Supplemental Figure 1 (goes with Figure 3)
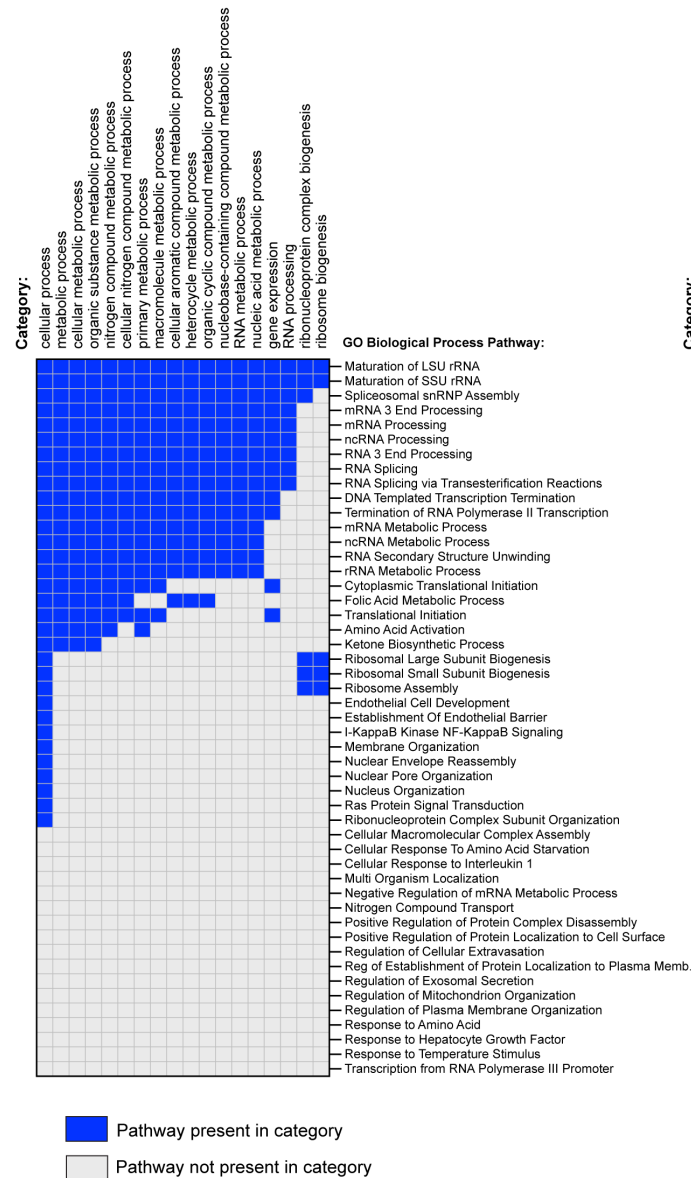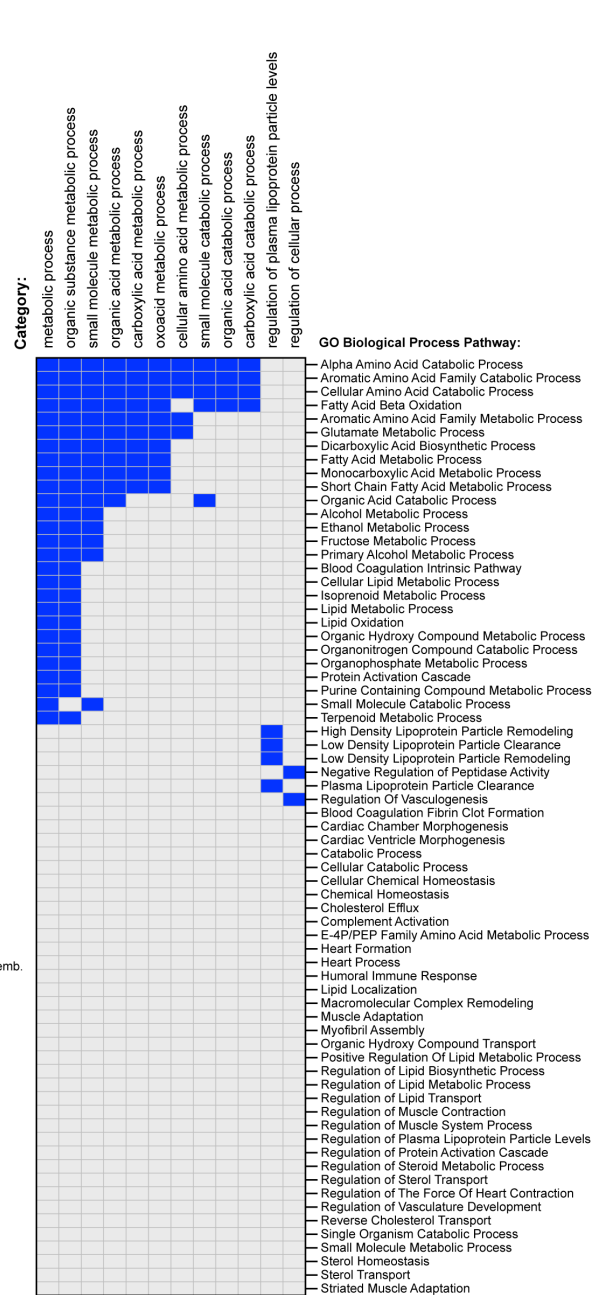
A Pathways induced by O₂ in WT and mitigated in *Cyp1b1*-null mice (49 pathways)

