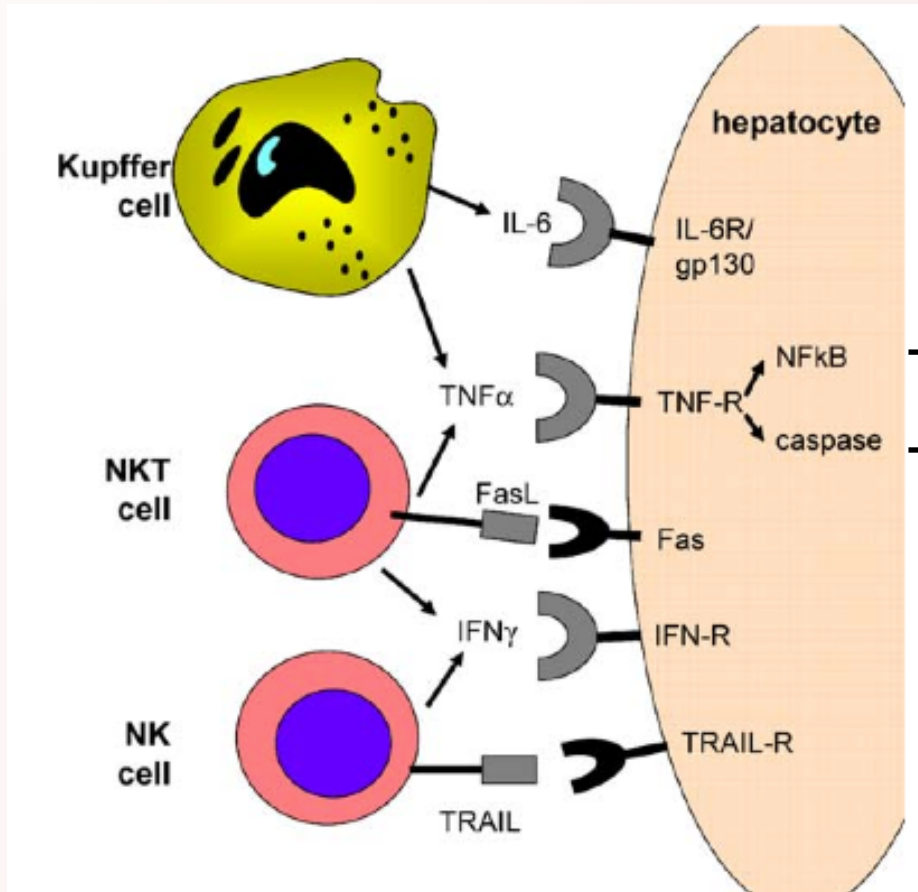
positive regulation of apoptosis
GO:0043065

still got
doubts?



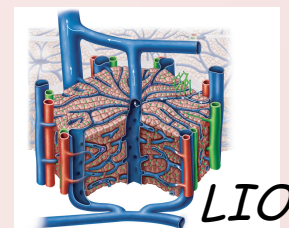
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The Curious Case of TNF and Cell Death: part II



Survival

Death



The CD40 conundrum

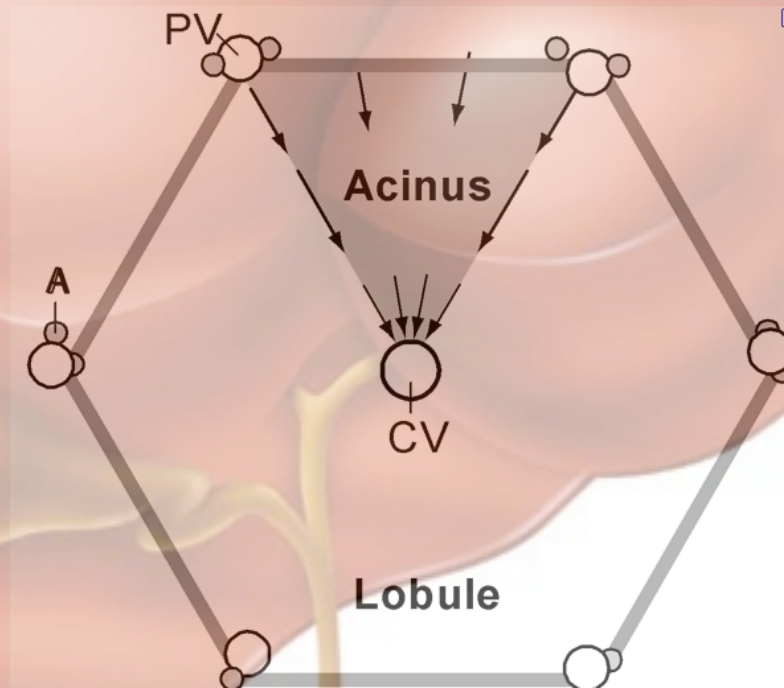
GO:2000353: Positive regulation of endothelial cell apoptotic process

