ESPERION®

Welcome to R&D Day

April 24, 2025

Forward-looking Statements & Disclosures

This investor presentation contains forward-looking statements that are made pursuant to the safe harbor provisions of the federal securities laws, including statements regarding marketing strategy and commercialization plans, current and planned operational expenses, future operations, commercial products, clinical development, plans for potential future product candidates, financial condition and outlook, including expected cash runway, and other statements containing the words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “suggest,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” and similar expressions. Any express or implied statements contained in this investor presentation that are not statements of historical fact may be deemed to be forward-looking statements. Forward-looking statements involve risks and uncertainties that could cause Esperion’s actual results to differ significantly from those projected, including, without limitation, the net sales, profitability, and growth of Esperion’s commercial products, clinical activities and results, supply chain, commercial development and launch plans, the outcomes and anticipated benefits of legal proceedings and settlements, and the risks detailed in Esperion’s filings with the Securities and Exchange Commission. Any forward-looking statements contained in this investor presentation speak only as of the date hereof, and Esperion disclaims any obligation or undertaking to update or revise any forward-looking statements contained in this investor presentation, other than to the extent required by law.

Leadership in Attendance

Sheldon Koenig

PRESIDENT AND CHIEF EXECUTIVE OFFICER

Ben Halladay

CHIEF FINANCIAL OFFICER

BJ Swartz

CHIEF BUSINESS OFFICER

Stephen Pinkosky, PhD

VP, EARLY & PRE-CLINICAL DRUG DISCOVERY

LeAnne Bloedon, MS, RD

VP, CLINICAL DEVELOPMENT

Satish Nachaegari

VP, GLOBAL REGULATORY AFFAIRS

Key Opinion Leaders & Advocacy Partners

Christos Mantzoros
MD, DSc, PhD h.c. mult

PROFESSOR OF MEDICINE
HARVARD MEDICAL SCHOOL

David E. Cohen
MD, PhD

CHIEF, DIVISION OF GASTROENTEROLOGY, HEPATOLOGY AND ENDOSCOPY, BRIGHAM AND WOMEN'S HOSPITAL

Mary Pressley Vyas

VP, STRATEGIC INITIATIVES
PSC PARTNERS

ESPERION R&D Day 2025

AGENDA

9:00 am	**Welcome and Opening Remarks** Sheldon Koenig, President and CEO, Esperion
9:05 am	**Next Gen ACLY Inhibition Discovery Program Introduction** Stephen Pinkosky, PhD, VP Early & Pre-Clinical Drug Discovery, Esperion
9:10 am	**ACLY as an Energy Nexus** Christos Mantzoros, MD, DSc, PhD h.c. mult, Professor of Medicine, Harvard Medical School
9:35 am	**Identification of Novel ACLY Pathways** Stephen Pinkosky, VP Early & Pre-Clinical Drug Discovery, Esperion
10:00 am	**Primary Sclerosing Cholangitis** David E. Cohen, MD, PhD Chief, Division of Gastroenterology, Hepatology and Endoscopy, Brigham and Women's Hospital
10:25 am	**Break**
10:35 am	**PSC Patient Voice: Insights from Patients and Advocates** Mary Pressley Vyas, VP Strategic Initiatives, PSC Partners
10:50 am	**Introduction to Lead Candidate & Market Opportunity** Stephen Pinkosky, PhD, VP Early & Pre-Clinical Drug Discovery, Esperion
11:05 am	**KOL Discussion** Christos Mantzoros, MD, DSc, PhD h.c. mult, Professor of Medicine, Harvard Medical School David E. Cohen, MD, PhD Chief, Division of Gastroenterology, Hepatology and Endoscopy, Brigham and Women's Hospital
11:30 am	**Q&A**
11:55 am	**Closing Remarks** Sheldon Koenig, President and CEO, Esperion

Three Pillar Strategy for Success

Expand Bempedoic Acid Franchise Globally

Strong and consistent prescription demand and increasing physician adoption continue to drive durable revenue growth

- Achieved **growth** since U.S. label expansion
- Supported by **global partnerships** who are making **significant progress** driving international revenue
- Developing **triple combination products** with Bempedoic Acid in the **U.S.**

Reach Sustainable Operating Profitability

Revenue growth, operating efficiency and expense discipline will pave the way to long-term profitability and free cash flow generation

Key Financial Data

FY 2025 R&D Guidance	$55 - 65 M
FY 2025 SG&A Guidance	$160 - 170 M
FY 2025 OpEx Guidance[1]	$215 - 235 M

Portfolio Expansion and Pipeline Advancement

Our strengthened balance sheet and capital structure support plans to expand our portfolio

- Advancing our **internally developed and wholly owned** development pipeline
- **Potential acquisition or in-licensing** of cardiometabolic products that are **synergistic with our commercial call point**

1. Includes ~$15 million of non-cash stock-based compensation expense

ESPERION®

Esperion's Next Generation ACLY Inhibition Discovery Program

Stephen Pinkosky, PhD

Vice President, Drug Discovery, Early Pre-Clinical Development

Expanding Our Pipeline Through ACLY Innovation and Expertise

Innovative Portfolio & Pipeline

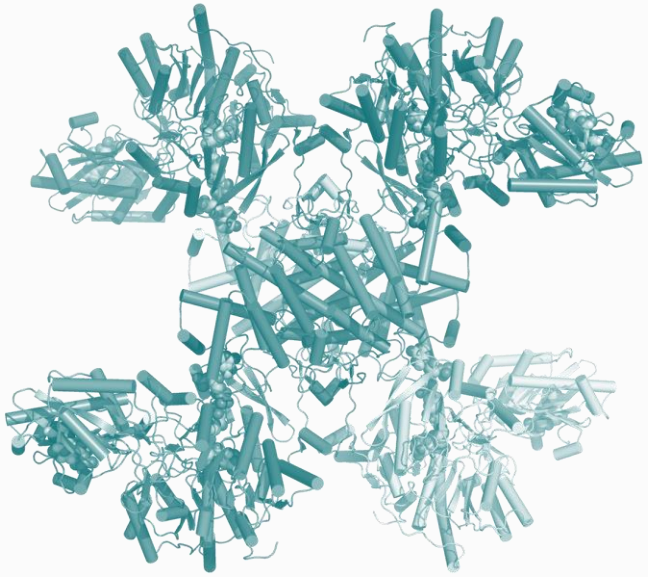
PRODUCT/PROGRAM	EXPLORATORY	LEAD ID	LEAD OPTIMIZATION	PRECLINICAL DEVELOPMENT	CLINICAL DEVELOPMENT	APPROVED / COMMERCIAL	MILESTONES
Cardiovascular Disease (LDL-C lowering / CV Risk reduction)							
NEXLETOL® bempedoic acid							Approved 2020 Expanded label 2024
NEXLIZET® bempedoic acid and ezetimibe							Approved 2020 Expanded label 2024
Triple Combination A bempedoic acid, ezetimibe, and atorvastatin							NDA: 2027
Triple Combination B bempedoic acid, ezetimibe, and rosuvastatin							NDA: 2027
Liver Diseases							
Primary Sclerosing Cholangitis (PSC)							IND: 2026
Renal Diseases							To Be Announced

ACLY: ATP citrate lyase; LDL-C: low-density lipoprotein cholesterol; CV: cardiovascular; NDA: New Drug Application; IND: Investigational New Drug

Leveraging Decades of Expertise in ACLY Inhibition

Objectives of the Next-Generation ACLY Inhibitor Discovery Program:

- **Use leading edge approaches and technology** to identify/design differentiated new chemical entity
- **Improve potency and specificity** several orders of magnitude vs current active site inhibitors
- **Target several cell types** important in disease pathogenesis
- **Identify potential indications and patient populations** using leading-edge bioinformatic approaches

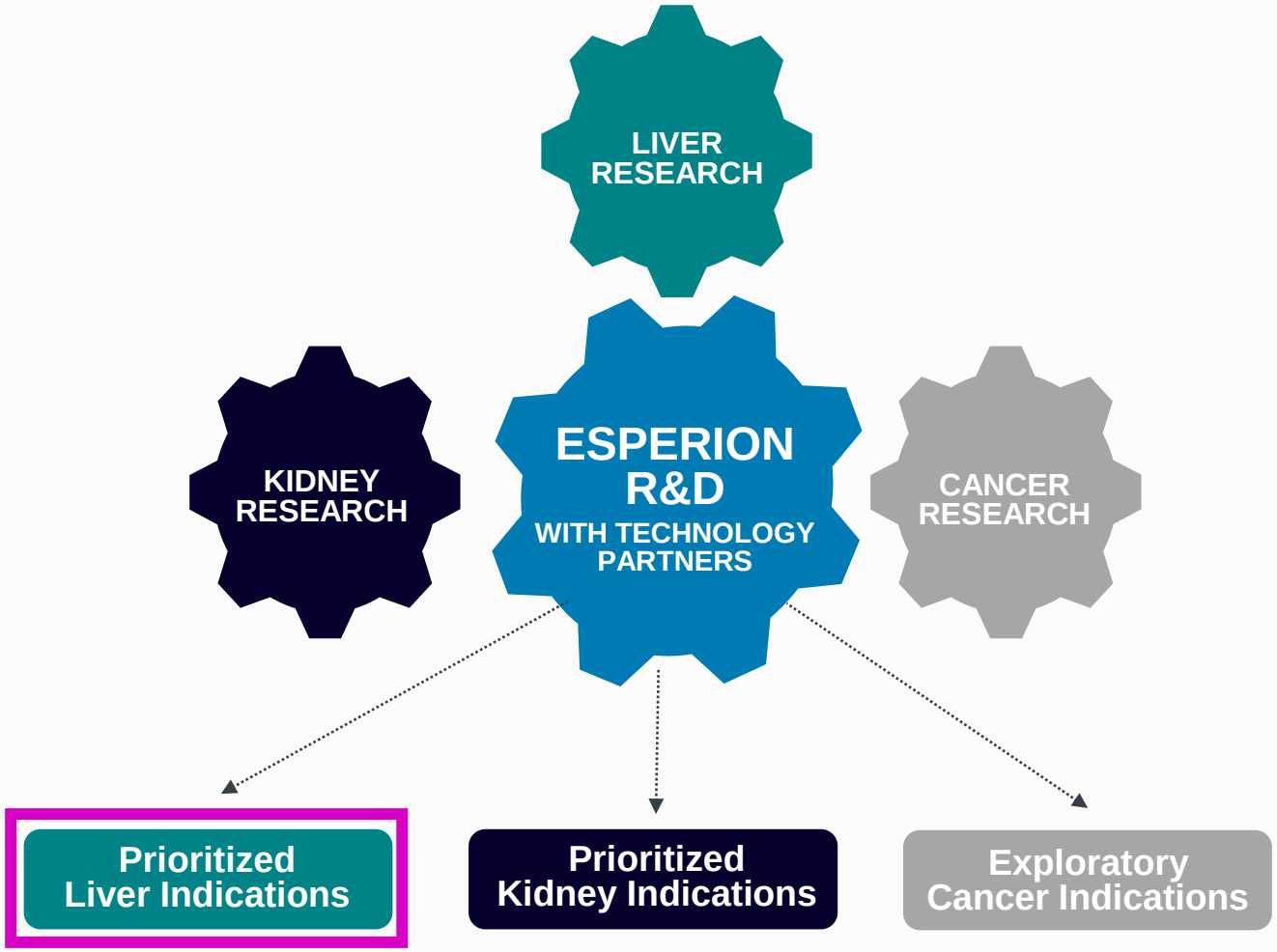


ACLY
(homotetramer)

ACLY: ATP citrate lyase

Graphic adapted from Verschueren KH, et al. *Nature*. 2019; **568** (7753): 571–575.

Target Validation Informs Esperion's Next-Generation Indication Selection



Identify novel ACLY pathways and links to diseases

Phenome-wide association studies

↓

Multi-omics

↓

Preclinical intervention studies

↓

Biomarkers

ACLY: ATP citrate lyase

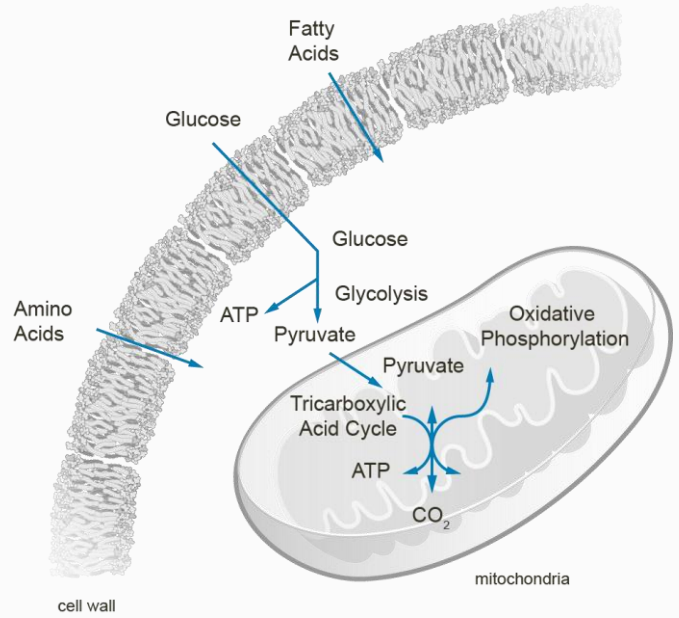
ESPERION®

ACLY as an Energy Nexus

Christos Mantzoros MD, DSc, PhD h.c. mult
Professor of Medicine, Harvard Medical School

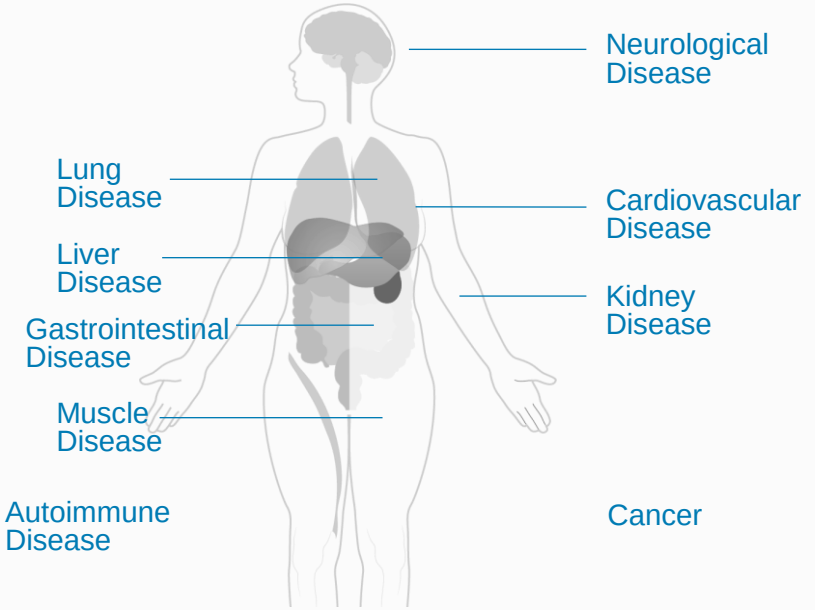
Dysregulated Cellular Energetics Drive Many Diseases[1-3]

Metabolic Energy Pathways



Dysregulation

Development of Disease



Cellular energetics are a fundamental aspect of biology describing how cells generate and utilize energy.

When dysregulated, there is disruption of normal energy production and utilization primarily linked to tricarboxylic acid (TCA) cycle function.

ATP: adenosine triphosphate

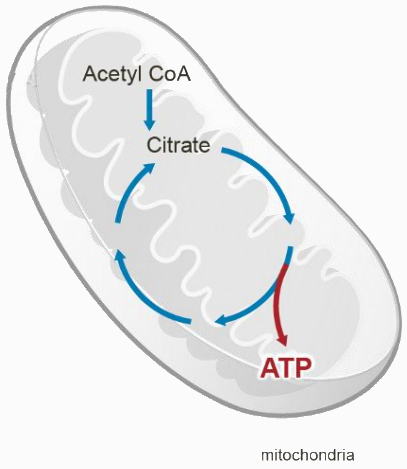
1. Ren J, et al. *J Mol Med*. 2010;88:993–1001; 2. Rocha M, et al. *Medicinal Research Reviews*. 2013;00:1–30; 3. Javadov S, et al. *Cells*. 2020;9:1177
Adapted from https://www.britannica.com/science/catabolism

ESPERION

The Canonical and Non-Canonical TCA Cycles are Critical Metabolic Pathways in All Cells[1-3]

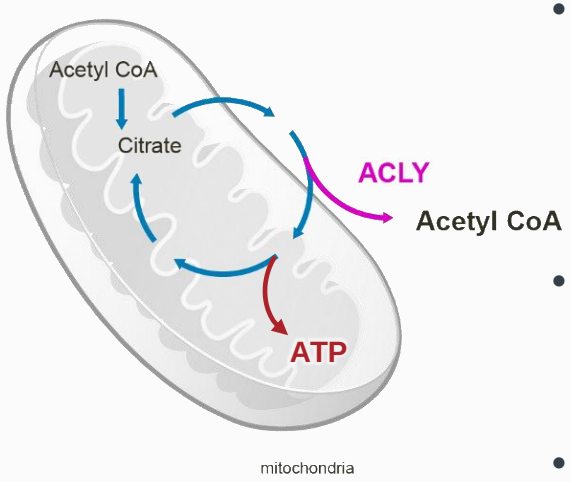
There are 2 versions of the TCA cycle which differentially control acetyl CoA within the cell

Canonical TCA (Krebs) Cycle



- Primarily **catabolic pathway** that consumes lipids and carbohydrates to **generate ATP—energy production**
- Occurs in **mitochondria only**

Non-Canonical TCA Cycle



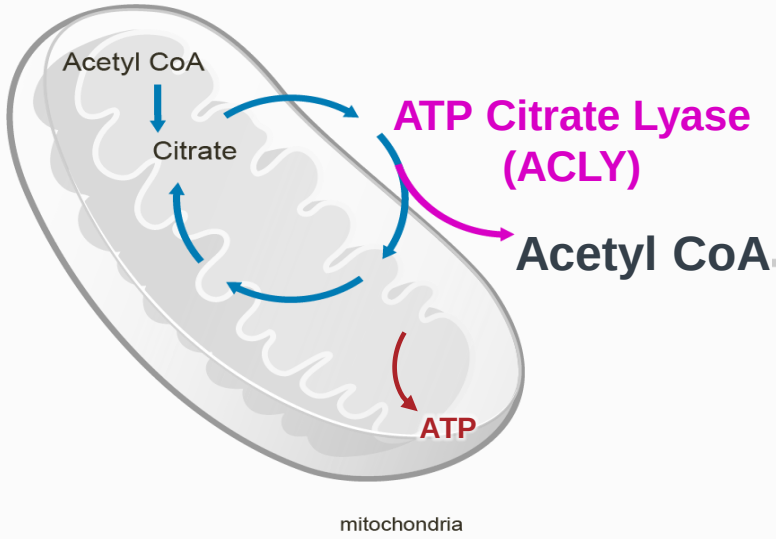
- Primarily **anabolic pathway** that supports cell states with high demands due to **accelerated proliferation and/or effector functions**
- Utilized by **highly proliferative cells**, cancer cells, and stem cells
- Occurs **across mitochondria, cytoplasm, and nucleus**