Category:
- cellular process
- metabolic process
- cellular metabolic process
- organic substance metabolic process
- nitrogen compound metabolic process
- cellular nitrogen compound metabolic process
- primary metabolic process
- macromolecule metabolic process
- cellular aromatic compound metabolic process
- heterocycle metabolic process
- organic cyclic compound metabolic process
- nucleobase-containing compound metabolic process
- RNA metabolic process
- nucleic acid metabolic process
- gene expression
- RNA processing
- ribonucleoprotein complex biogenesis
- ribosome biogenesis

GO Biological Process Pathway:
- Maturation of LSU rRNA
- Maturation of SSU rRNA
- Spliceosomal snRNP Assembly
- mRNA 3 End Processing
- mRNA Processing
- ncRNA Processing
- RNA 3 End Processing
- RNA Splicing
- RNA Splicing via Transesterification Reactions
- DNA Templated Transcription Termination
- Termination of RNA Polymerase II Transcription
- mRNA Metabolic Process
- ncRNA Metabolic Process
- RNA Secondary Structure Unwinding
- rRNA Metabolic Process
- Cytoplasmic Translational Initiation
- Folic Acid Metabolic Process
- Translational Initiation
- Amino Acid Activation
- Ketone Biosynthetic Process
- Ribosomal Large Subunit Biogenesis
- Ribosomal Small Subunit Biogenesis
- Ribosome Assembly
- Endothelial Cell Development
- Establishment Of Endothelial Barrier
- I-KappaB Kinase NF-KappaB Signaling
- Membrane Organization
- Nuclear Envelope Reassembly
- Nuclear Pore Organization
- Nucleus Organization
- Ras Protein Signal Transduction
- Ribonucleoprotein Complex Subunit Organization
- Cellular Macromolecular Complex Assembly
- Cellular Response To Amino Acid Starvation
- Cellular Response to Interleukin 1
- Multi Organism Localization
- Negative Regulation of mRNA Metabolic Process
- Nitrogen Compound Transport
- Positive Regulation of Protein Complex Disassembly
- Positive Regulation of Protein Localization to Cell Surface
- Regulation of Cellular Extravasation
- Reg of Establishment of Protein Localization to Plasma Memb.
- Regulation of Exosomal Secretion
- Regulation of Mitochondrion Organization
- Regulation of Plasma Membrane Organization
- Response to Amino Acid
- Response to Hepatocyte Growth Factor
- Response to Temperature Stimulus
- Transcription from RNA Polymerase III Promoter

■ Pathway present in category

▢ Pathway not present in category

B Pathways suppressed by O₂ in WT and mitigated in *Cyp1b1*-null mice (69 pathways)

Category:
- metabolic process
- organic substance metabolic process
- small molecule metabolic process
- organic acid metabolic process
- carboxylic acid metabolic process
- oxoacid metabolic process
- cellular amino acid metabolic process
- small molecule catabolic process
- organic acid catabolic process
- carboxylic acid catabolic process
- regulation of plasma lipoprotein particle levels
- regulation of cellular process