In Liver context

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

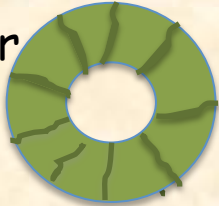
Evidence for HCAECs PMID: 12885753

Liver functional unit



Portal triade

Interlobular
Bile duct



Portal vein

Hepatocyte



HSC
Disse space

Sinusoid

KC

Central vein

EC

Disse space

Hepatocyte



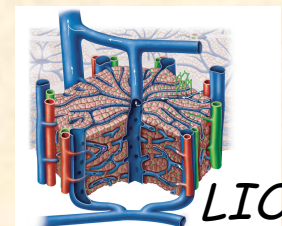
Hepatic arteriole



EC Endothelial cell

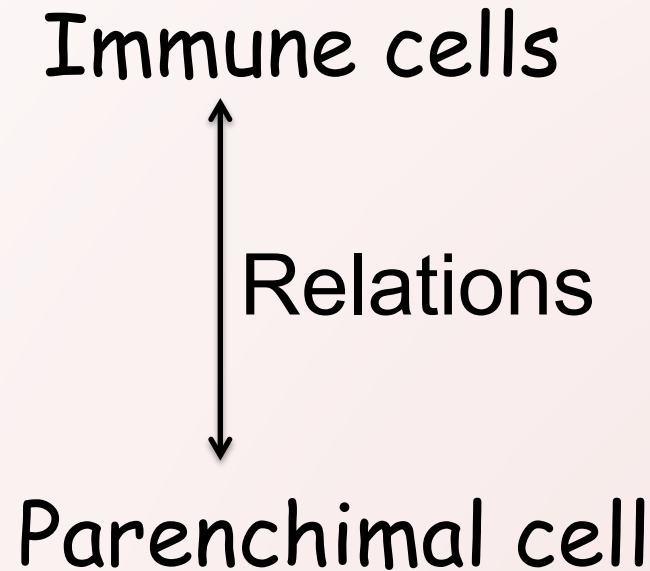
KC Kupffer cell

HSC Hepatic Stellate cell

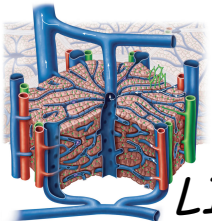
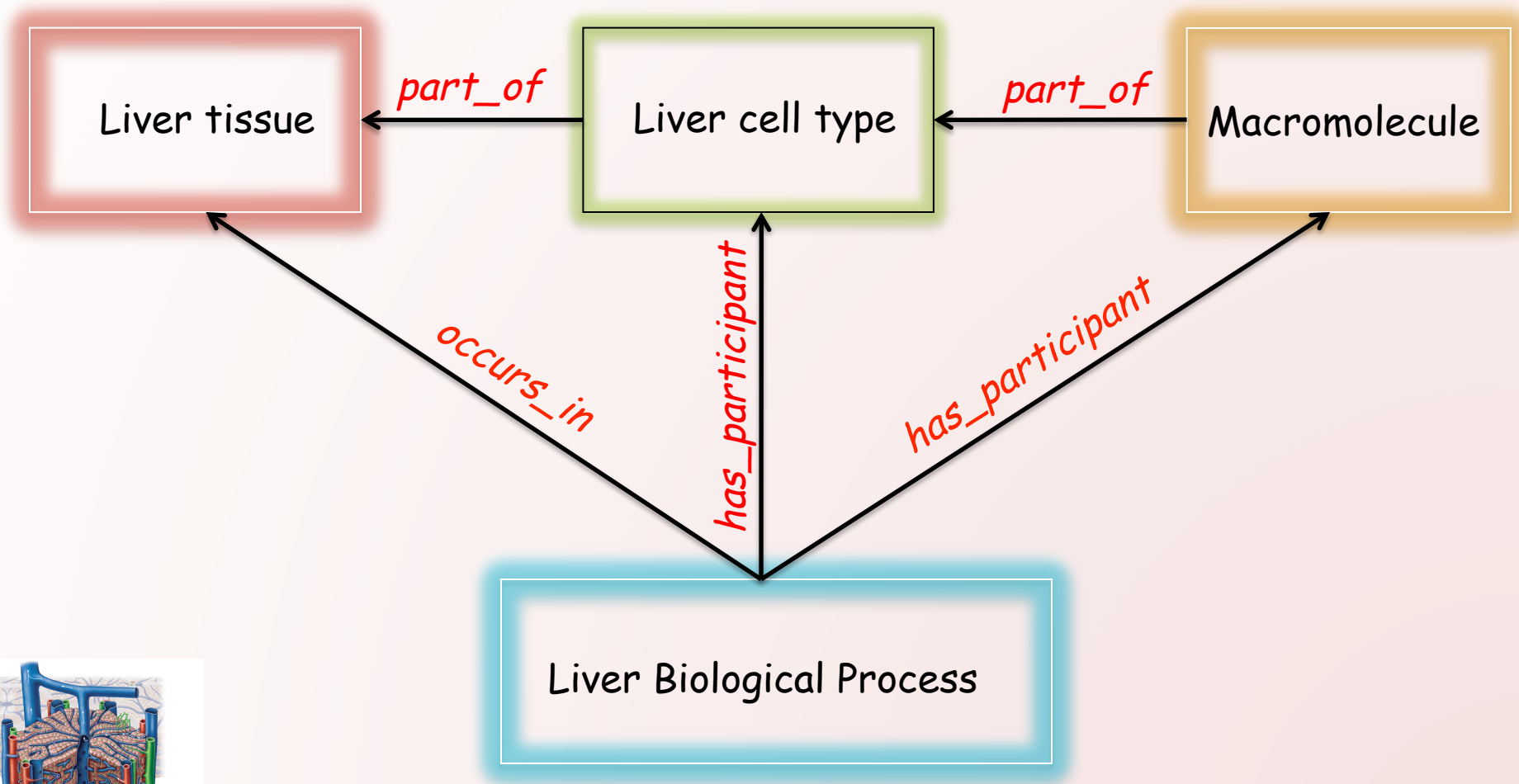