ACLY: ATP citrate lyase; TCA: tricarboxylic acid; ATP: adenosine triphosphate; Acetyl CoA: acetyl coenzyme A

1. Arnold PK, et al. *Nature*. 2022;603:477–481; 2. Mateska I, Alexaki VI. *Sig Transduct Target Ther*. 2022;7:201; 3. Chen G, et al. *Biomedicine & Pharmacotherapy*. 2023;168:115741

ACLY is the Key Enzyme in the Non-Canonical TCA Cycle[1,2]

A combination of genetic and lifestyle factors promote maladaptation of the ACLY-dependent energy-sensing nexus and lead to upregulation *in multiple cell types*



Energetic/Metabolic Processes Regulated by Acetyl CoA Production

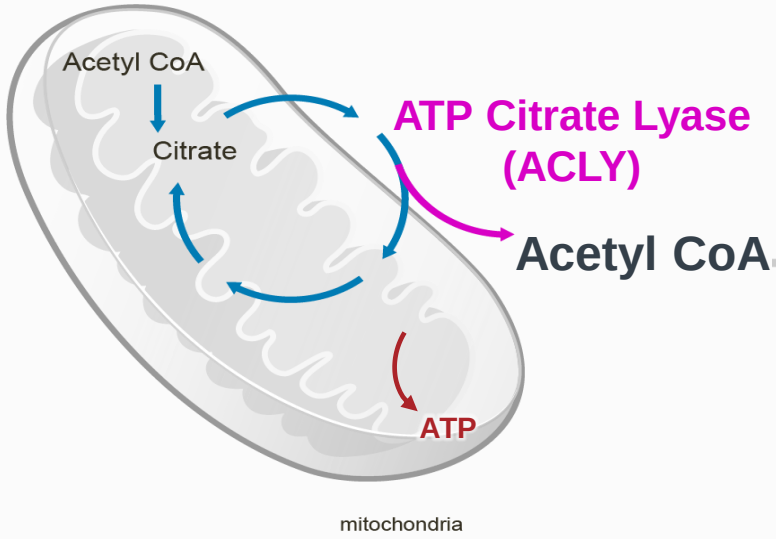
- Cholesterol/Bile Acid Synthesis
- Epigenetic Regulation
- Protein Regulation
- De Novo Lipogenesis

ACLY: ATP citrate lyase; TCA: tricarboxylic acid; ATP: adenosine triphosphate; Acetyl CoA: acetyl coenzyme A

1. Mateska I, Alexaki VI. *Sig Transduct Target Ther*. 2022;7:201; 2. Chen G, et al. *Biomedicine & Pharmacotherapy*. 2023;168:115741

ACLY is the Key Enzyme in the Non-Canonical TCA Cycle[1,2]

A combination of genetic and lifestyle factors promote maladaptation of the ACLY-dependent energy-sensing nexus and lead to upregulation *in multiple cell types*



Energetic/Metabolic Processes Regulated by Acetyl CoA Production

- Cholesterol/Bile Acid Synthesis
- Epigenetic Regulation
- Protein Regulation
- De Novo Lipogenesis

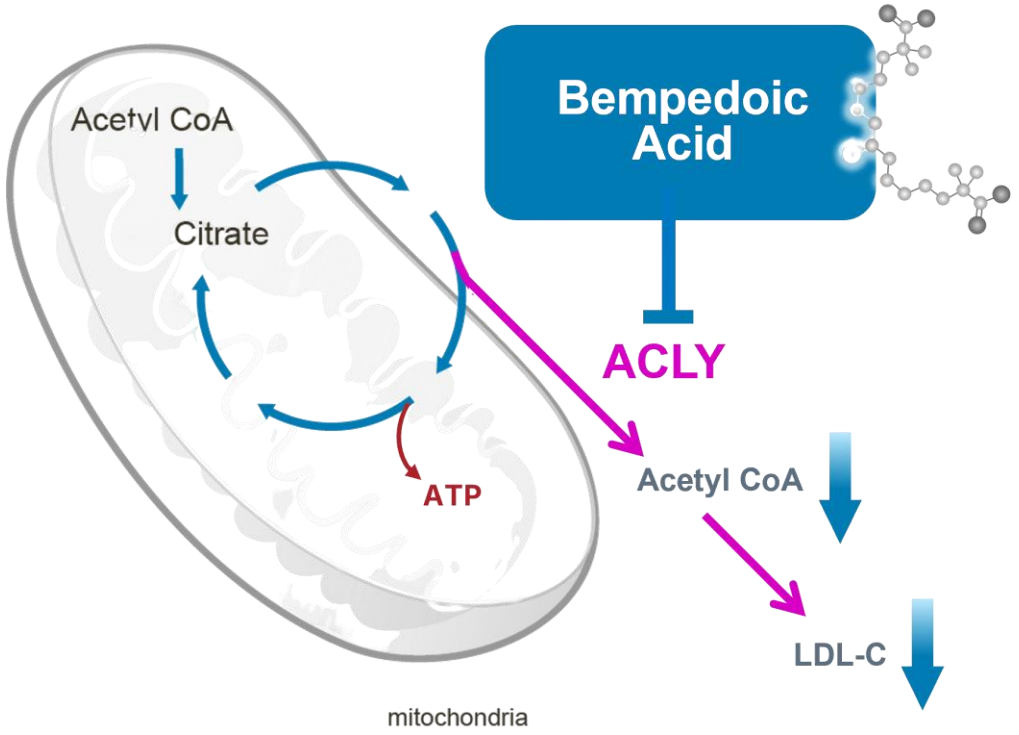
ACLY: ATP citrate lyase; TCA: tricarboxylic acid; ATP: adenosine triphosphate; Acetyl CoA: acetyl coenzyme A

1. Mateska I, Alexaki VI. *Sig Transduct Target Ther*. 2022;7:201; 2. Chen G, et al. *Biomedicine & Pharmacotherapy*. 2023;168:115741

Bempedoic Acid is an Active Site Hepatocellular ACLY Inhibitor[1-3]

Developed by Esperion, bempedoic acid:[1,2]

- Is the first and only approved ACLY inhibitor
- FDA-approved to lower LDL-cholesterol and to reduce the risk of MI and coronary revascularization in adults

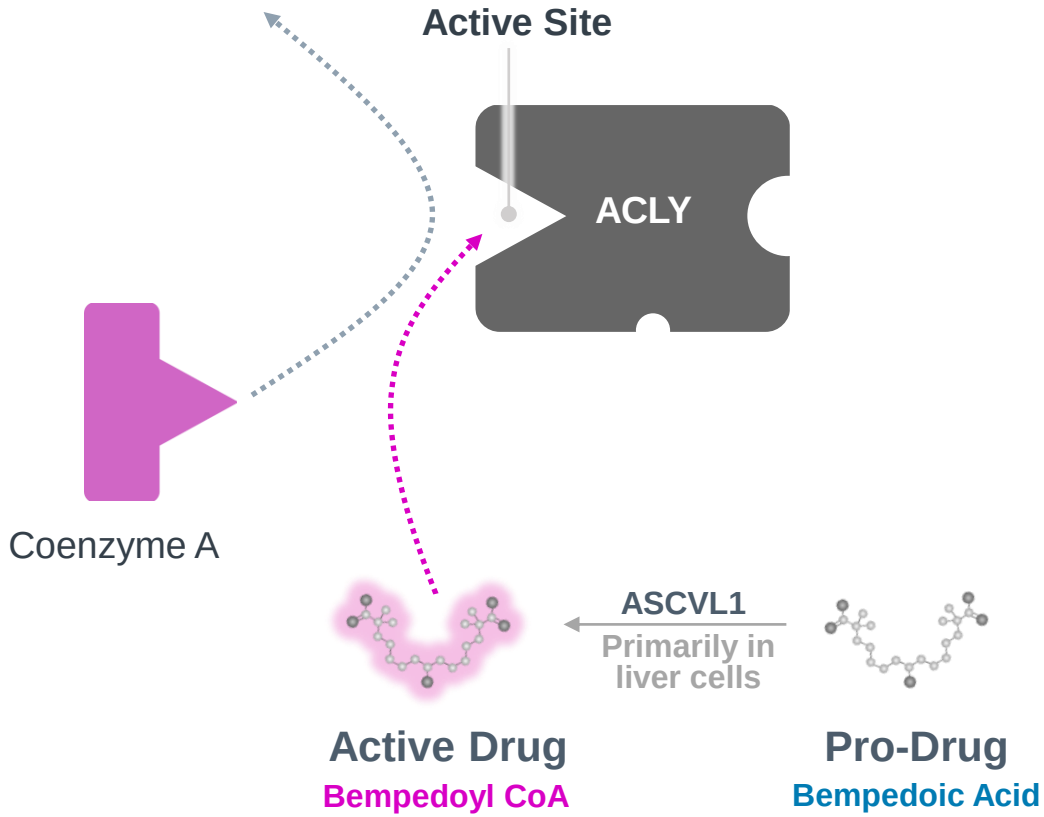


ACLY: ATP citrate lyase; LDL-C: low density lipoprotein cholesterol; Acetyl CoA: acetyl coenzyme A; MI: myocardial infarction

1. Batchuluun B, et al. *Nat Rev Drug Discov*. 2022;21:283–305
2. Pinkosky SL, et al. *Trends Mol Med*. 2017;23(11):1047-1063
3. Biolo G, et al. *Front. Cardiovasc. Med*. 2022;9:1028355

Bempedoic Acid Activity is Restricted to Hepatocytes[1-3]

- **Bempedoic acid** is a pro-drug converted in hepatocytes to its active drug form, Bempedoyl CoA[1,2]
- **Bempedoyl CoA** inhibits ACLY by directly competing for the active site with coenzyme A[1,2]



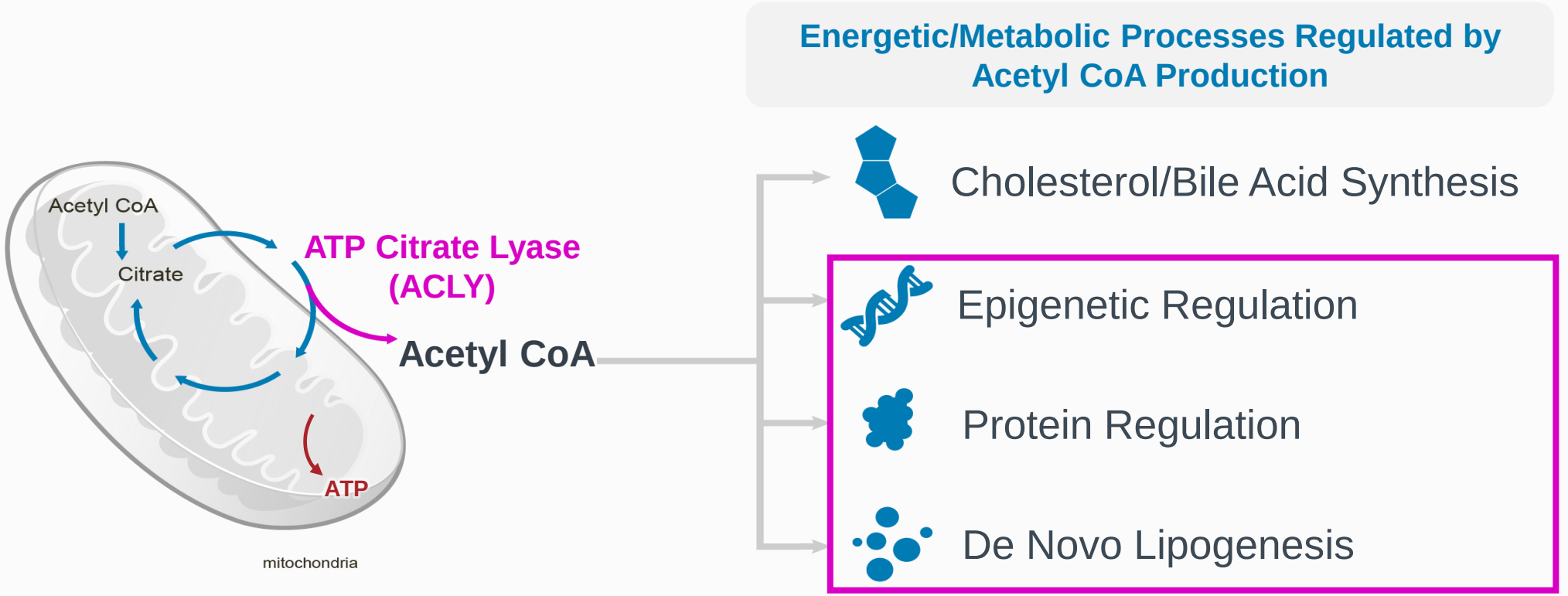
ACLY: ATP citrate lyase; LDL-C: low density lipoprotein cholesterol; MI: myocardial infarction

1. Brandts J, & Ray KK. *Expert Opinion on Investigational Drugs*. 2020;29(8):763–770; 2. Biolo G, et al. *Front. Cardiovasc. Med.* 2022;9:1028355.

ESPERION

ACLY is the Key Enzyme in the Non-Canonical TCA Cycle[1,2]

A combination of genetic and lifestyle factors promote maladaptation of the ACLY-dependent energy-sensing nexus and lead to upregulation *in multiple cell types*



ACLY: ATP citrate lyase; TCA: tricarboxylic acid; ATP: adenosine triphosphate; Acetyl CoA: acetyl coenzyme A

1. Mateska I, Alexaki VI. *Sig Transduct Target Ther*. 2022;7:201;
2. Chen G, et al. *Biomedicine & Pharmacotherapy*. 2023;168:115741

Preclinical & Clinical Studies Demonstrate Marked Upregulation of ACLY in Metabolic Dysfunction-Associated Liver Diseases (MASLD)[1,2]

ACLY expression is upregulated in livers of *db/db* mice with obesity, fatty liver, and T2D[1]

ACLY mRNA levels ~1.4-fold higher in macrophages from patients with MASH vs controls[2]

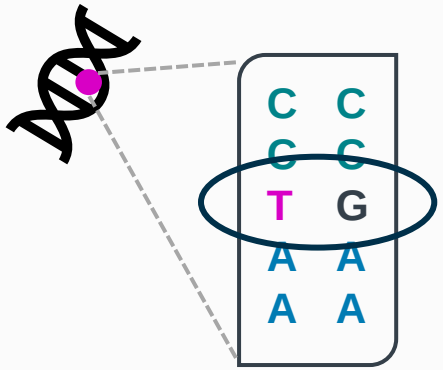
ACLY protein levels are increased in livers of patients with MASH & MASLD vs controls[2]

ACLY: ATP citrate lyase; T2D: type 2 diabetes; MASH: metabolic dysfunction-associated steatohepatitis

1. Guo L, et al. *J Biol Chem*. 2019;294(31):11805-11816;
2. Convertini P, et al. *J Transl Med*. 2023;21(1):568.

ESPERION®

Mechanistic Validation of ACLY Inhibition and Identification of Potential New Therapeutic Indications



Specific Genetic Variant of Interest

ICD codes from EHR

Phenome-wide Phenotypes

PheCode	Phenotype Description
573	Liver Disorders
155	Liver Cancer

All Phenotypes Associated with a Variant

Phenome-wide association studies (PheWAS) use large data sets to search for phenotypes (an observed trait such as a disease state) associated with a specific genetic variant[1]

Phenome: sum of all physical and chemical traits of an organism; ICD: international classification of disease; EHR: electronic health record

1. JN Learning. *Genetics and Genomics*. Phenome-wide association studies. 2022. https://edhub.ama-assn.org/jn-learning/audio-player/18737946

UK BioBank Allows for Mechanistic Validation of ACLY Inhibition in Liver Disease

Population-based prospective cohort study of ~500,000 adults aged 40-69 years recruited in 2006-2010

The study continues to collect extensive phenotypic and genotypic detail for a wide range of health-related outcomes[1]

- Questionnaires
- Physical measures
- Sample assays
- Accelerometry
- Disease/Cancer registry
- Hospital EHR data
- Multimodal imaging

Baseline Characteristics of UK BioBank Participants

46% Male

93% Current Alcohol Drinkers

56.7 years old*

34% Lightly Physically Active

27.4 kg/m^2 BMI*

138 mg/dL LDL-C

*mean; UK: United Kingdom; BMI: body mass index; EHR:electronic health record; LDL-C: low density lipoprotein cholesterol

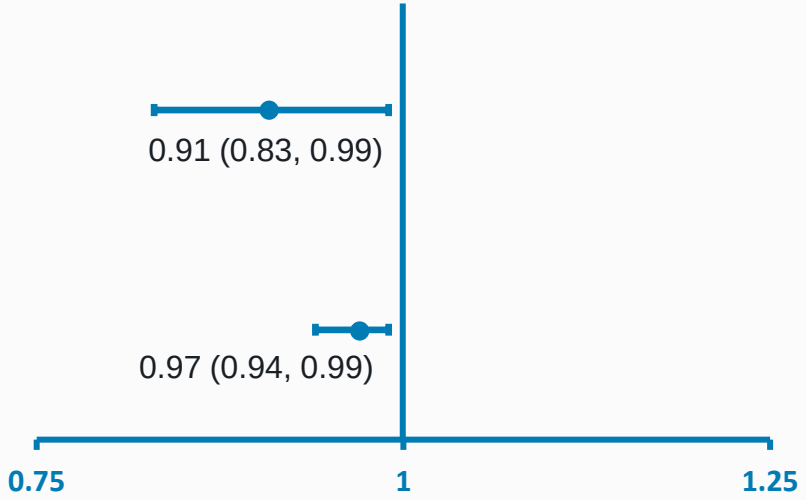
1. Sudlow C, et al. UK Biobank: An Open Access Resource for Identifying the Causes of a Wide Range of Complex Diseases of Middle and Old Age. *PLOS Medicine.* 2015;12(3):e1001779.