GO Biological Process Pathway:
- Alpha Amino Acid Catabolic Process
- Aromatic Amino Acid Family Catabolic Process
- Cellular Amino Acid Catabolic Process
- Fatty Acid Beta Oxidation
- Aromatic Amino Acid Family Metabolic Process
- Glutamate Metabolic Process
- Dicarboxylic Acid Biosynthetic Process
- Fatty Acid Metabolic Process
- Monocarboxylic Acid Metabolic Process
- Short Chain Fatty Acid Metabolic Process
- Organic Acid Catabolic Process
- Alcohol Metabolic Process
- Ethanol Metabolic Process
- Fructose Metabolic Process
- Primary Alcohol Metabolic Process
- Blood Coagulation Intrinsic Pathway
- Cellular Lipid Metabolic Process
- Isoprenoid Metabolic Process
- Lipid Metabolic Process
- Lipid Oxidation
- Organic Hydroxy Compound Metabolic Process
- Organonitrogen Compound Catabolic Process
- Organophosphate Metabolic Process
- Protein Activation Cascade
- Purine Containing Compound Metabolic Process
- Small Molecule Catabolic Process
- Terpenoid Metabolic Process
- High Density Lipoprotein Particle Remodeling
- Low Density Lipoprotein Particle Clearance
- Low Density Lipoprotein Particle Remodeling
- Negative Regulation of Peptidase Activity
- Plasma Lipoprotein Particle Clearance
- Regulation Of Vasculogenesis
- Blood Coagulation Fibrin Clot Formation
- Cardiac Chamber Morphogenesis
- Cardiac Ventricle Morphogenesis
- Catabolic Process
- Cellular Catabolic Process
- Cellular Chemical Homeostasis
- Chemical Homeostasis
- Cholesterol Efflux
- Complement Activation
- E-4P/PEP Family Amino Acid Metabolic Process
- Heart Formation
- Heart Process
- Humoral Immune Response
- Lipid Localization
- Macromolecular Complex Remodeling
- Muscle Adaptation
- Myofibril Assembly
- Organic Hydroxy Compound Transport
- Positive Regulation Of Lipid Metabolic Process
- Regulation of Lipid Biosynthetic Process
- Regulation of Lipid Metabolic Process
- Regulation of Lipid Transport
- Regulation of Muscle Contraction
- Regulation of Muscle System Process
- Regulation of Plasma Lipoprotein Particle Levels
- Regulation of Protein Activation Cascade
- Regulation of Steroid Metabolic Process
- Regulation of Sterol Transport
- Regulation of The Force Of Heart Contraction
- Regulation of Vasculature Development
- Reverse Cholesterol Transport
- Single Organism Catabolic Process
- Small Molecule Metabolic Process
- Sterol Homeostasis
- Sterol Transport
- Striated Muscle Adaptation

Supplemental Figure 2 (goes with Figure 6)

A

IPF Signature:	GSE93606	GSE53845	GSE35145	GSE24206	GSE110147
WT: O_2 over RA	0.00	0.00	0.00	0.00	0.55
Cyp1a1 KO: O_2 over RA	0.34	0.00	0.00	0.00	0.36
Cyp1a2 KO: O_2 over RA	0.00	0.00	0.00	0.00	0.00
Cyp1b1 KO: O_2 over RA	0.33	0.00	0.00	0.00	0.00
Cyp1a1 KO O_2 over WT O_2	0.00	0.00	0.00	0.00	0.00
Cyp1a2 KO O_2 over WT O_2	0.00	-0.50	-0.73	-0.63	-0.81
Cyp1b1 KO O_2 over WT O_2	0.00	-0.54	0.00	-0.60	0.00

Pearson correlation (r)
-1   0   1

B

GSE110147
WT: O_2 over RA
r = 0.55
p=0.000891

0 = no IPF (n=11)
1 = IPF (n=22)

GSE53845
Cyp1b1 KO O_2 over WT O_2
r = −0.54
p=0.000079

0 = no IPF (n=4)
1 = IPF (n=4)

GSE24206
Cyp1b1 KO O_2 over WT O_2
r = −0.60
p=0.019055

0 = no IPF (n=6)
1 = IPF (n=9)

summed Z-score