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Liver immune response



LIVER IMMUNOLOGY ONTOLOGY



LIVER IMMUNOLOGY ONTOLOGY

FMA

CL

PRO, SO, CheBi

Liver tissue

part_of

Liver cell type

part_of

Macromolecule

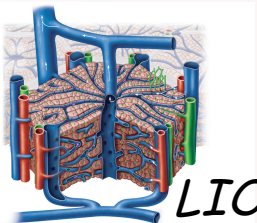
occurs_in

has_participant

has_participant

Liver Biological Process

GO



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GO:0050663

Cytokine secretion

isA

LiverSinusoidalEndothelialCellCytokineSecretion

LIO

OccursIn

hasParticipant

FMA:17543

hepatic sinusoid

hasQuality

PATO:0001167

damaged

LiverSinusoidalEndothelialCell

CL:1000398

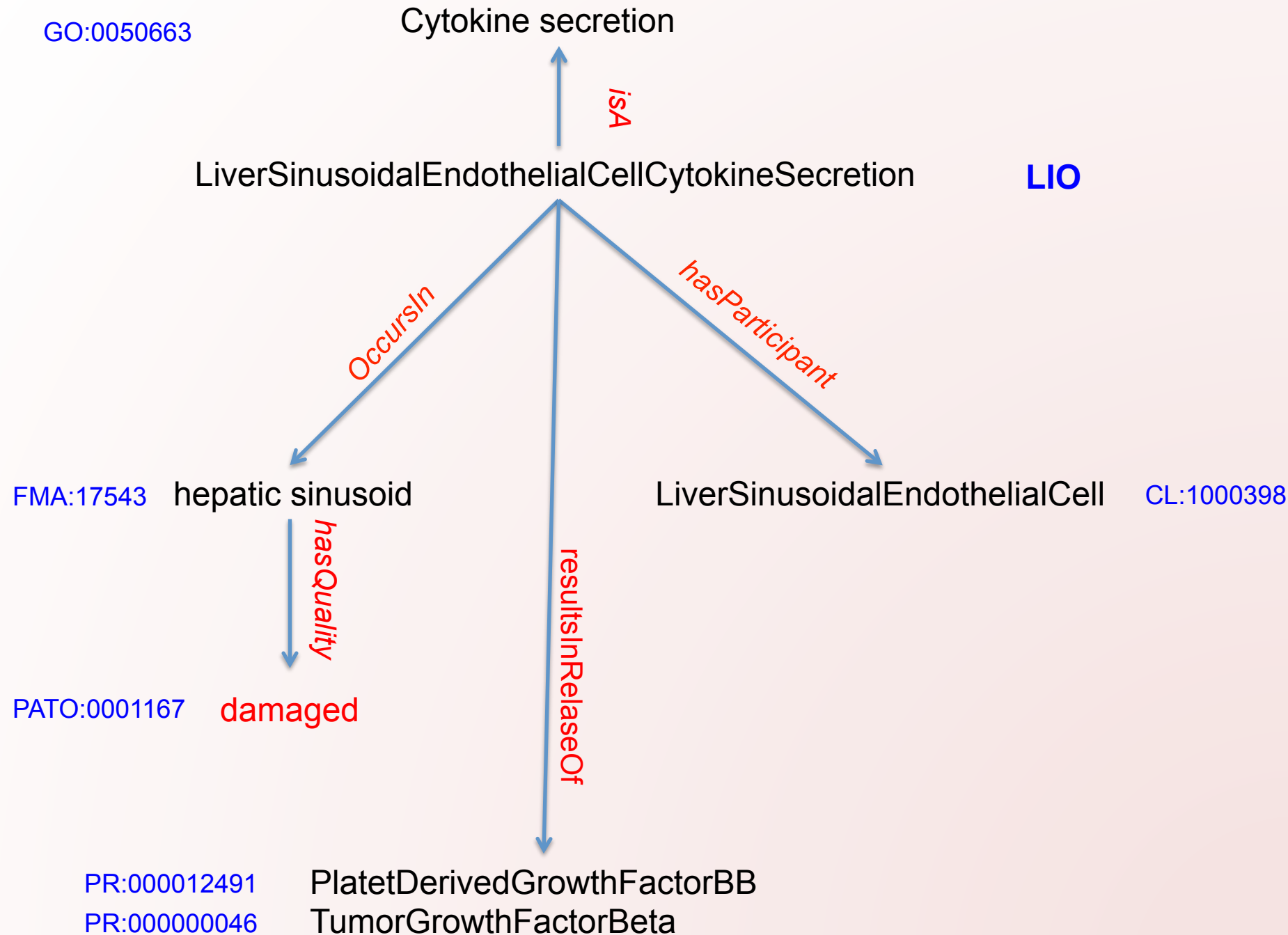
resultsInReleaseOf

PR:000012491

PlatetDerivedGrowthFactorBB

PR:000000046

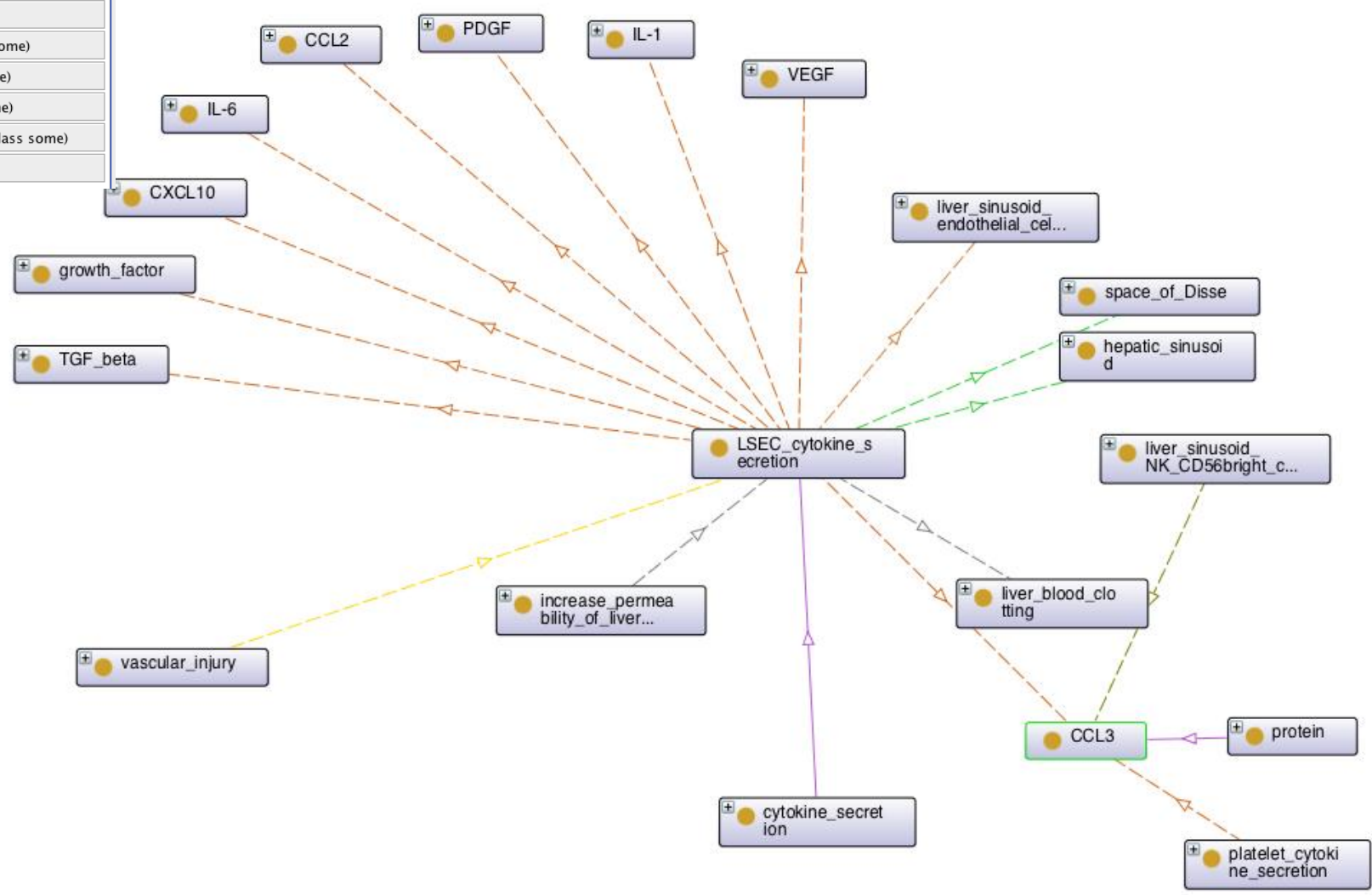