ESPERION

ACLY Inhibition May Have Protective Effects on Reducing Risk of Liver Cancer and Disorders

Individual-level data (n=385,917) from the UK BioBank was utilized to infer lifelong effects of ACLY inhibition across a range of liver outcomes through PheWAS

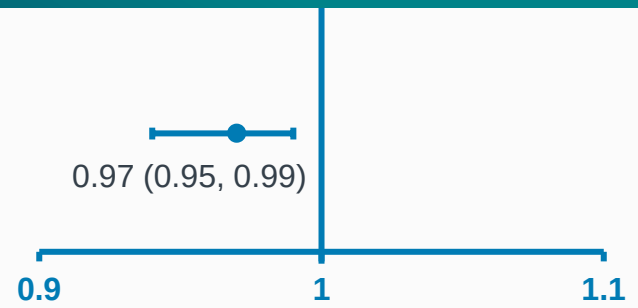
Phenotype Description	Lower Genetically Predicted ACLY Gene Expression Odds Ratio (95% CI)	P-Value
Liver Cancer (n = 474)	0.91 (0.83, 0.99)	0.047
Liver Disorders (n = 4391)	0.97 (0.94, 0.99)	0.028



UK: United Kingdom; ACLY: ATP citrate lyase

Genetically Predicted ACLY Inhibition is Significantly Associated with Decreased Risk of Composite Hepatic Events

Phenotype Description	Lower Genetically Predicted ACLY Gene Expression Odds Ratio (95% CI)	P-Value
Composite Hepatic Events (n = 6352)	0.97 (0.95, 0.99)	0.015



Composite Hepatic Events Components

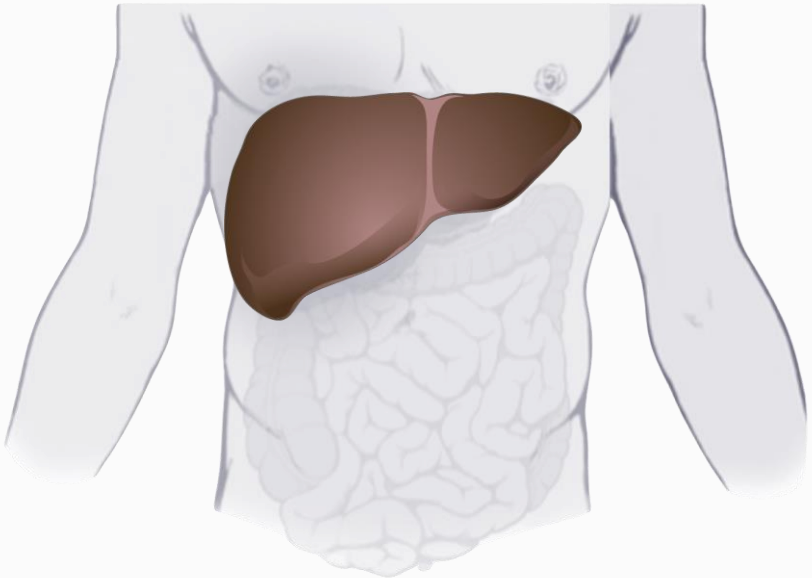
- Hepatic Encephalopathy
- Hepatic Decompensation
- New-Onset or Deterioration of Ascites
- Variceal Bleeding
- Acute-on-Chronic Liver Failure
- Hepatocellular Carcinoma

ACLY: ATP citrate lyase

PheWAS Data Supports the Causal Role of ACLY Dysregulation in Multiple Liver Disorders

Examples from the Liver Disorders PheWAS Code[1]

- Metabolic Dysfunction-Associated Steatotic Liver Disease
- Chronic Active Hepatitis
- Hepatopulmonary Syndrome
- Liver Transplant

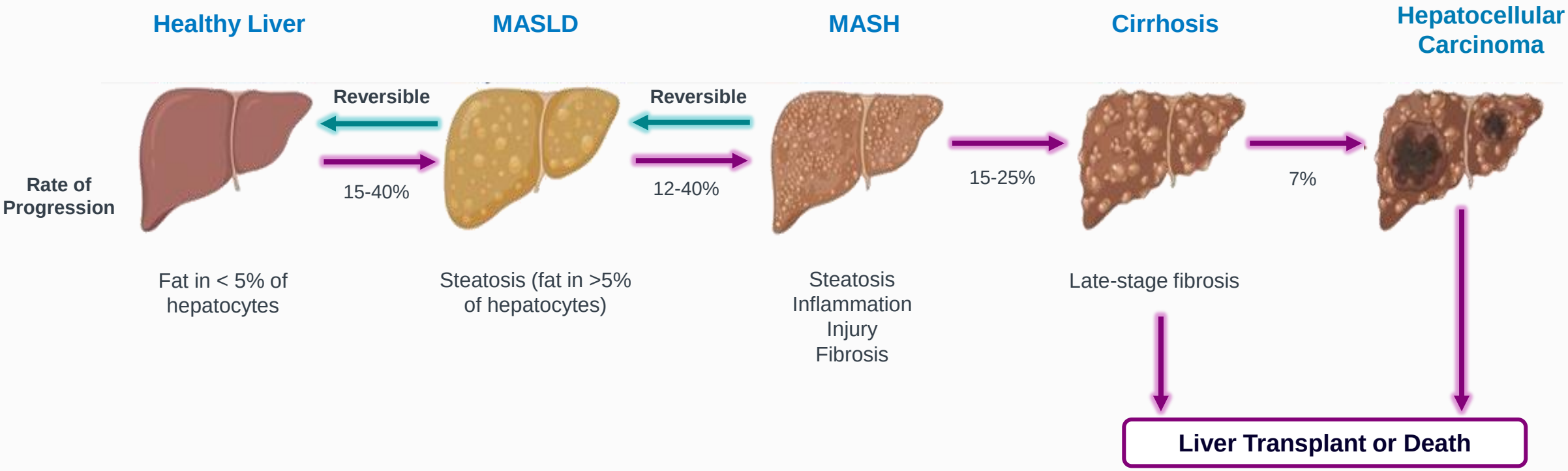


ACLY: ATP citrate lyase

1. CIPHER - VA. Ornl.gov. Published 2025. Accessed March 21, 2025. https://phenomics.va.ornl.gov/web/cipher/phenotype-viewer/details?id=3265&name=Other_disorders_of_liver__MAP_

MASLD Provides Broad Population to Mechanistically Validate ACLY Inhibition in Liver Disease

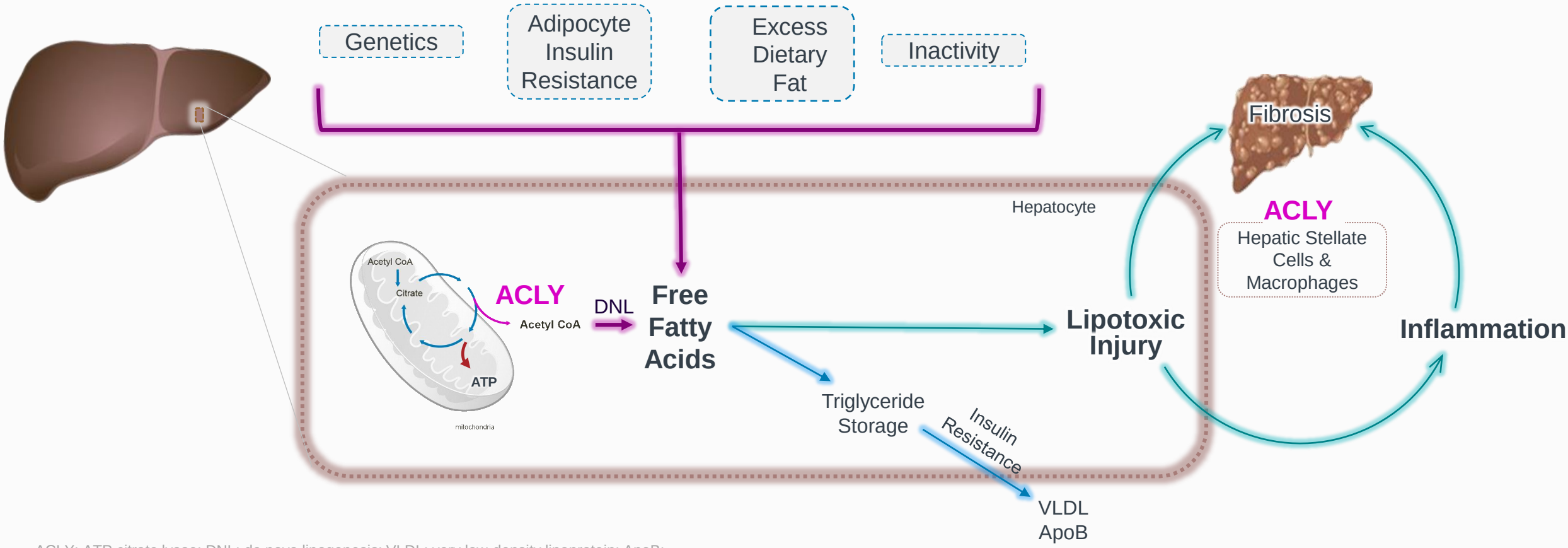
Inflammation, oxidative stress, insulin resistance, altered lipid metabolism, and fibrosis contribute to the progression of MASLD



ACLY: ATP citrate lyase; MASH: metabolic dysfunction-associated steatohepatitis, MASLD: metabolic-associated steatotic liver disease

1. Miao, Lei, et al. Trends in Endocrinology & Metabolism. 2024;35(8):697-707; 2. Younossi ZM, et al. Clin Gastroenterol Hepatol. 2024 Oct;22(10):1999-2010.e8; 3. Yanai H, et al. Int J Mol Sci. 2023 Oct 23;24(20):15473

Proposed Pathophysiologic Role of ACLY in Progression of MASLD/MASH



ACLY: ATP citrate lyase; DNL: de novo lipogenesis; VLDL: very low-density lipoprotein; ApoB: Apolipoprotein B; MASH: metabolic dysfunction-associated steatohepatitis, MASLD: metabolic-associated steatotic liver disease; Acetyl CoA: acetyl coenzyme A

In normal liver physiology, these are bidirectional processes to maintain homeostasis

1. Valenzuela-Vallenjo L, Guatibona-Garcia V, Mantzoros CS. *Metabolism.* 2022 Nov:136:155248.

ACLY Inhibition has Broad Applicability to Reduce Liver Disease

ACLY is the key enzyme in the non-canonical TCA cycle, an energy nexus in all cells

Genetically predicted associations of decreased risk of liver disorders through ACLY inhibition justifies deeper investigation through multi-omic analyses

MASLD provides a broad population to investigate novel connections of ACLY to liver disease

ACLY: ATP citrate lyase; TCA: tricarboxylic acid; MASLD: metabolic dysfunction-associated steatotic liver disease

ESPERION®

Identification of Novel ACLY Pathways and New Indications Using Human Multi-omics

Stephen Pinkosky, PhD

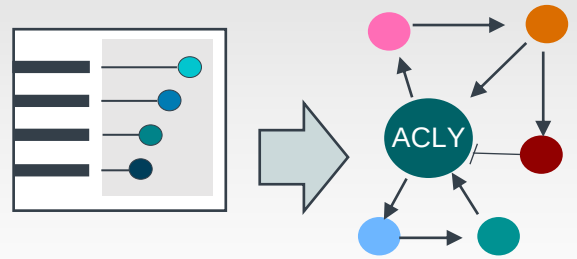
Vice President, Drug Discovery, Early Pre-ClinicalDevelopment

Novel Insights into ACLY Biology and Disease Associations Using Multi-omics Methodology

Data Set Selection

Liver Multi-omic Network

In-Depth Contextualization



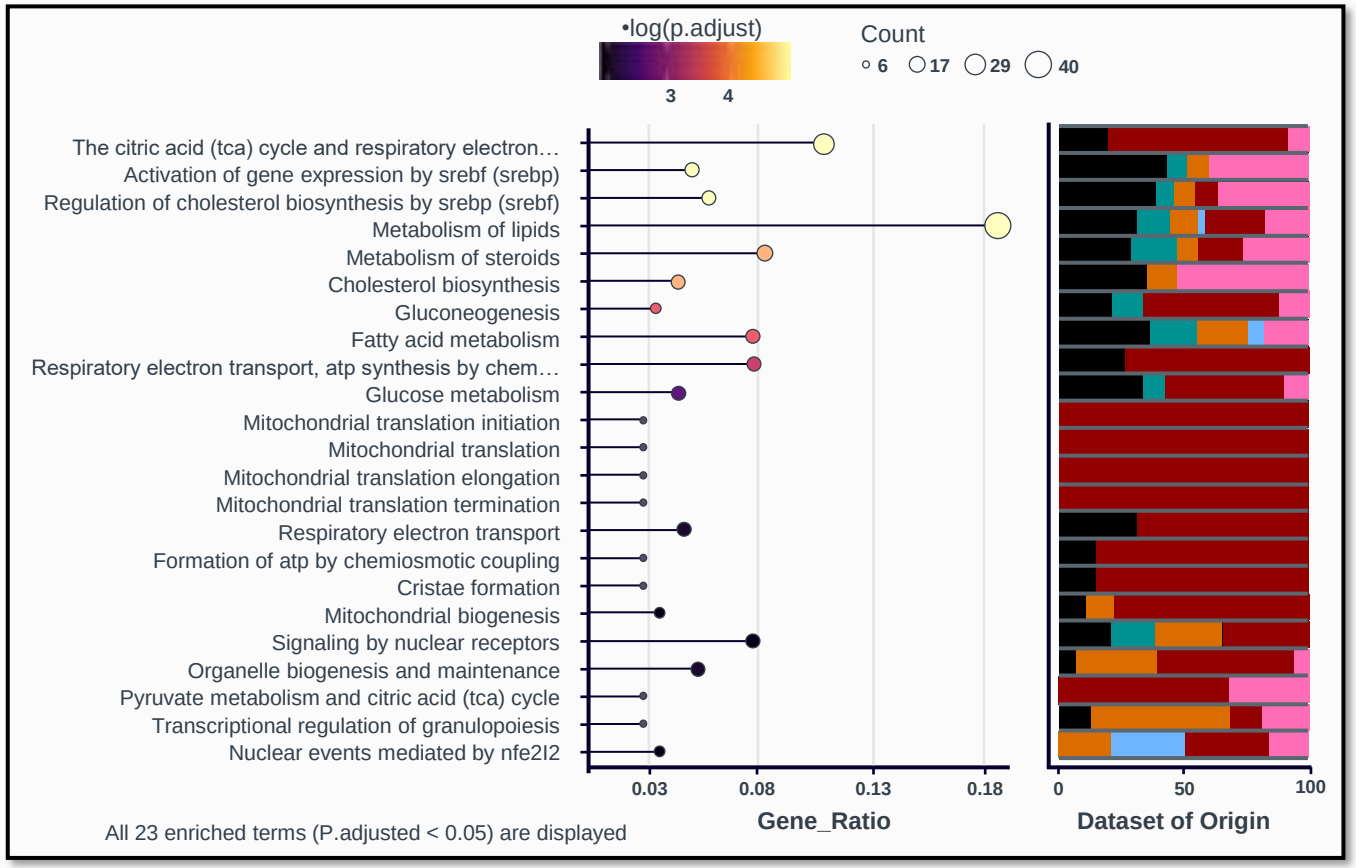
Select data for pathway insight into liver disease

Infer new associations across layers

Identify novel ACLY pathways to inform indication selection & drug discovery criteria

ACLY: ATP citrate lyase; MASH: metabolic dysfunction-associated steatohepatitis, MASLD: metabolic-associated steatotic liver disease

Multi-omics Network Identifies Known and Novel Pathways Connected to ACLY in Liver Disease



Liver bulk RNA-Seq **Cirrhosis cholangiocytes scRNA-seq** **Serum proteomics**

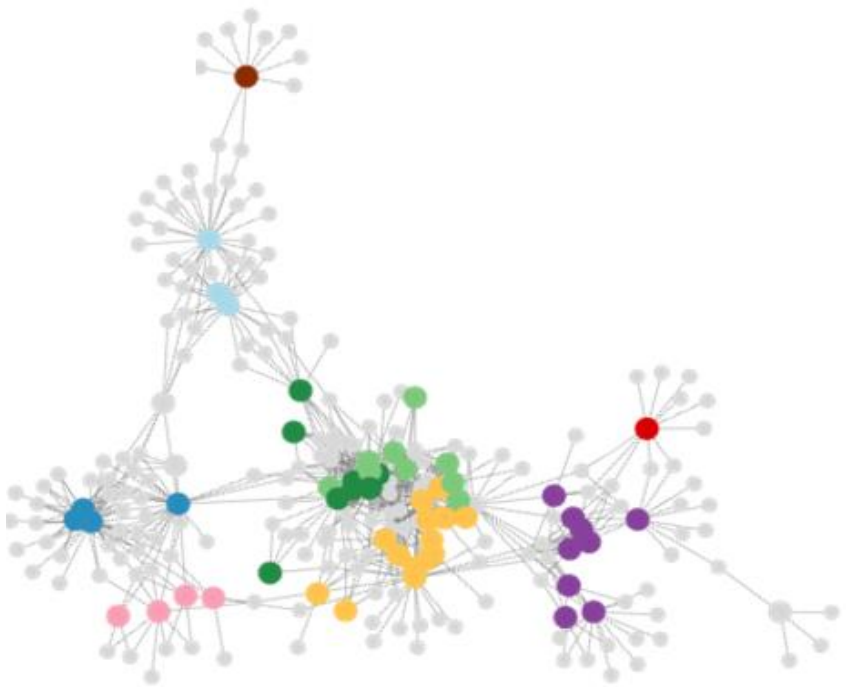
Obesity microarray **Obesity/fibrosis fibroblasts snRNA-seq**

Pathway Enrichment: ACLY Connections in Liver Disease

- ☑ Multiple expected pathways validated
- ☑ Several novel pathways identified
- ☑ **Cholangiocyte** data set enriched for numerous novel connections

ACLY: ATP citrate lyase; RNA: ribonucleic acid

Interrogating New ACLY Signatures Through Known and Novel Disease Pathway Connections



Cholesterol/Bile Acid Synthesis

- Cholesterol biosynthesis and lipid metabolism

Epigenetic & Protein Regulation

- ECM regulation
- Drug metabolism
- Cellular stress response
- Transcriptional regulation
- Cellular respiration
- Protein metabolism-associated signaling
- Peptide metabolism

De Novo Lipogenesis

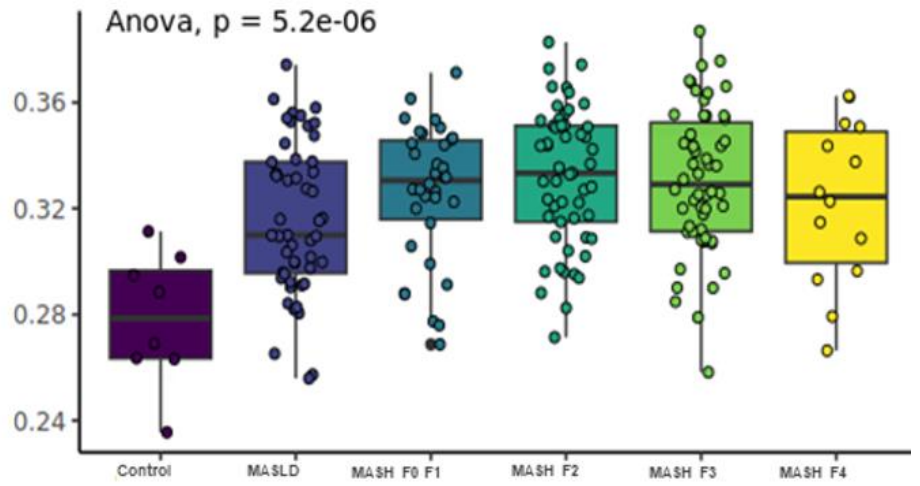
- Cholesterol biosynthesis and lipid metabolism
- Metabolic and homeostatic regulation

ACLY: ATP citrate lyase; ECM: extracellular matrix

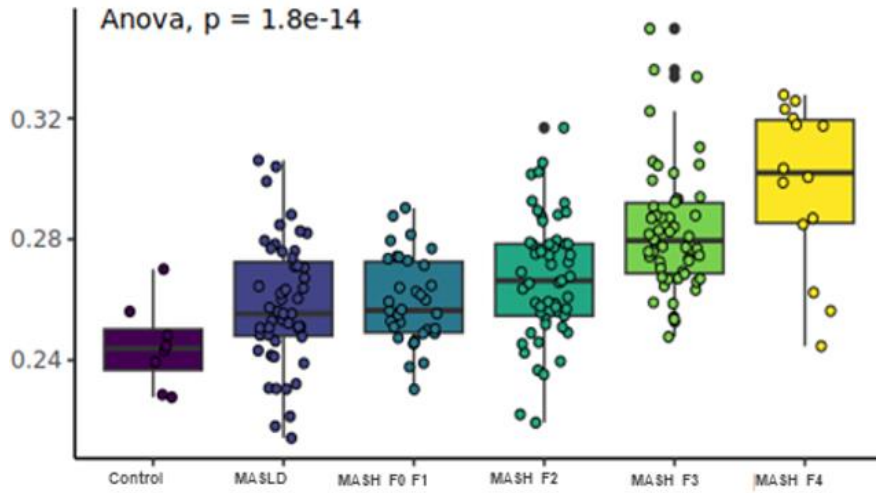
ESPERION

Newly Identified ECM Mechanism of ACLY is Associated with Progression of Liver Fibrosis

Cholesterol biosynthesis and lipid metabolism



Extracellular Matrix (ECM) Regulation



Development of fibrosis resulting from liver injury, inflammation and immune cell recruitment is the culminative process in liver disease progression

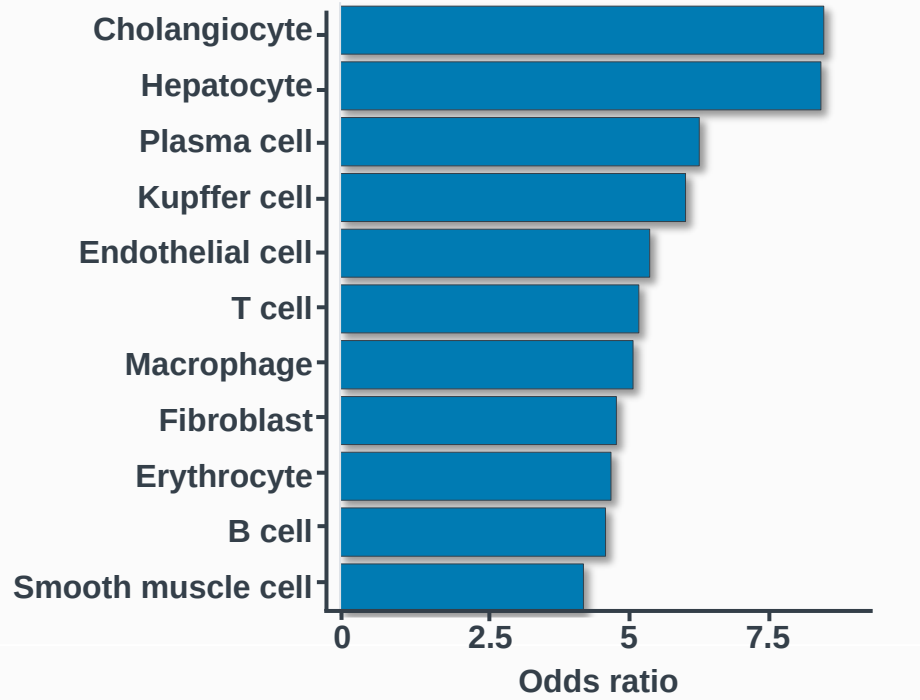
Analyses were conducted using liver bulk RNA-Seq; ACLY: ATP citrate lyase; ECM: extracellular matrix; ANOVA: analysis of covariance

Multi-component Mechanism of ACLY is Relevant in Multiple Liver Diseases

Top Disease Associations

0.61	Hepatic insufficiency
0.61	Cholangitis
0.58	Hepatitis, alcoholic
0.57	Metabolic dysfunction-associated steatotic liver disease (MASLD)
0.57	Hepatomegaly
0.55	Chronic hepatitis c virus infection
0.55	Alcoholic liver disease
0.54	Hepatitis a virus infection
0.53	Drug-induced liver injury
0.53	Hepatitis

Key Cell Types Responsible for Mediating ACLY Effects



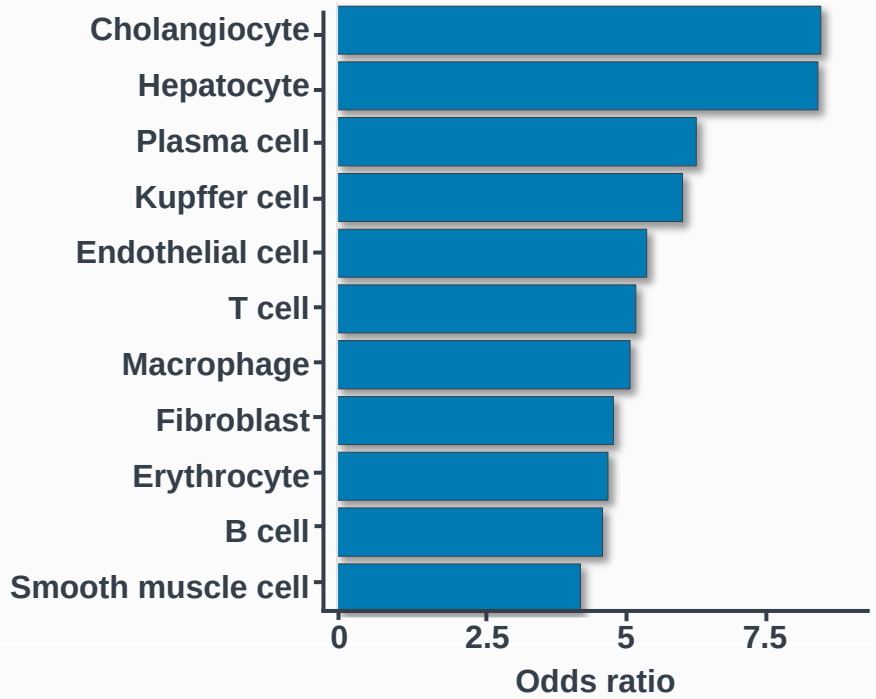
ACLY: ATP citrate lyase

Multi-omics Analysis Indicates Cholangitis and MASLD are Highly Associated with ACLY Pathways

Top Disease Associations

0.61	Hepatic insufficiency
0.61	Cholangitis
0.58	Hepatitis, alcoholic
0.57	Metabolic dysfunction-associated steatotic liver disease (MASLD)
0.57	Hepatomegaly
0.55	Chronic hepatitis c virus infection
0.55	Alcoholic liver disease
0.54	Hepatitis a virus infection
0.53	Drug-induced liver injury
0.53	Hepatitis

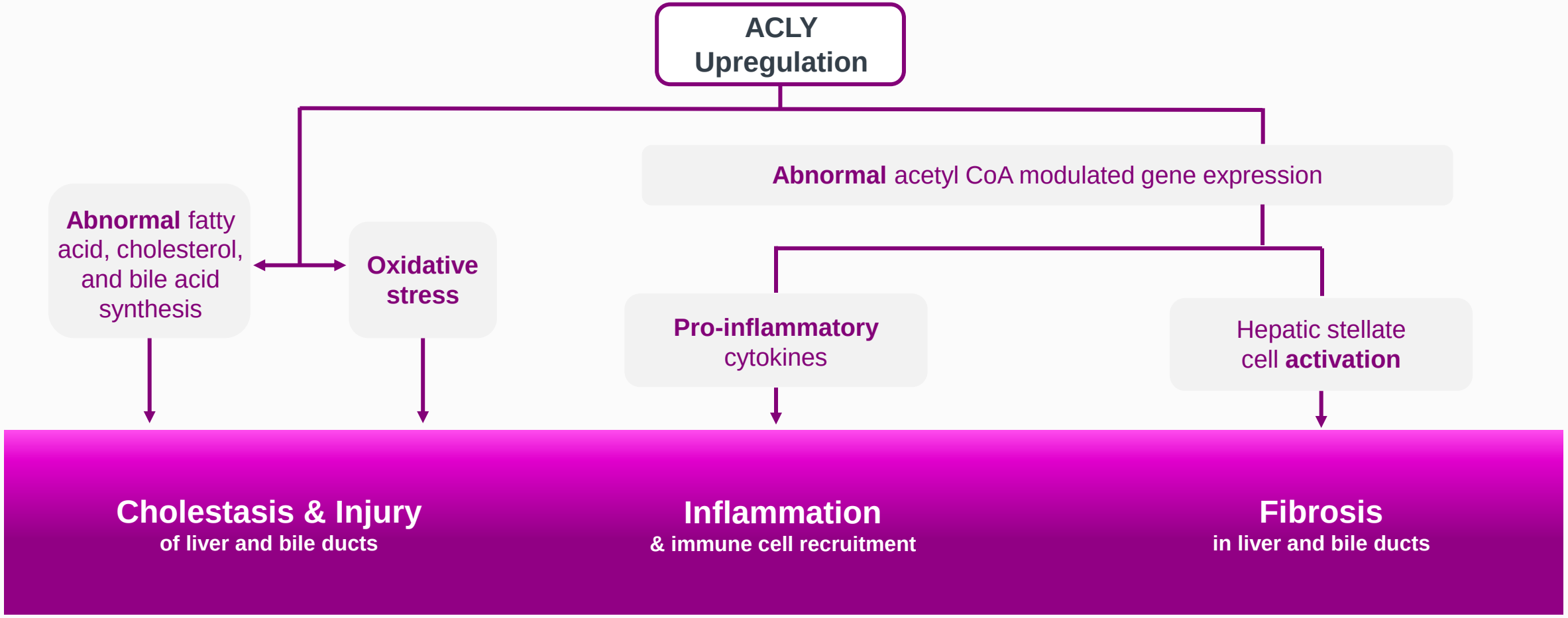
Key Cell Types Responsible for Mediating ACLY Effects



Strong rationale for prioritizing PSC given ACLY gene networks link to cholangitis via chronic immune and bile acid-related mechanisms

ACLY: ATP citrate lyase

ACLY Upregulation is Directly Related to Multiple Mechanisms of PSC Progression



ACLY: ATP citrate lyase; PSC: primary sclerosing cholangitis; Acetyl CoA: acetyl coenzyme A

Accumulating Evidence Suggest ACLY Inhibition is a Rational Target for PSC

- Human genetic evidence link ACLY to multiple liver disorders
- New pathway connections, including fibrosis, were identified along with known ACLY mechanisms
- Cell types with roles in liver disease progression (e.g. cholangiocytes, hepatocytes, Kupffer cells) mediate ACLY pathways and effects
- ACLY upregulation is related to mechanisms of PSC progression (liver cholestasis and injury, inflammation, and fibrosis)

ACLY: ATP citrate lyase; PSC: primary sclerosing cholangitis; Acetyl CoA: acetyl coenzyme A

ESPERION®

Independent Validation of ACLY in Hepatic Stellate Cell Activation

David E. Cohen MD, PhD

Chief, Division of Gastroenterology, Hepatology and Endoscopy, Brigham and Women's Hospital

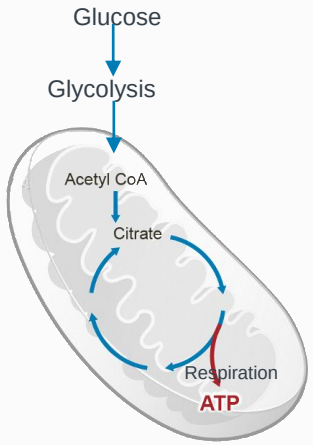
Research Collaboration Established to Deepen the Connection Between ACLY Biology and Fibrosis in PSC

Activation of hepatic stellate cells (HSC) is coupled to non-canonical TCA cycle and is dependent on ACLY activity

Activation of HSCs requires upregulation of glycolysis and respiration to fuel fibrogenesis and proliferation

Activation of HSCs via injury signals is a primary driver of liver fibrosis in PSC

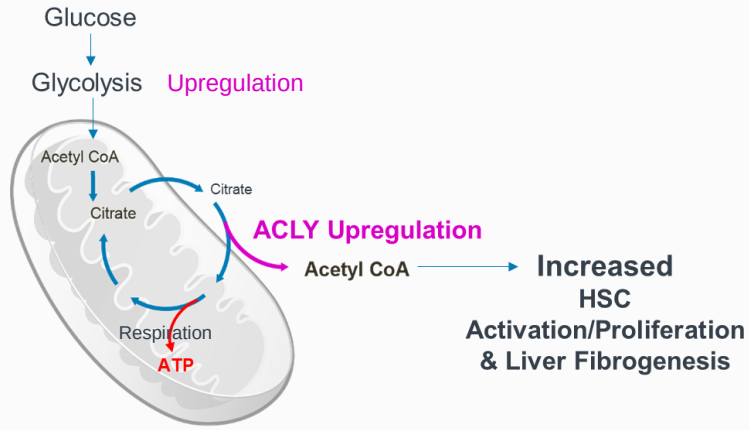
Canonical TCA pathway



Quiescent HSC
(Baseline energy demand)

PSC-related injury signals (*e.g.*TGFβ)

Non-canonical TCA pathway

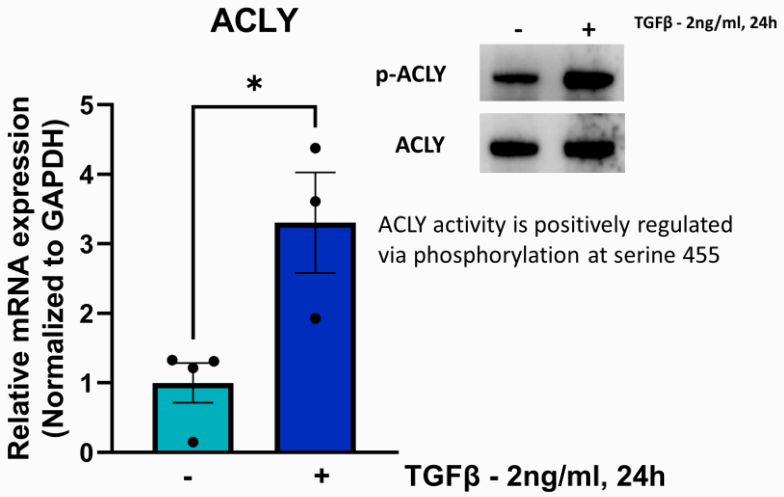


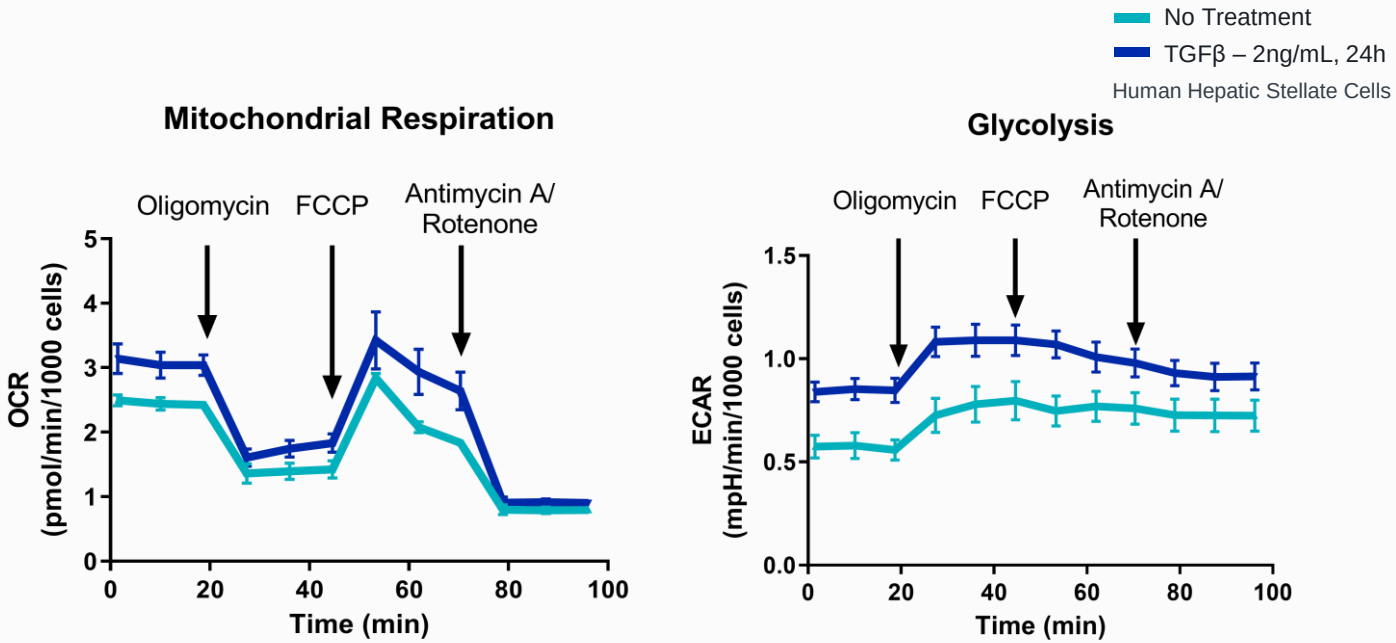
Activated HSC
(Increased energy and substrate demand)