TumorGrowthFactorBeta

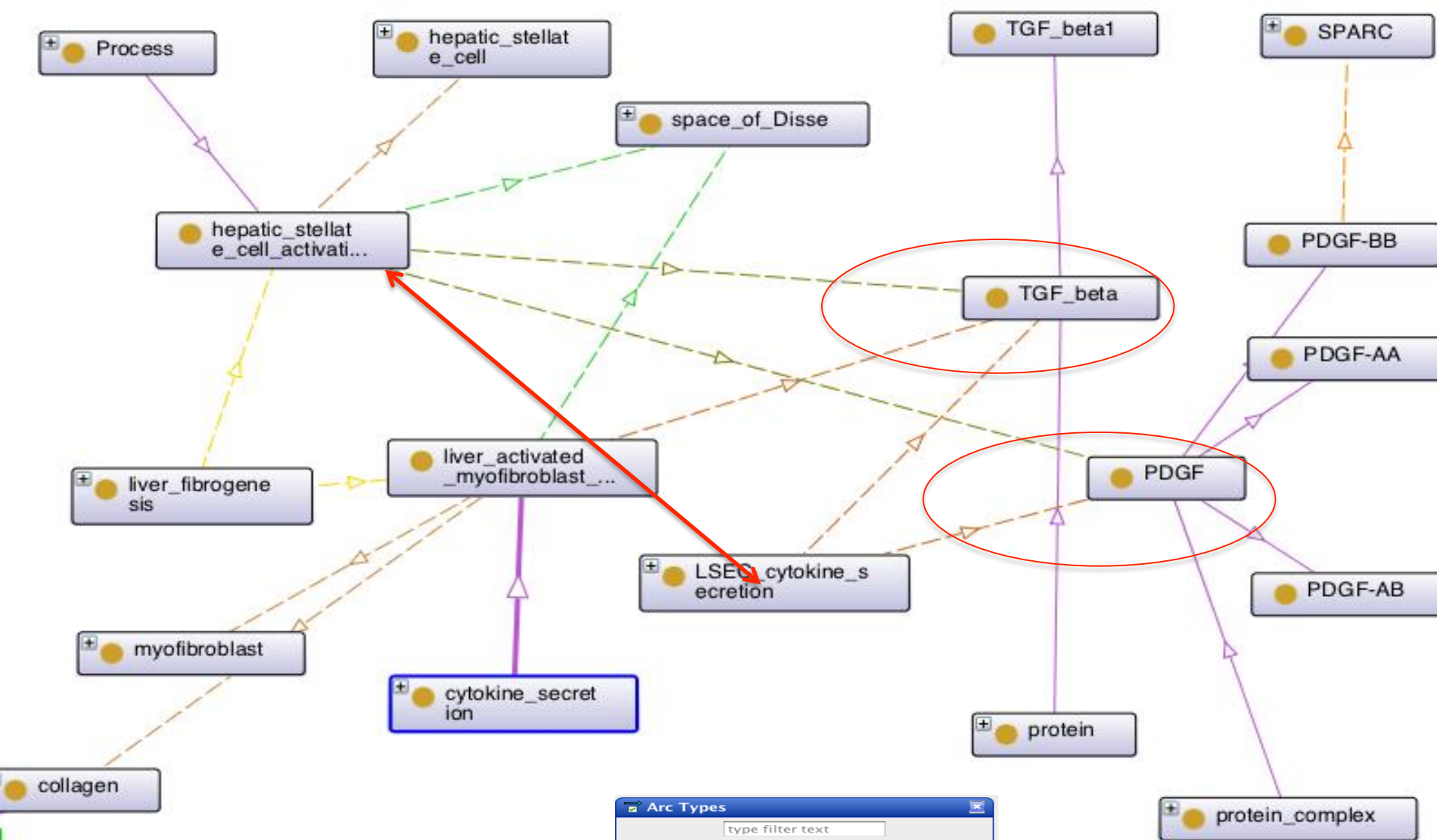


Arc Types

type filter text

- ☒ has individual
- ☒ has subclass
- ☒ has_function(Subclass some)
- ☒ has_part(Subclass some)
- ☒ has_participant(Subclass some)
- ☒ preceded_by(Subclass some)
- ☒ regulated_by(Subclass some)
- ☒ results_in_release_of(Subclass some)
- ☒ unfolds_in(Subclass some)





Arc Types	
	type filter text
<input checked="" type="checkbox"/>	has individual
<input checked="" type="checkbox"/>	has subclass
<input checked="" type="checkbox"/>	has_function(Subclass some)
<input checked="" type="checkbox"/>	has_part(Subclass some)
<input checked="" type="checkbox"/>	has_participant(Subclass some)
<input checked="" type="checkbox"/>	precedes_by(Subclass some)
<input checked="" type="checkbox"/>	regulated_by(Subclass some)
<input checked="" type="checkbox"/>	results_in_release_of(Subclass some)
<input checked="" type="checkbox"/>	unfolds_in(Subclass some)

connective tissue replacement involved in inflammatory response wound healing

[Term information](#) ↓ [Term neighborhood](#) ↓ [External references](#) ↓ [13 gene product associations](#) ↗

Term Information

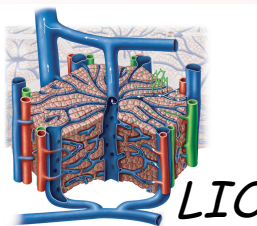
Accession GO:0002248

Ontology **Biological Process**

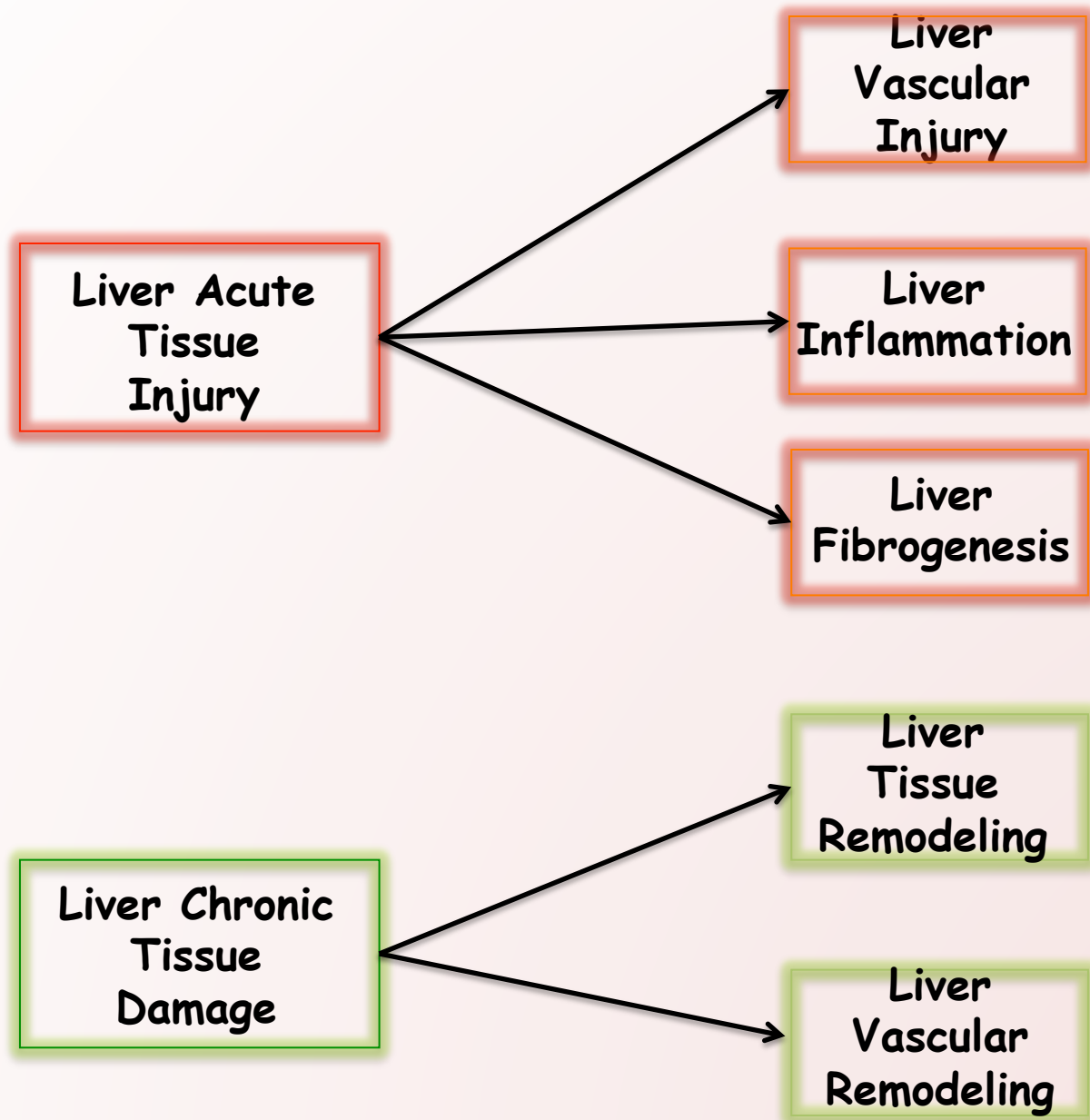
Synonyms **related:** connective tissue replacement during inflammatory response
narrow: fibrosis during inflammatory response

Definition This series of events leading to growth of connective tissue when loss of tissues that are incapable of regeneration occurs, or when fibrinous exudate cannot be adequately cleared that contribute to an inflammatory response.