Hypothesis: ACLY-dependent changes in cell energy metabolism drives hepatic stellate cell (HSC) activation via injury/fibrosis signals

ACLY: ATP citrate lyase; PSC: primary sclerosing cholangitis; TCA, tricarboxylic acid; TGFB: transforming growth factor beta; Acetyl CoA: acetyl coenzyme A; ATP: adenosine triphosphate

Mimicking Inflammation and Injury, TGFβ Upregulates ACLY Expression & Activity





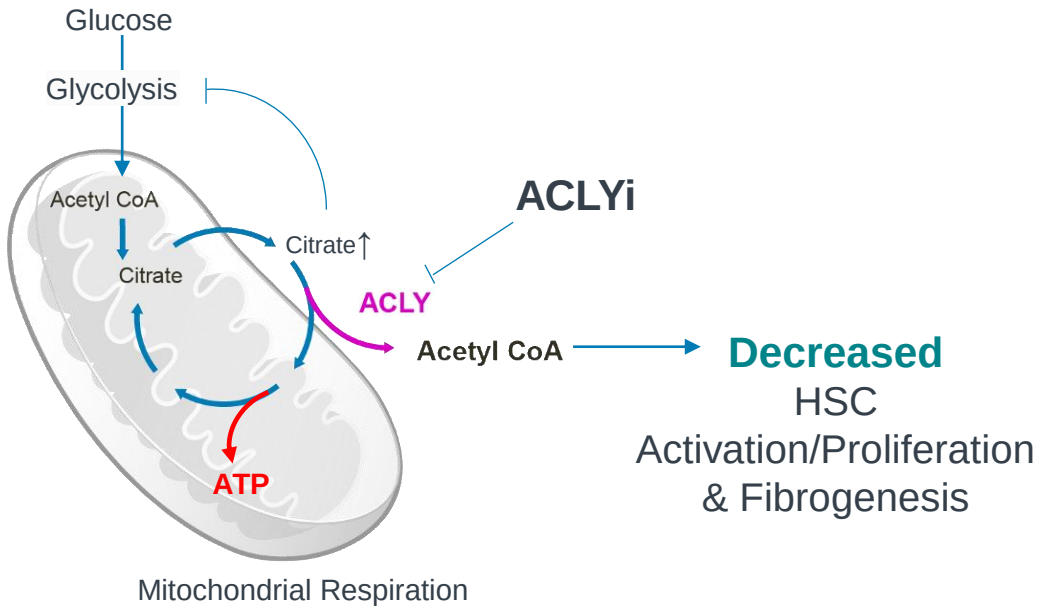
TGFβ stimulates ACLY upregulation

TGFβ activation increases basal and maximal values of mitochondrial respiration and glycolysis

ACLY: ATP citrate lyase; TGFB: transforming growth factor beta; HSC: hepatic stellate cells

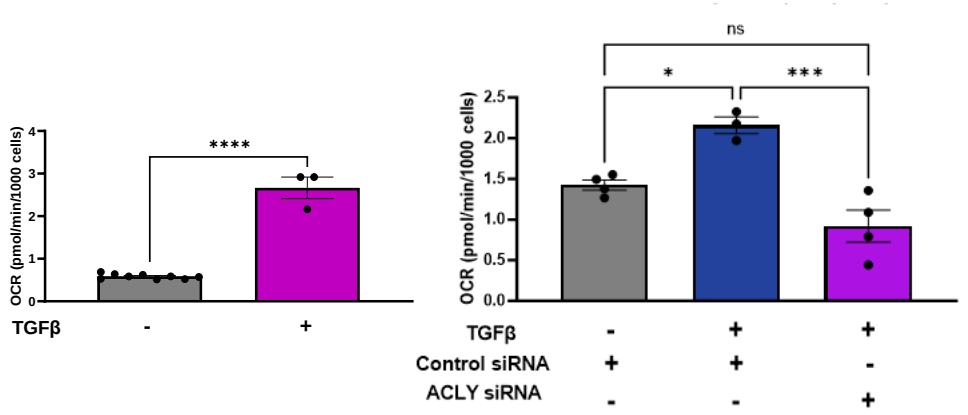
Oligomycin: inhibitor of ATP synthase that decreases mitochondrial respiration.
FCCP: uncoupler that maximizes mitochondrial respiration of the cell.
Antimycin A and Rotenone: inhibitors of complexes III and I that abrogate mitochondrial respiration.

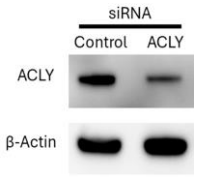
ACLY Inhibition: A Potential Therapeutic Target in Fibrosis via HSC Activation Pathways



Hypothesis: ACLY inhibition decreases HSC activation/proliferation and liver fibrogenesis

Maximal Respiratory Capacity



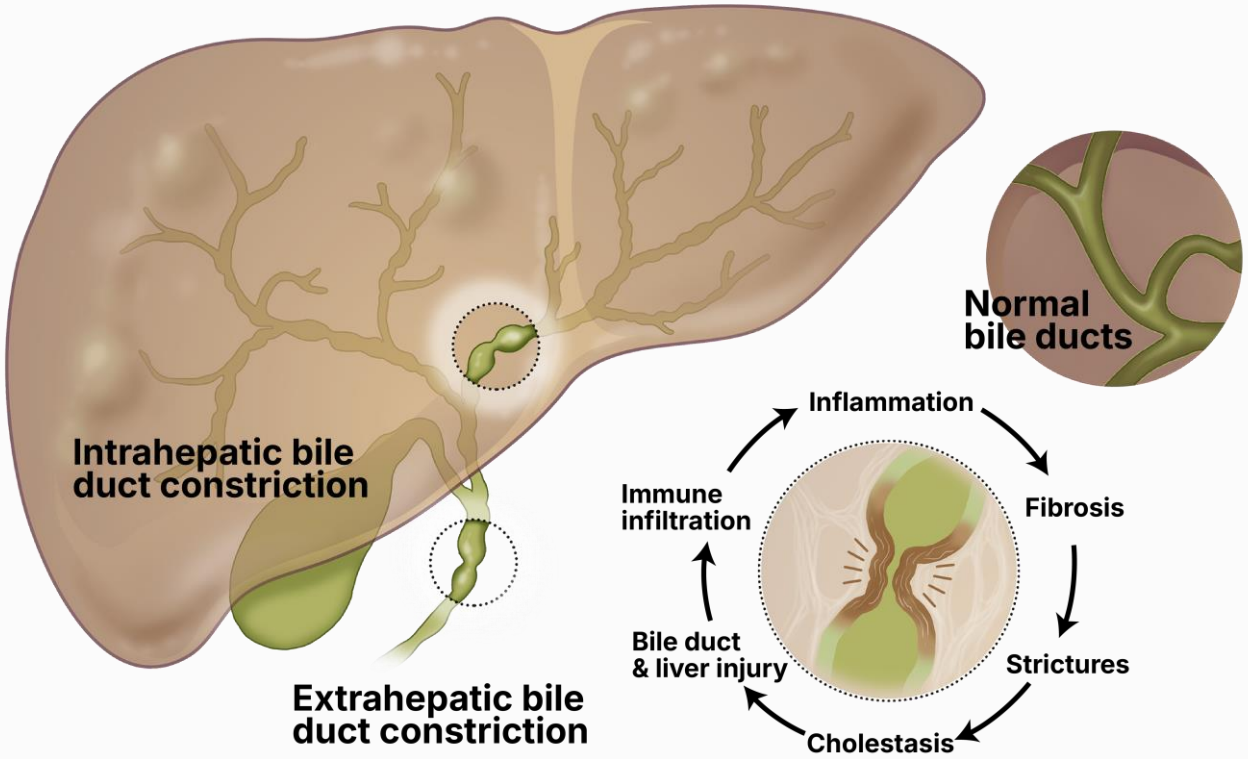


Conclusion: Knockdown of ACLY blunts metabolic response (mitochondrial respiration) of HSC activation/proliferation by TGFβ

ACLY: ATP citrate lyase; TGFB: transforming growth factor beta; HSC: hepatic stellate cells; Acetyl CoA: acetyl coenzyme A; siRNA: small interfering ribonucleic acid

Primary Sclerosing Cholangitis (PSC)

PSC: A Complex Disease with Great Unmet Need



Progressive inflammatory and fibrotic disease that injures bile ducts[1]

The etiology of PSC is unclear but likely due to multiple mechanisms[1]

No approved therapies to cure or halt PSC progression[1]

Death or liver transplantation expected within 1-2 decades after diagnosis[2]

PSC: primary sclerosing cholangitis

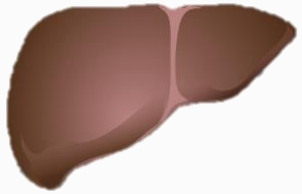
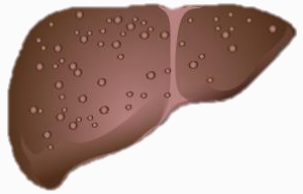
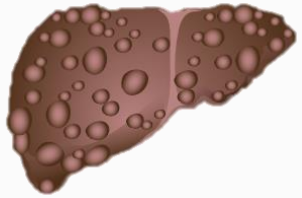
1. Saner FH, et al. Transplantation for Primary Sclerosing Cholangitis: Outcomes and Recurrence. J Clin Med. 2023 May 11;12(10):3405; 2. Bowlus C, Arrivé L, Bergquist A, et al. AASLD practice guidance on primary sclerosing cholangitis and cholangiocarcinoma Hepatology. 2023;77(2):659-702.

ESPERION®

PSC Progression: From Silent Onset to Rapid Decline[1-7]

The average time between PSC diagnosis and liver transplant or death is 10 to 20 years

Addressable PSC Population: Stages 0-3

Stage 0	Stage 1	Stage 2	Stage 3	Stage 4	Liver Transplantation or Death
					
	Mild fibrosis	**Moderate fibrosis**	**Severe fibrosis**		
Abnormal liver function only	Cholangitis or portal hepatitis	Periportal fibrosis or periportal hepatitis	Septal fibrosis or bridging necrosis	Biliary cirrhosis or cholangiocarcinoma	Liver failure

Cholestatic Symptoms

0 years **~15 years**

PSC: primary sclerosing cholangitis

1. Steele IL, et al. *MedGenMed*. 2007;9(2):20.; 2. Rupp C, et al. *United European Gastroenterol J*. 2018;6(2):255-262.; 3. Singh S, Talwalkar JA. *Clin Gastroenterol Hepatol*. 2013;11(8):898-907.; 4. Karlsen TH, et al. *J Hepatol*. 2017;67(6):1298-1323; 5. Skarby AJ, et al. *JHEP Rep*. 2024;6(1):100609.; 6. Thylin M, et al. *Liver Int*. 2024;44(9):2351-2358.; 7. Hilscher MB, et al. *Hepatol Commun*. 2018;2(7):836-844.

ESPERION

PSC is a Rare Disease± with Increasing Prevalence

6-16 cases per 100,000 estimated in North America and Western Europe[1]

~46,000

patients diagnosed with PSC across **United States**[2-3]

~30,000

patients diagnosed with PSC across **Europe**[4-7]

70% of PSC cases are diagnosed in men[1]

25 to 45 years of age

peak incidence of PSC is during the most productive years of life[1]

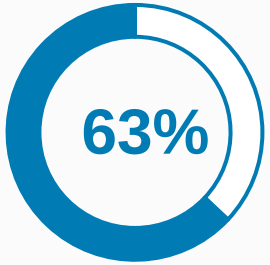
±The FDA defines a rare disease as a disease or condition that affects less than 200,000 people in the United States.

PSC: primary sclerosing cholangitis

1. Bowlus C, Arrivé L, Bergquist A, et al. *Hepatology*. 2023;77(2):659-702; 2. Bakhshi Z, et al. *J Gastroenterol*. 2020 May;55(5):523-532; 3. Nguyen A, et al. *Front Gastroenterol (Lausanne)*. 2022;1:1076788.; 4. Liang H, et al. *Medicine (Baltimore)*. 2017;96(24):e7116. 5. Boonstra K, et al. *Hepatology*. 2013;58(6):2045-55; 6. Krampe, J, et al. Poster presented at: ISPOR 2024; Nov 2, 2024; Barcelona, Spain; 7. Lindkvist B, et al. *Hepatology*. 2010;52(2):571-7..

ESPERION

Pediatric Patients with PSC Currently Face a Lifetime of Disease Without Treatment Options



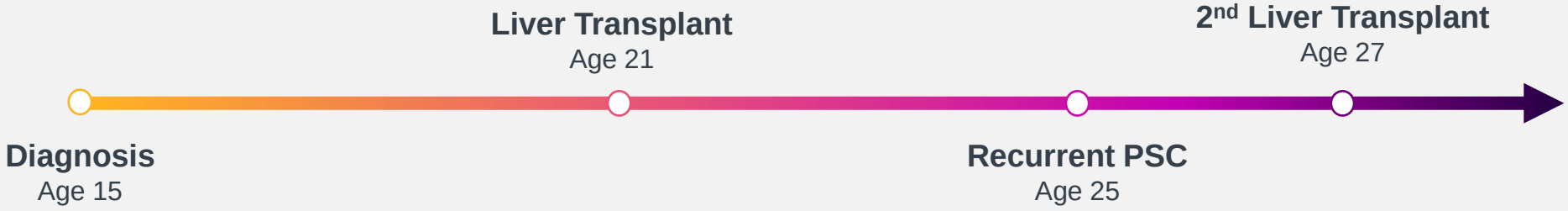
Children with PSC who experience clinical complications* within 10 years of diagnosis[1-2]

~1.5 cases per 100,000

Estimated in United States pediatrics[3-4]

Children with PSC who require liver transplant within 10 years of diagnosis[5]

Example Pediatric to Early Adulthood Disease Progression Timeline



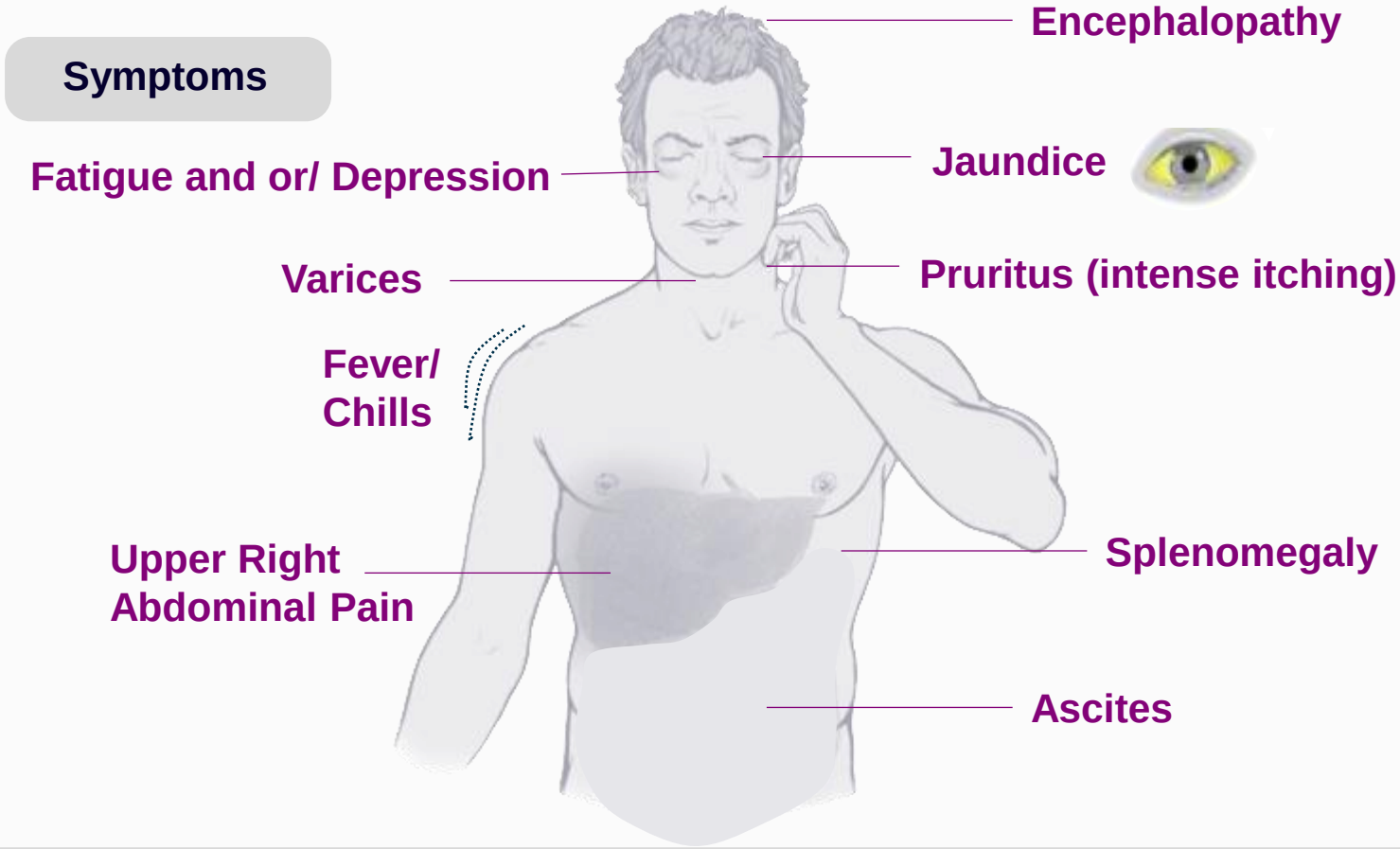
PSC: primary sclerosing cholangitis

1. Fuchs Y, Valentino PL. Clin Liver Dis (Hoboken). 2023 Jan 13;21(2):47-51; 2. Deneau MR, et. al. Hepatology 2017;66:518–27; 3. Deneau M, et al. Hepatology. 2013 Oct;58(4):1392-400. Epub 2013 Aug 13; 4. Kaplan GG, Am J Gastroenterol. 2007;102:10429; 5. Laborda TJ. World J Hepatol 2019; 11(1): 19-36

ESPERION

Living with PSC: Balancing Life and Disease

With no available treatments to slow or reverse PSC progression, *the standard of care is to treat the symptoms of disease*[1]



PSC: primary sclerosing cholangitis

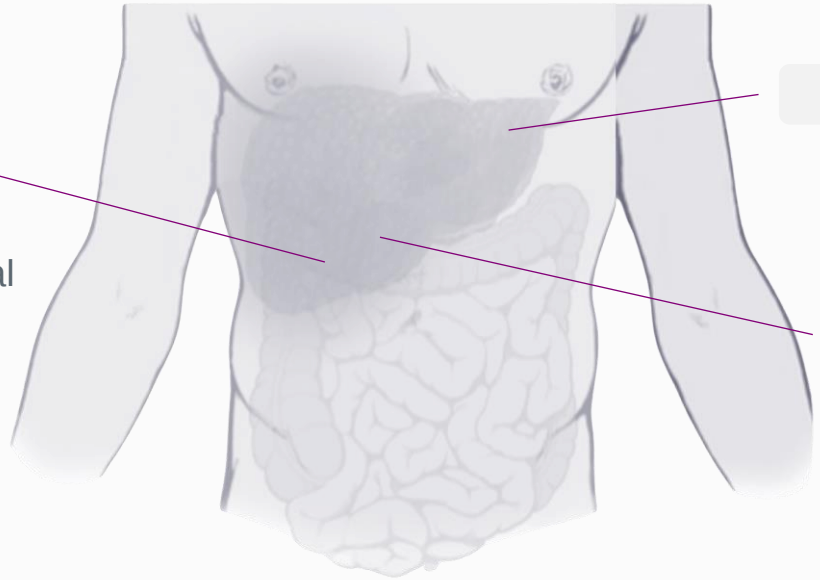
1. Bowlus C, Arrivé L, Bergquist A, et al. *Hepatology*. 2023;77(2):659-702.