Source: GOC:jal, ISBN:0721601871



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**Liver
Vascular
Injury**

Injured liver platelet aggregation

Injured liver platelet degranulation

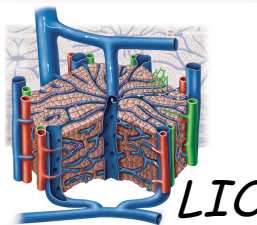
Injured liver blood clotting

Injured liver cytokine secretion

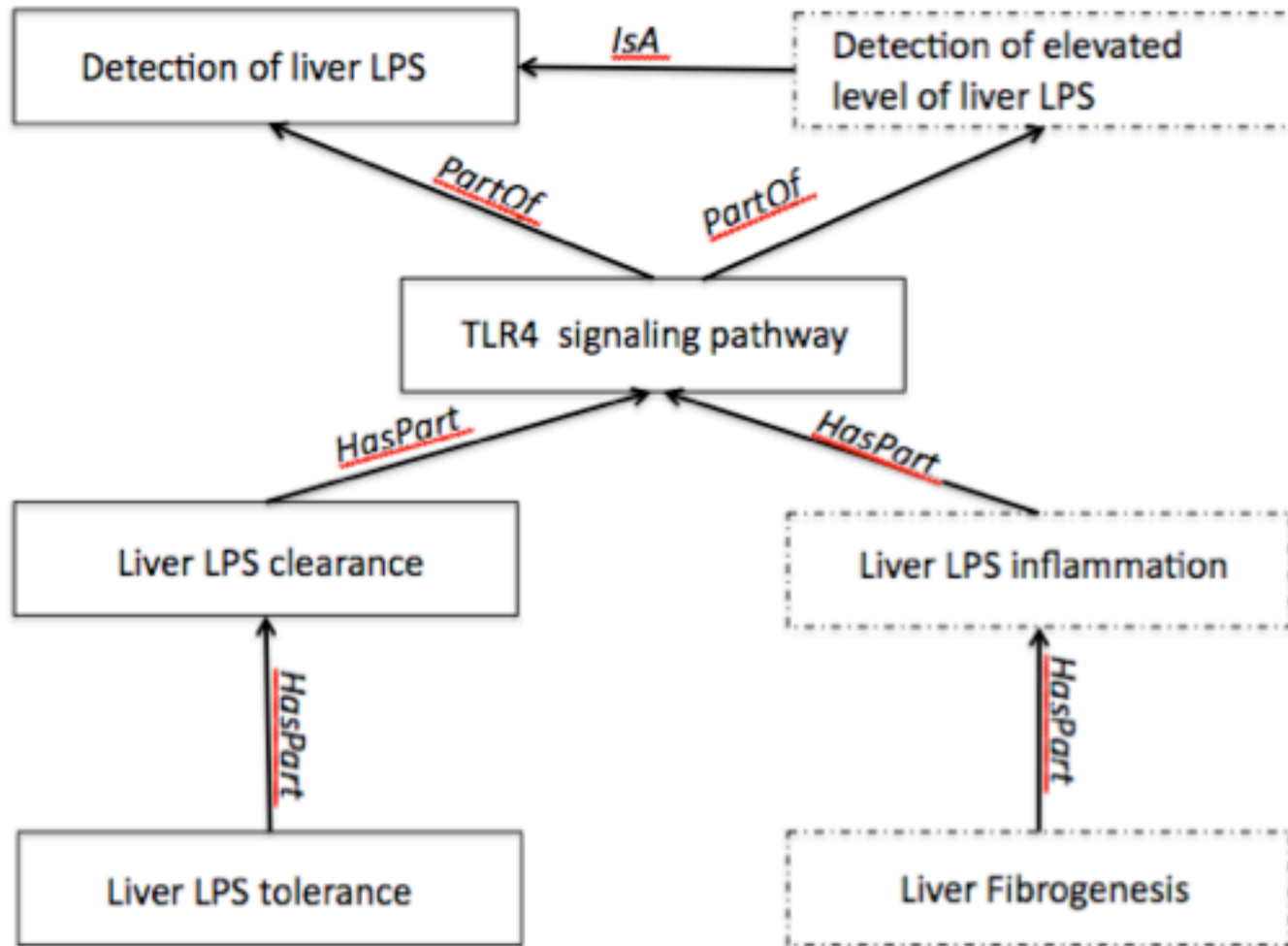
Injured liver positive regulation of vascular permeability