PSC is Undoubtedly a Premalignant Condition[1]

Patients with PSC have *40 times the risk* of a primary hepatobiliary cancer compared to the general population[1]. Unfortunately, these cancers are also challenging to diagnose.

Gallbladder Carcinoma

- 1%-3.5% lifetime incidence
- 10x the risk compared to general population



Hepatocellular Carcinoma (HCC)

- 0.3%-2.8% lifetime incidence

Cholangiocarcinoma (CCA)

- Up to 20% lifetime incidence
- 400-1500x risk compared to general population

PSC: primary sclerosing cholangitis

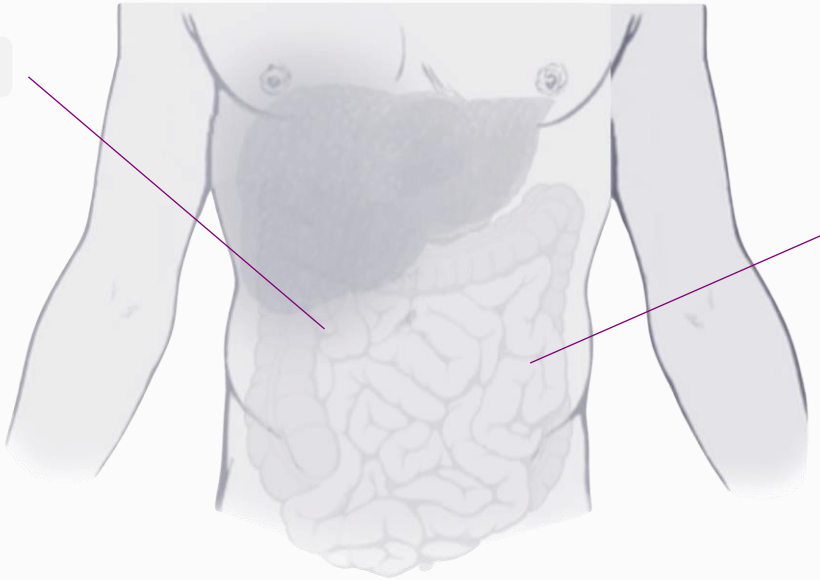
1. Fung BM, et al. *World J Gastroenterol*. 2019;25(6):659-671.

PSC & Inflammatory Bowel Disease: Closely Linked Conditions[1]

PSC-associated IBD is more likely to progress to colorectal malignancy

Inflammatory Bowel Disease (IBD)

- Over 70% of patients with PSC have IBD with 2 of 3 diagnosed with ulcerative colitis (UC)



Colorectal Cancer (CRC)

In patients with both PSC and IBD:

- 20-30% lifetime risk
- 10x the risk compared to general population
- 4x the risk compared to those with UC alone

ERCP: endoscopic retrograde cholangiopancreatography; IBD: inflammatory bowel disease; PSC: primary sclerosing cholangitis

1. Tsaitas C, et al. *World J Hepatol*. 2014;6(4):178-87.

PSC Places Continual Physical and Psychological Burden on Patients

Routine Monitoring[1,2]

- Blood Draws Every 3-6 Months
- Ultrasounds Every 6-12 Months
- Colonoscopy Every 1-2 Years
- Yearly Magnetic Resonance Cholangiography
- Invasive Endoscopic Procedure (ERCP) as needed

7-12 PSC related hospital days annually[3,4]

Hospitalized PSC patients are acutely ill[4]

- 83% with major/extreme severity of illness
- 60% with major/extreme risk of dying

Frequency of monitoring may vary based on disease progression and complications, patient status, and clinical decision making.

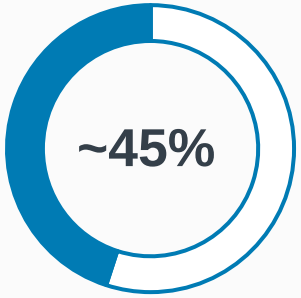
ERCP: endoscopic retrograde cholangiopancreatography; PSC: Primary sclerosing cholangitis

1. Vlăduţ C, et al. J Clin Med. 2020 Mar 11;9(3):754 2. Bowlus CL, et al. Hepatology. 2023 Feb 1;77(2):659-702; 3. Van Munster KN, et al. *Liver Int.* 2023;43:639-648.; 4. Vohra I, et al. *Diagnostics (Basel)*. 2024;14(22):2493..

Ongoing Need to Develop Disease Modifying Therapies for PSC

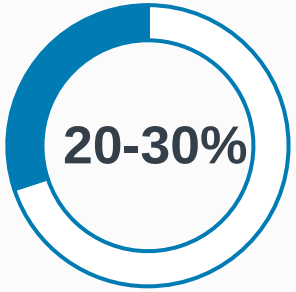
Despite severity of illness, the vast majority of the 46,000 US patients living with PSC do not meet current criteria to receive liver transplantation.

Only
387
PSC-related liver transplants[1]
(in 2024, United States)



Die within 10 years **without** a liver transplant[2-5]

30% of liver transplant recipients die within 10 years[6]



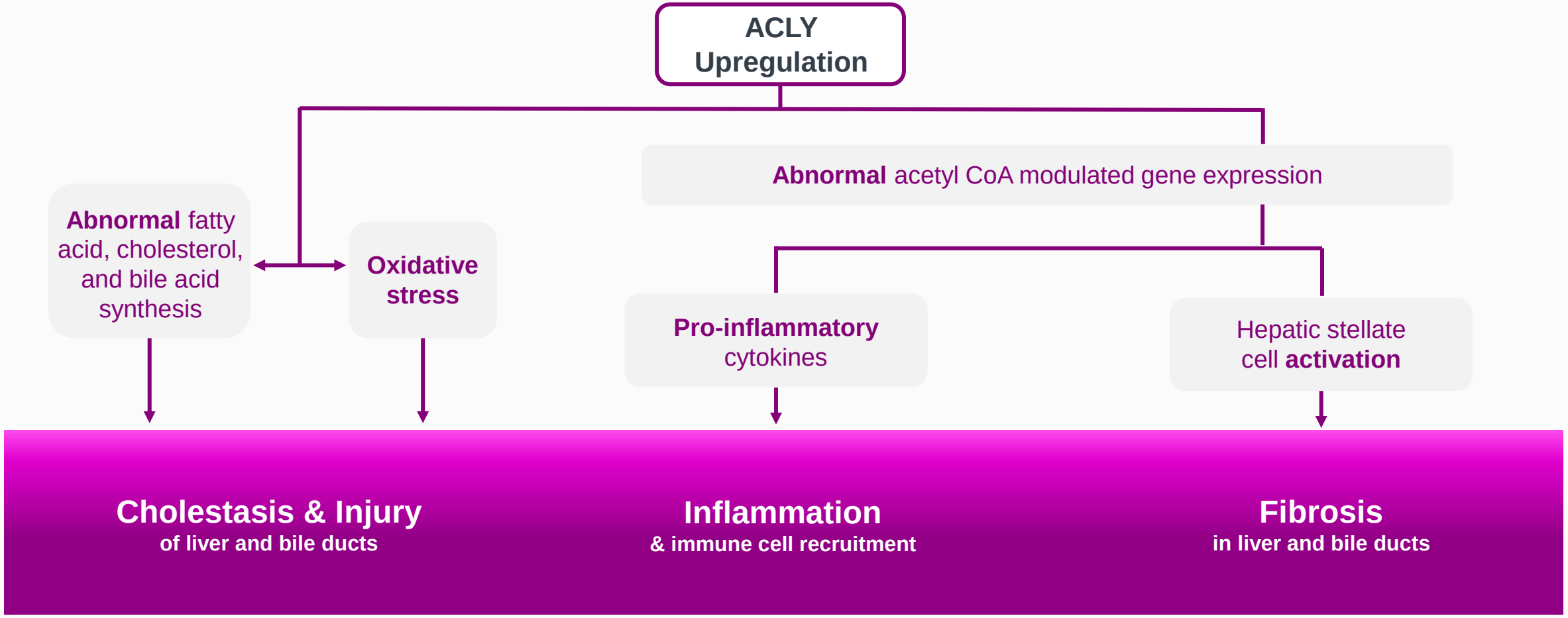
Patients who receive a liver transplant experience **recurrent PSC**[7]

PSC: primary sclerosing cholangitis

1. UNOS.org/data 2. Horwich B, *AASLD*. February 27, 2024; 3. LaRusso NF, et al. *Hepatology*. 2006;44(3):746-64; 4. Ponsioen C, et al. *Gastroenterol Hepatol (N Y)*. 2013;9(7):453-65; 5. Ueda Y, et al. *Transplant Direct*. 2017;3(12):e334; 6. Visseren T, et al. *Transplant Direct*. 2021; 34(8): e1329-1575; 7. Bowlus C, Arrivé L, Bergquist A, et al. *Hepatology*. 2023;77(2):659-702.

ESPERION

ACLY Upregulation is Directly Related to Multiple Mechanisms of PSC Progression



ACLY: ATP citrate lyase; PSC: primary sclerosing cholangitis; Acetyl CoA: acetyl coenzyme A

ESPERION®

Break

(10-min)

ESPERION®

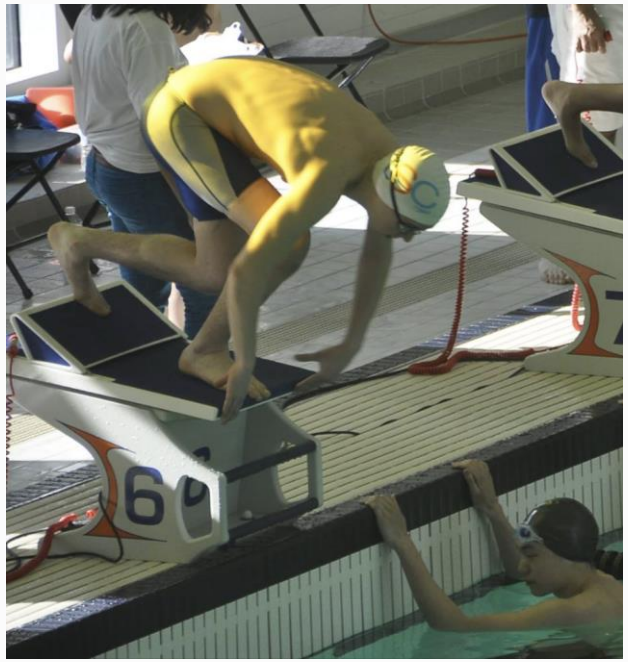
The PSC Patient Voice: Insights from Patients and Advocates

Mary Pressley Vyas

VP, Strategic Initiatives, PSC Partners

Our PSC Journey

10 Years Ago



PSC PARTNERS SEEKING A CURE

ESPERION

Our PSC Journey

DIAGNOSIS

PSC PARTNERS SEEKING A CURE

TESTS

- Blood
- Ultrasound
- MRCP
- Liver biopsy
- Scopes
- ERCP
- Bile duct brushings
- Bone density

DIAGNOSIS

- PSC
- Fibrosis
- Autoimmune hepatitis
- Ulcerative colitis

RISKS

- Cholangiocarcinoma
- Hepatocellular cancer
- Colectomy
- Cirrhosis
- End-stage liver disease

CONCERNS

- Chronic & progressive
- No cure, no proven treatments
- No reliable prognostic models (10-20 years)
- Organ system deprioritizes PSC patients
- High chance of PSC returning post liver transplant (~30%)

SYMPTOMS

Highly variable across the PSC population, but in this case

- Weight loss
- Brain fog
- Debilitating fatigue

ESPERION

PSC Partners Seeking a Cure

PSC PARTNERS SEEKING A CURE

Mission Statement

To drive research to identify treatments and a cure for PSC while providing education and support for those impacted by this rare disease

Established and impactful patient advocacy organization dedicated to working with an engaged and actively participating PSC patient community, industry, and global organizations to find treatment solutions

Prioritize and support drug development by providing impactful ways to de-risk and support clinical trials through various initiatives, including novel regulatory-grade real-world data

Founded in 2005 by Ricky Safer after being diagnosed with PSC herself

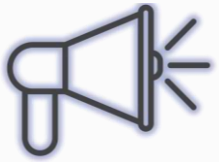
Located in Denver, CO and Toronto, ON

Initiatives to Support the PSC Community

PSC PARTNERS SEEKING A CURE

Support & Education

- PSCPartners.org website
- Annual Conference
- Webinars & Online Support
- Mentorship Program



Advocacy

- PSC Forum at the Center for Collaborative Research
- Pediatric Cholestatic Liver Disease Forum
- Patient Focused Drug Development with FDA
- Engagement with rare disease networks
- Critical Path Innovation Meeting (Regulatory Engagement)

Research Programs

- WIND-PSC Prospective Synthetic Cohort
- Research Grants Program
- Patient Registry
- International Collaborative Research Network
- PSC Symptom Assessment Project
- Cholangiocarcinoma Patient Survey
- Acute Cholangitis Patient Survey

ESPERION

WIND-PSC: A Strategic Advantage for PSC Drug Development

PSC PARTNERS SEEKING A CURE
WIND-PSC

A Study Design That Improves on Natural History Cohorts

- **Global**, prospective, multi-center, observational cohort with patients followed up to 5 years
- Up to **2,000 patients** will be enrolled in **North America and Europe** by **2027**
- Data collection system is **compliant** with **FDA standards** for submission
  - Liver-related endpoints consistent with current FDA guidance
  - Medical records, laboratory tests, procedures and medications

Uniquely Designed for Regulatory Purposes

- **Provides regulatory-grade, adjudicated longitudinal data to support accelerated clinical trial study design**
- Enables use as **a synthetic placebo arm** for Phase 4 or open label extension trials following initial accelerated approval
- Creates a large clinical and biomarker data set to **establish individual and/or composite surrogate endpoints** for eventual use in an accelerated approval pathway

ESPERION

ESPERION®

Esperion’s Lead PSC Candidate

Stephen Pinkosky, PhD

Vice President, Drug Discovery, Early Pre-Clinical Development

No Approved Therapy with Proven Efficacy to Cure or Halt PSC Progression

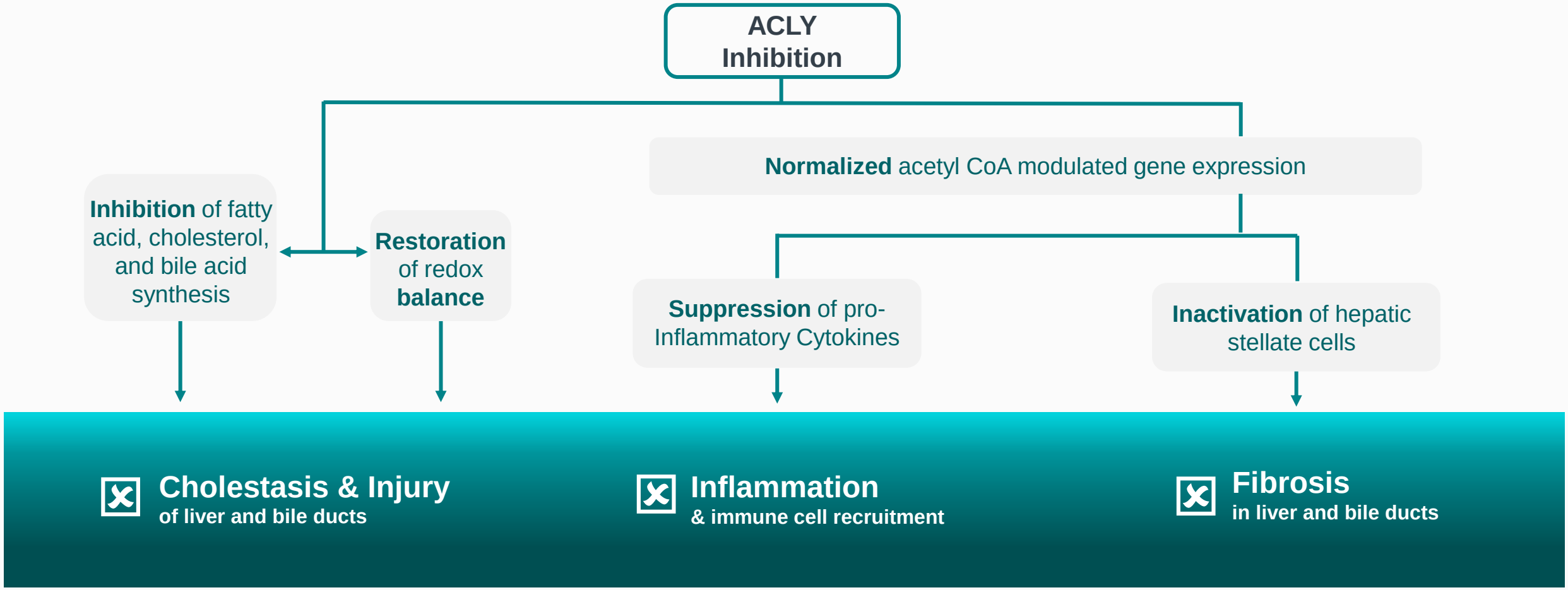
Esperion's oral next generation ACLY inhibitor has the potential to be the only agent to directly inhibit all 3 mechanisms of PSC disease progression

- **Cholestasis & Injury**
  of liver and bile ducts
- **Inflammation**
  & immune cell recruitment
- **Fibrosis**
  in liver and bile ducts

ACLY: ATP citrate lyase; PSC: primary sclerosing cholangitis

ESPERION

ACLY Inhibition is a Rational Therapeutic Target to Halt Multiple Mechanisms of PSC Progression