Injured liver neutrophil cellular extravasation

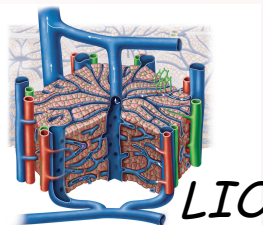
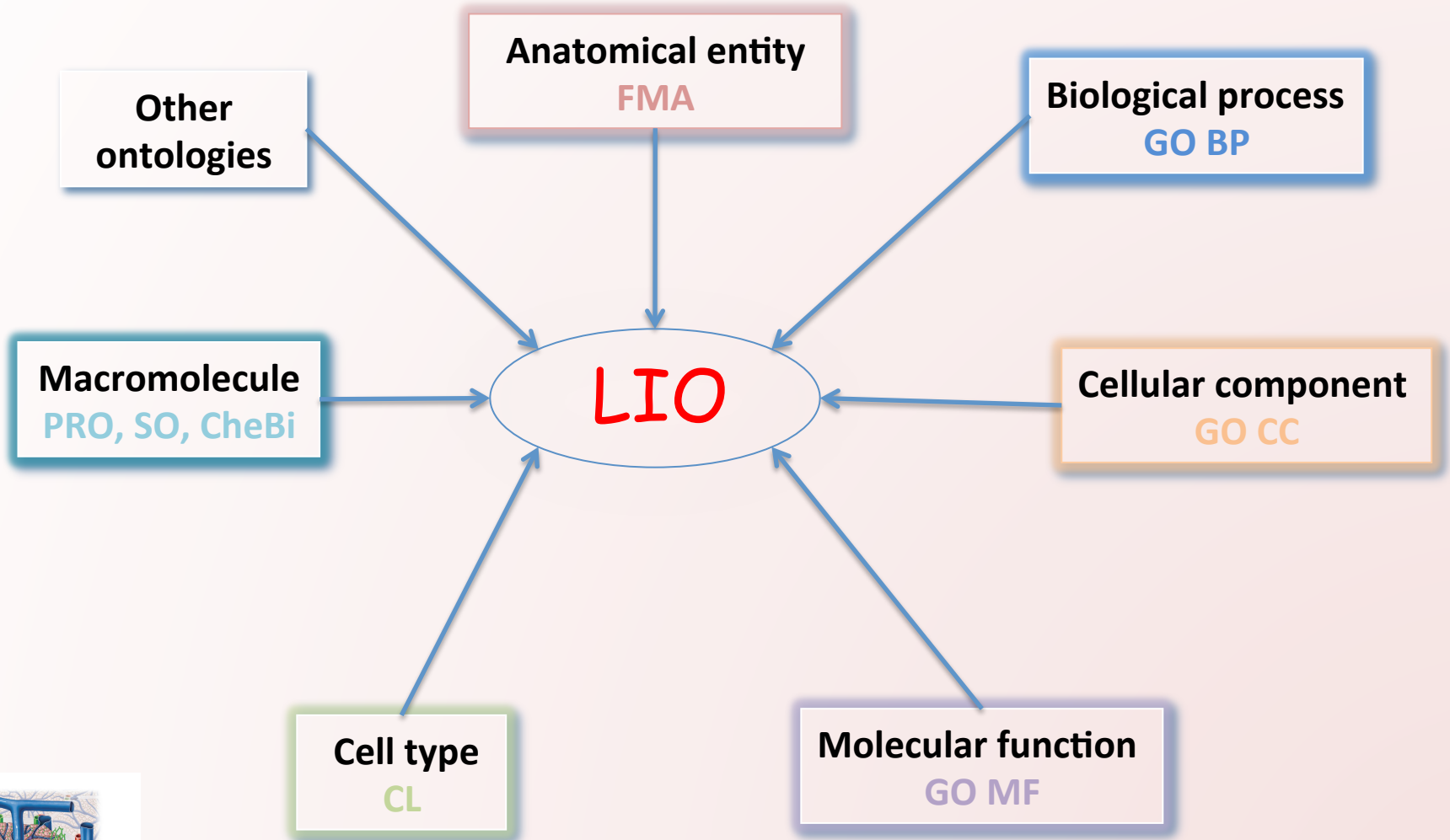
Injured liver neutrophil cell degranulation



LIO has the ability to capture differences between physiological and pathological responses

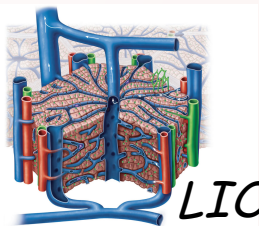


Bridging biological ontologies



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



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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

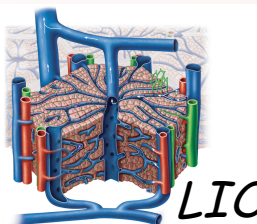
Bernard de Bono
Pierre Grenon

Department of Gastroenterology,
Duke University

Anna Mae Diehl

UT Southwestern Medical Center

Lindsay Cowell



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**EVERYTHING SHOULD BE MADE AS SIMPLE AS POSSIBLE,
BUT NOT SIMPLER**

A. EINSTEIN