ACLY: ATP citrate lyase; PSC: primary sclerosing cholangitis; Acetyl CoA: acetyl coenzyme A

Identification of Lead Candidates for PSC

Virtual Screening

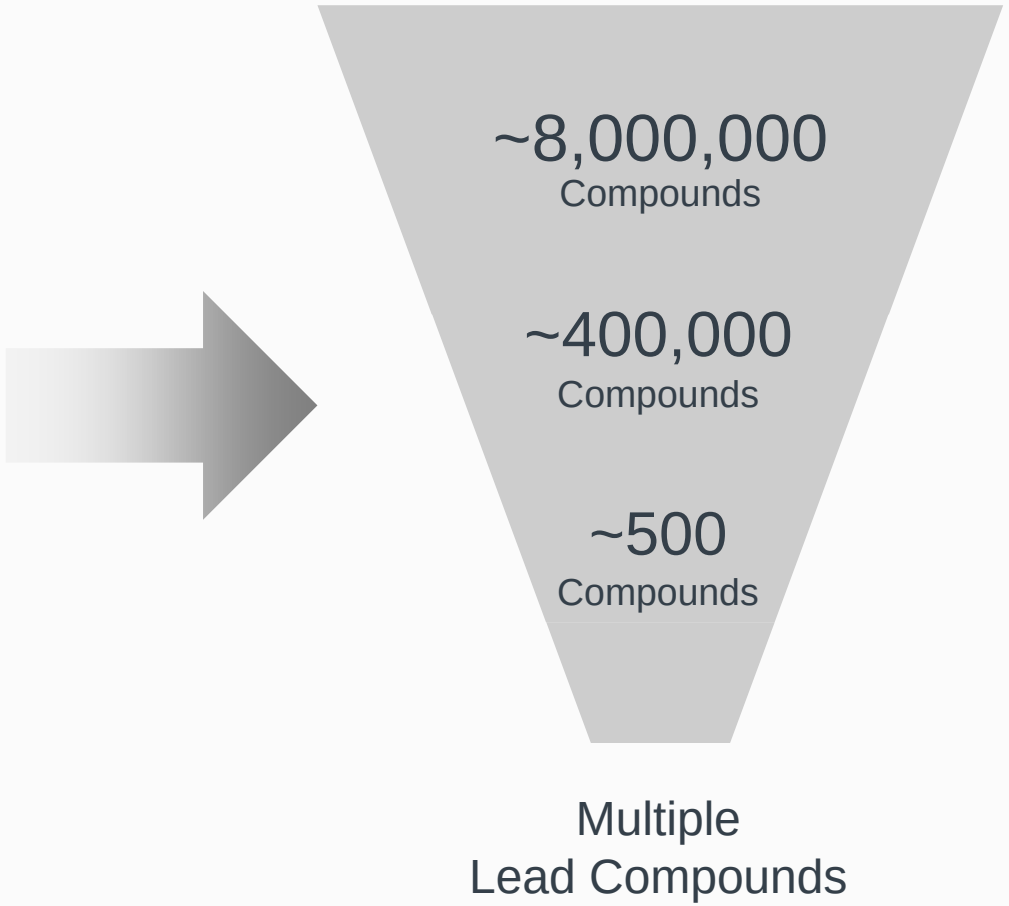
Structure & ligand based virtual screening toolbox

Knowledge Base

Structure-based approach using in-house protein structures

High Throughput Screening

Novel rapid-fire mass spectrometry

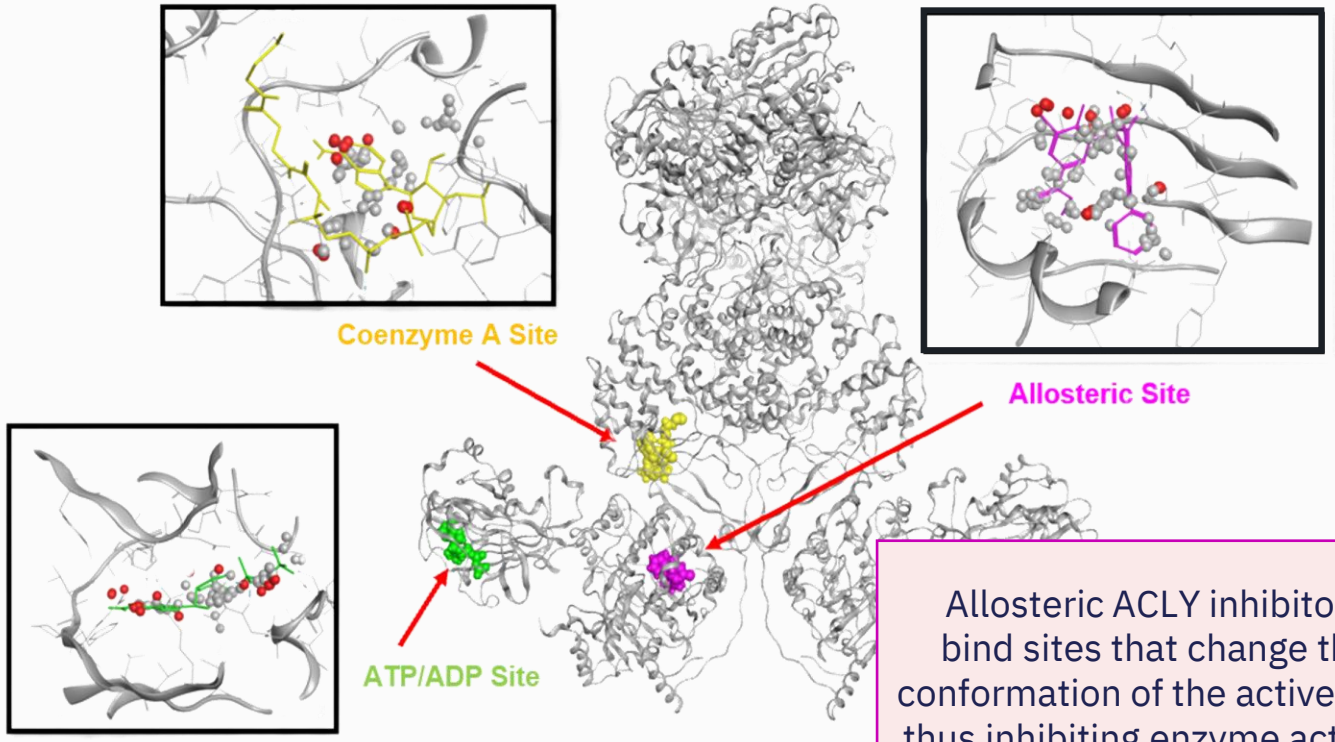


ACLY: ATP citrate lyase

Lead Candidates Will Leverage Advantages of Allosteric Inhibition

Potential Advantages of Allosteric Inhibition

- Improved Potency
- Enhanced Specificity
- Fewer Side Effects
- Less Drug Resistance



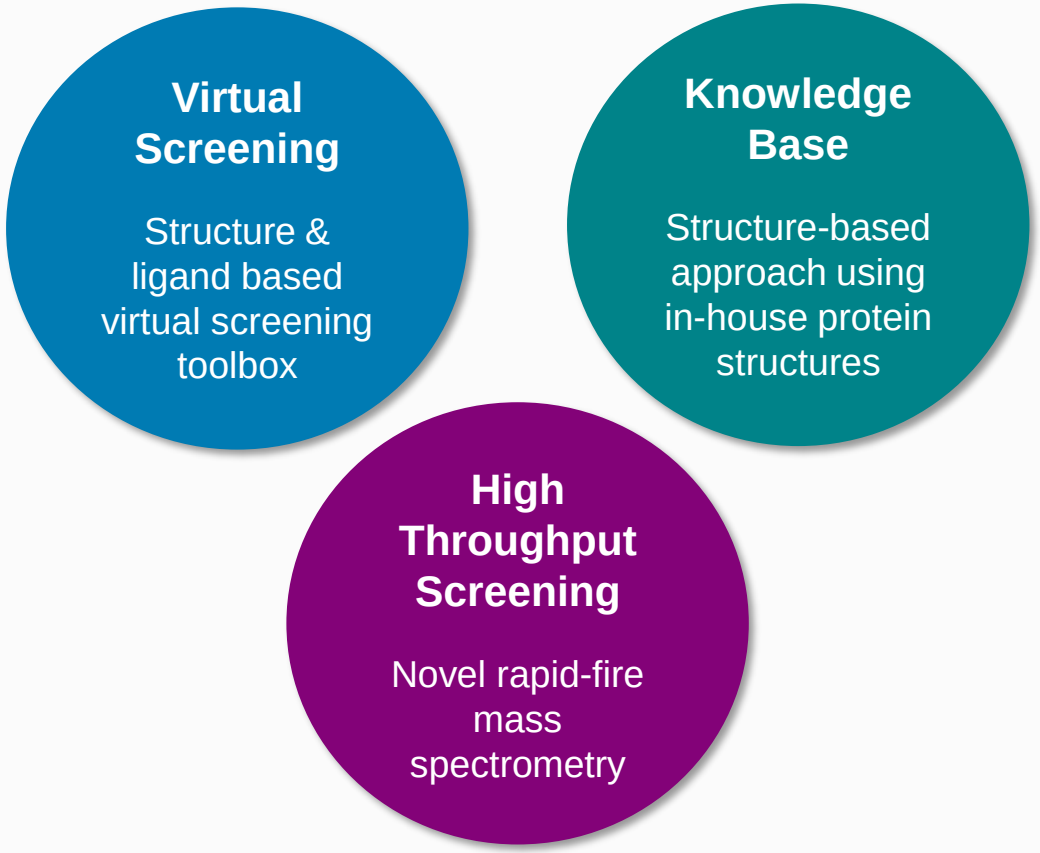
Allosteric ACLY inhibitors bind sites that change the conformation of the active site, thus inhibiting enzyme activity

ACLY: ATP citrate lyase; ATP: adenosine triphosphate; ADP: adenosine diphosphate

Identification of Lead Candidates for PSC

World-Class Approach

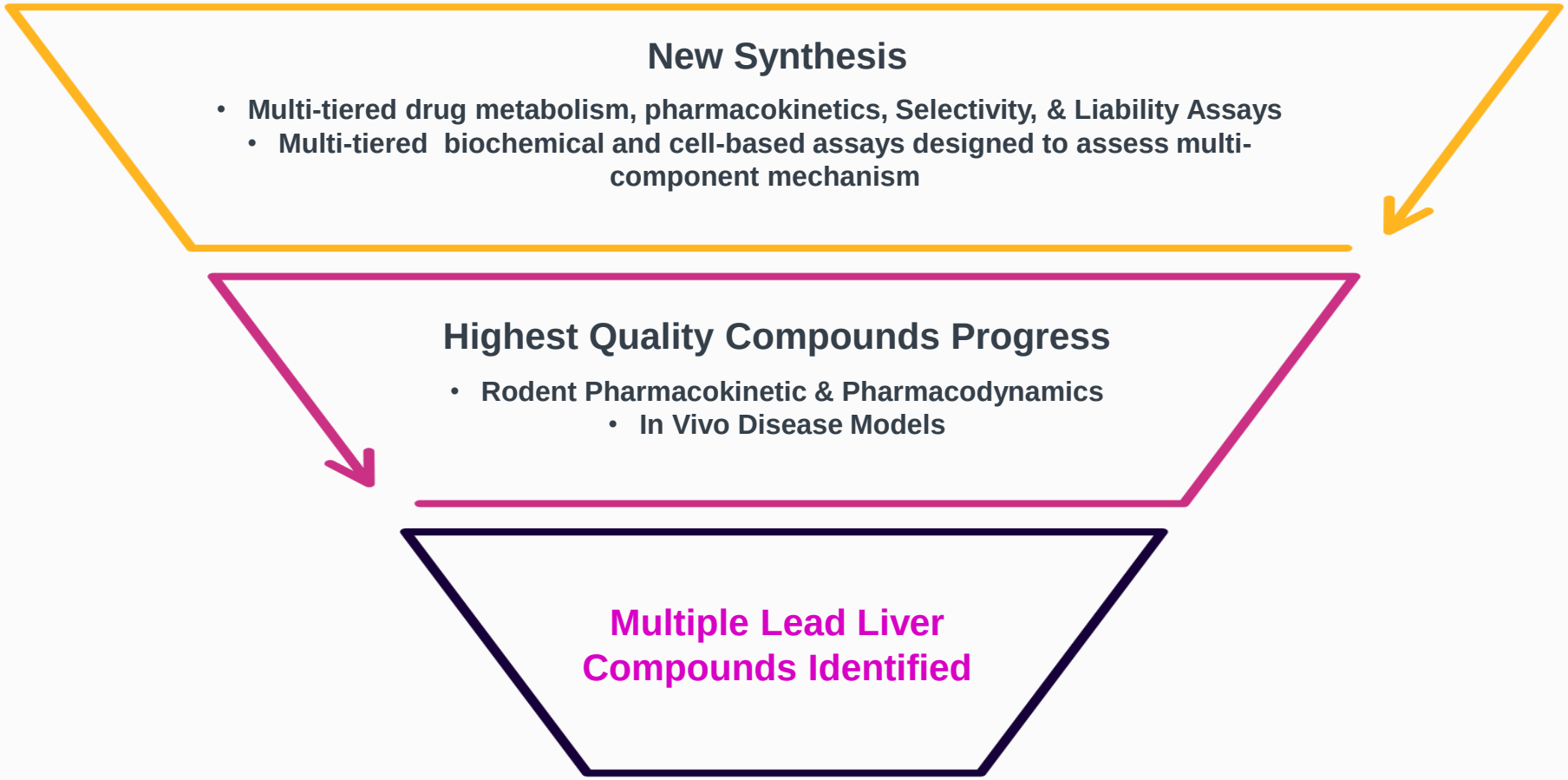
- ☑ nM biochemical and cellular potency
- ☑ Compound activity confirmed using orthogonal readouts
- ☑ Ligand-bound cryo-EM structure
- ☑ Direct binding demonstrated
- ☑ Strong (multiple log) SAR
- ☑ Highly differentiated from bempedoic acid
- ☑ Established high-quality assay suite and screening cascade for subsequent optimization



ACLY: ATP citrate lyase; SAR: structure-activity relationship; nM: nanomolar; cryo-EM: cryogenic electron microscopy

Esperion's Liver-Targeted Multi-tiered Activity and Liability Screening Cascade

Activity Optimization and Liability Counterscreening



Cryo EM: cryo-electron miscroscopy: IV, intravenous: PO, oral

Stringent Acceptance Criteria Ensure Selection of the Highest Quality Compounds

Metrics Used to Assess

Safety

Toxicity

Off-Target Liability

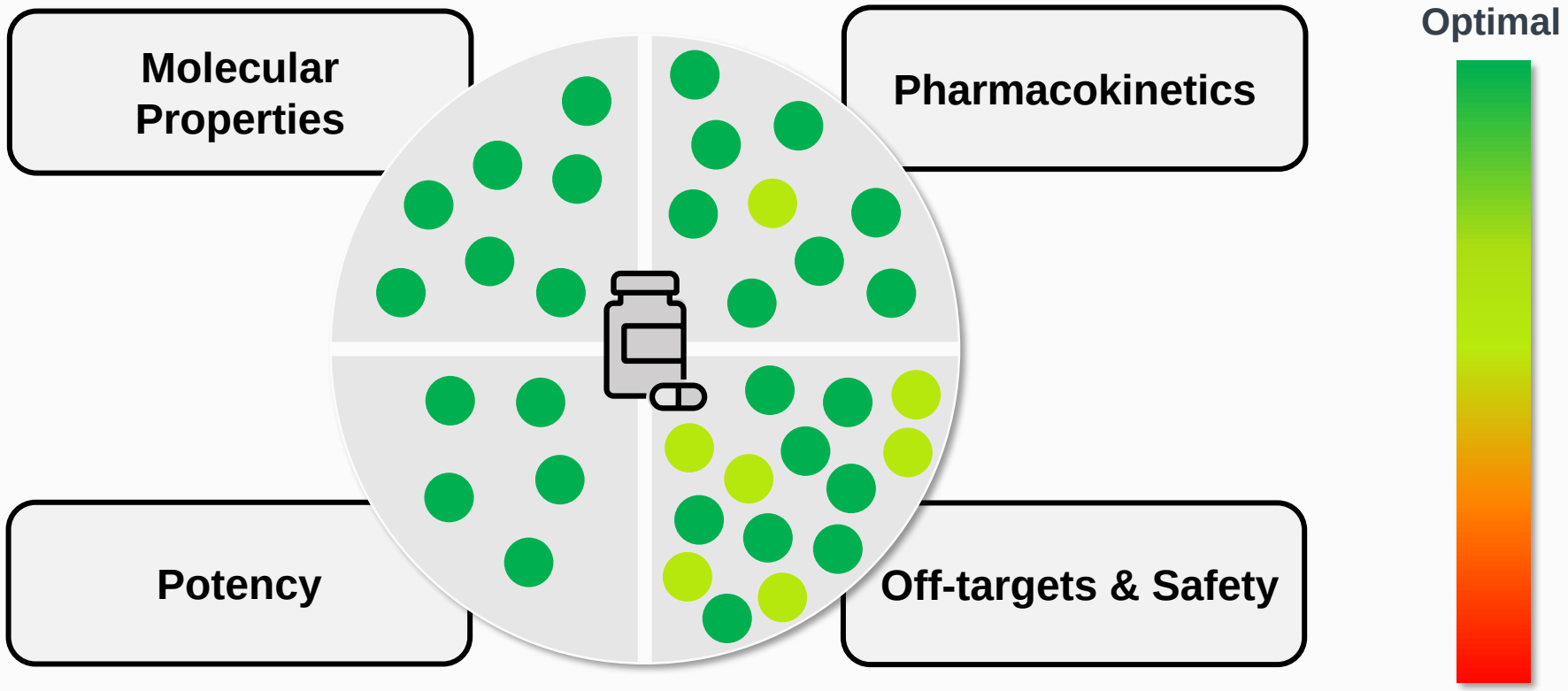
Potency/Specificity

Efficacy in Disease Models

A few **high-quality lead compounds** identified for advancement into pre-IND de-risking activities

IND: Investigational New Drug

Lead Compounds are Well-Characterized with Data In Vitro and In Vivo Supporting Once Daily Oral Dosing



No Anticipated Liabilities

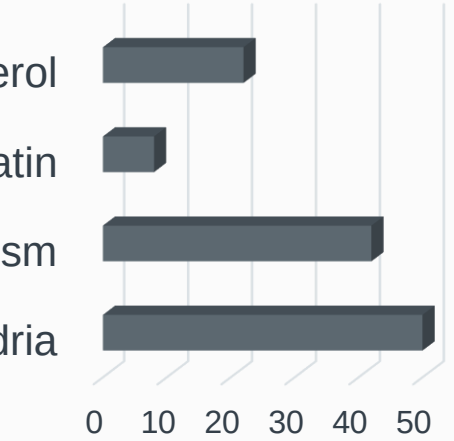
Esperion Lead Candidate ESP-1336: Specificity In Vitro and In Vivo

ESP-1336 Transcriptomics Demonstrate Expected Metabolic Processes by ACLYi in Primary Human Liver Cells

Expected Metabolic Mechanisms

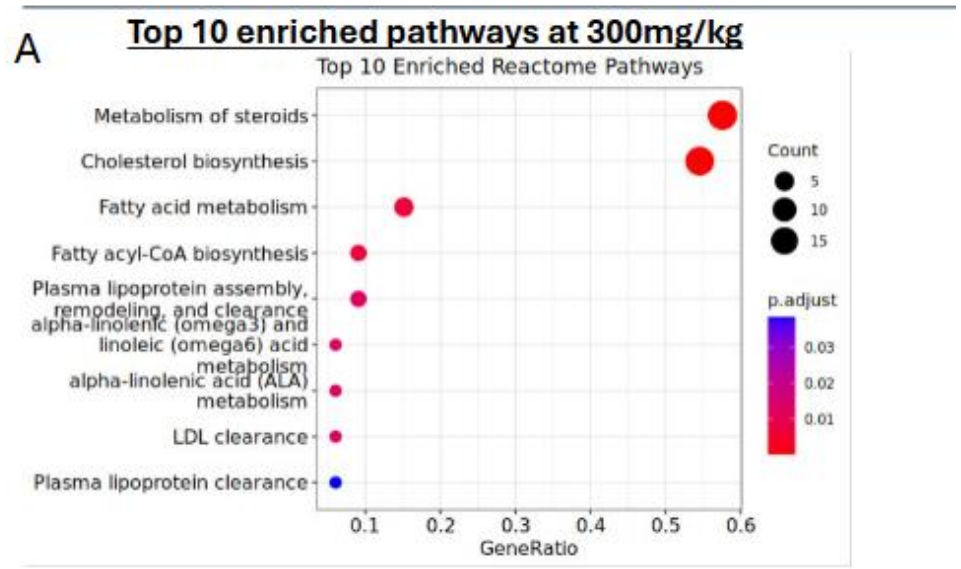
- Cholesterol/ Bile Acid Synthesis
- Epigenetic Regulation
- Protein Regulation
- De Novo Lipogenesis

Expected Metabolic Pathway Counts

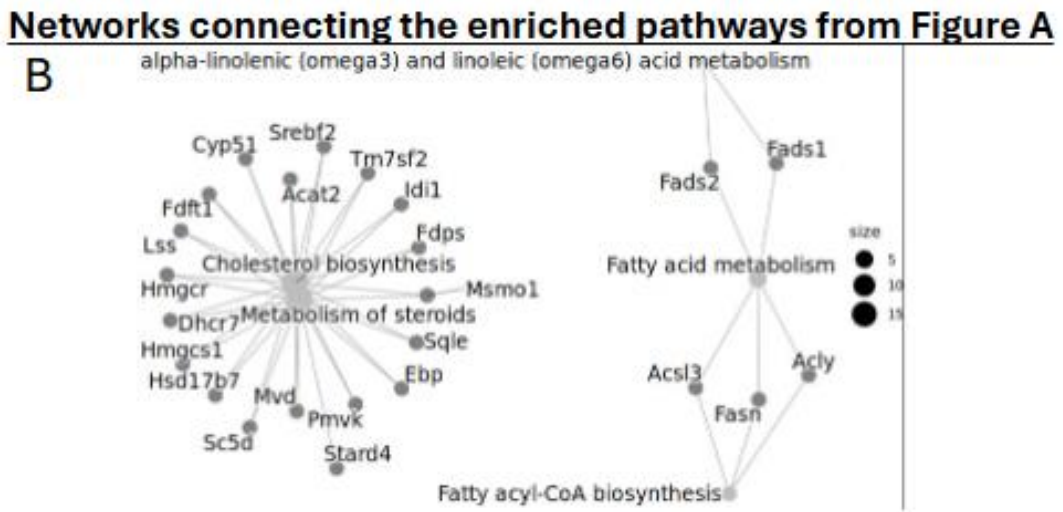


ACLYi: ATP citrate lyase inhibitor

Transcriptional Response With ESP-1336 Confirms ACLY Specificity at High Doses In Vivo



Effects of ESP-1336 are on-target for fatty acid and cholesterol metabolism/synthesis and lipoprotein metabolism



These enriched pathways of ACLY inhibition cluster into fatty acid and cholesterol synthesis inhibition as predicted

Transcriptomics in liver (rats) assessed after 4 days dosing at > 100-fold effective dose; ACLY:ATP citrate lyase

ESPERION®

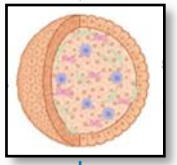
Characterizing ESP-1336 in Preclinical Disease Models

ESP-1336 Reduces Fibrosis in Human Liver Microtissues

ACLY inhibition results in concentration-dependent reduction in fibrosis, unlike ACC inhibitors

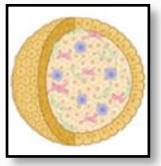
Hepatocytes
Liver Endothelial Cells
Kupffer Cells
Stellate Cells

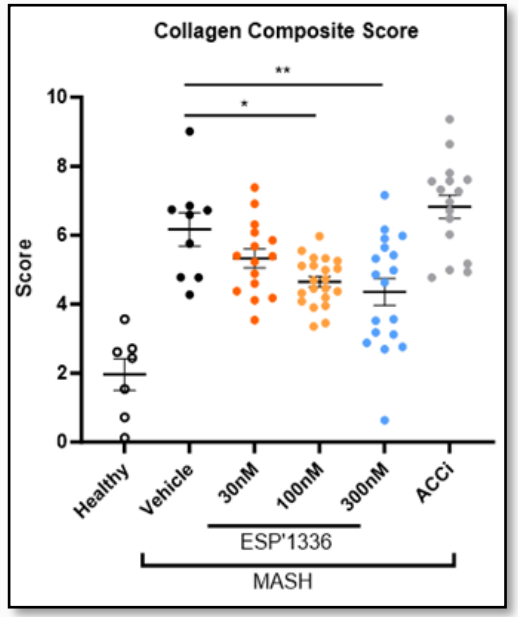
Aggregation



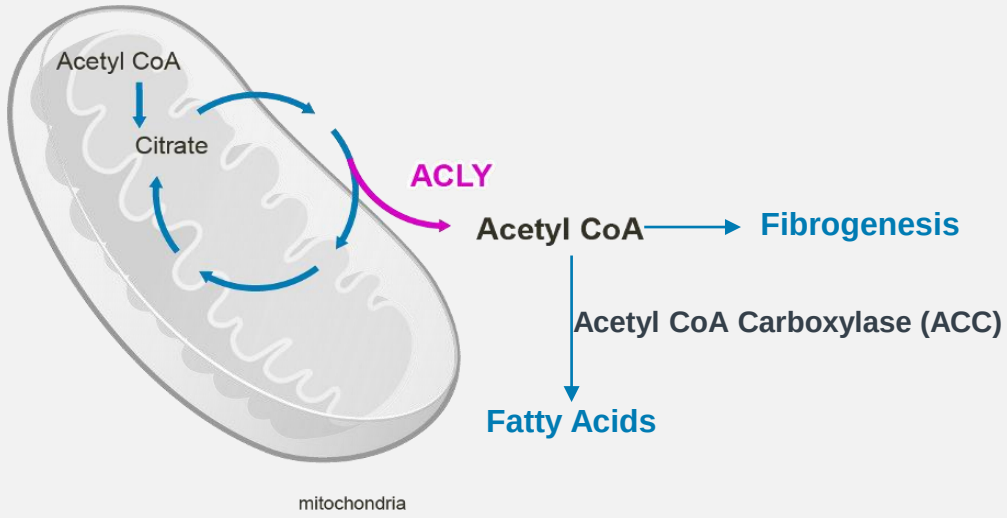
MASH stimulus

Fibrosis



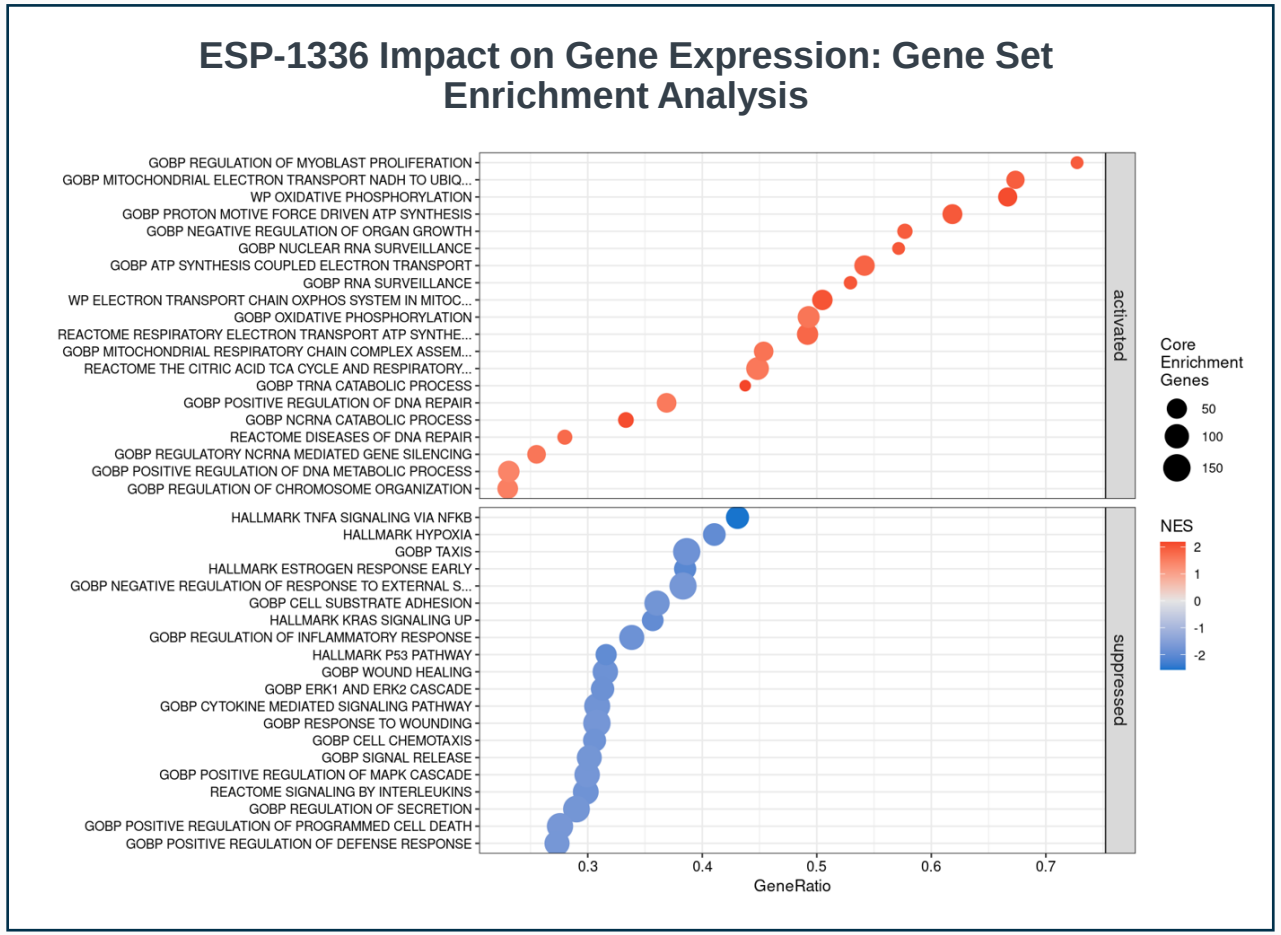


ACLYi and ACCi have opposite effects on Acetyl CoA



MASH: metabolic dysfunction-associated steatohepatitis ACLY: ATP-citrate lyase; ACLYi: ATP-citrate lyase inhibitor; ACCi: ACC inhibitor; CoA: coenzyme A

ESP-1336 Effects Pathways of Injury, Inflammation, and Fibrosis in Primary Human Liver Microtissues



Fibrosis
in bile and liver ducts

- Wound healing
- Myofibroblast proliferation

Inflammation
& immune cell recruitment

- Inflammatory Signaling
  - TNFα
  - NFkB
  - Interleukin
- Cell chemotaxis

Cholestasis & Injury
of bile and liver ducts

- Respiration/oxidative phosphorylation
- TCA cycle
- Cholesterol biosynthesis
- Apoptosis

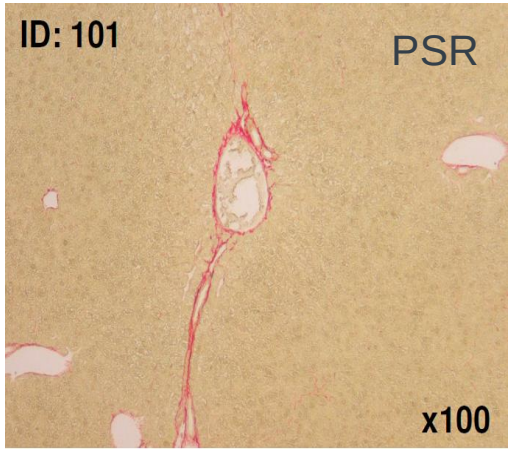
TCA: tricarboxylic acid ;TNFa: Tumor necrosis factor alpha; NFKB: Nuclear factor kappa-light-chain-enhancer of activated B cells

ESP-1336 Reduces Liver Inflammation and Fibrosis in a Chemical-Induced Injury Model

Inflammation
& immune cell recruitment

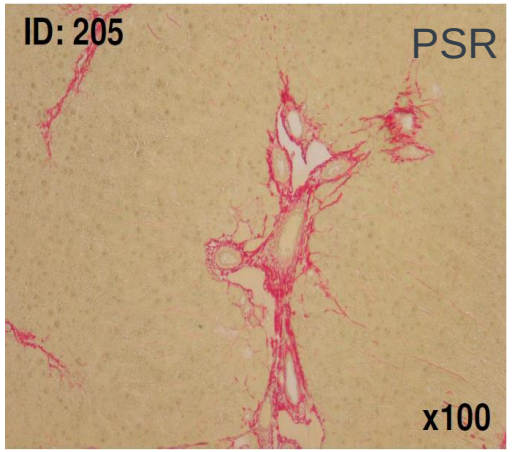
Fibrosis
in bile and liver ducts

Control



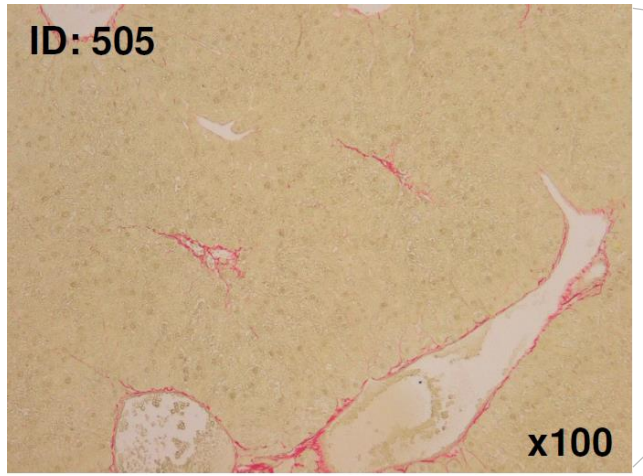
No Toxin

CCl_4 Toxin-Induced Liver Injury

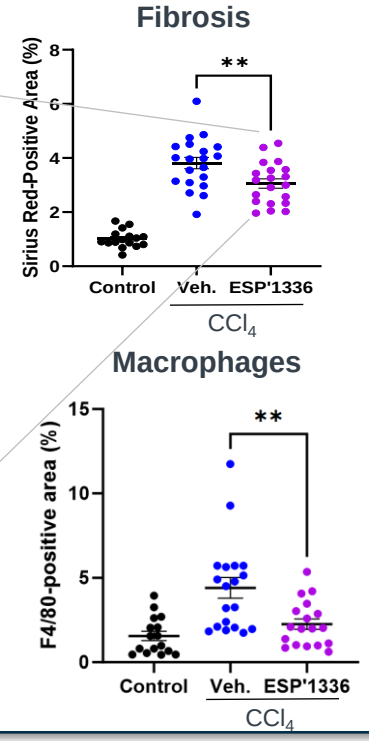


CCl_4 induced nonspecific inflammation & fibrosis

ESP-1336 + CCl_4



ESP-1336 reduced markers of liver inflammation and fibrosis



**One-way ANOVA vs. Vehicle p<0.01

ACLYi: ATP citrate lyase inhibitor; CCl_4: carbon tetrachloride

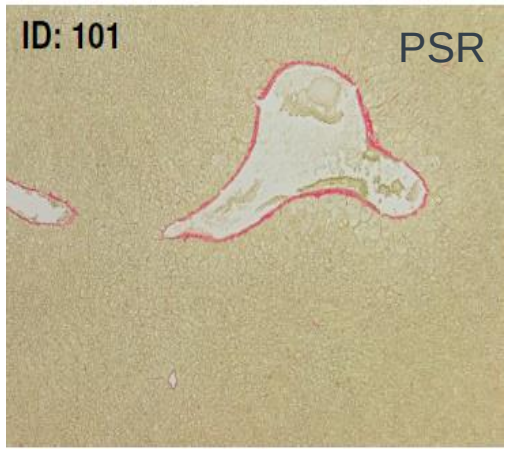
ESPERION

ACLY Improves Liver Injury and Fibrosis in a Model of Progressive Biliary Obstruction

Cholestasis & Injury
of bile and liver ducts

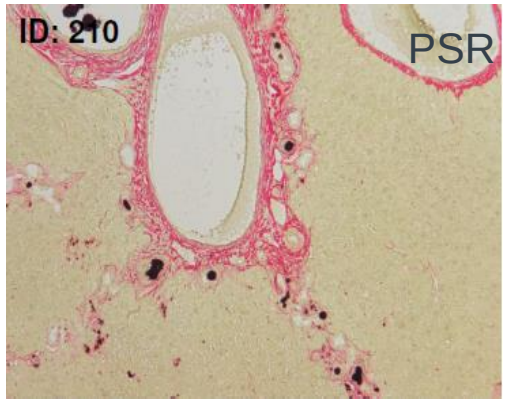
Fibrosis
in bile and liver ducts

Control



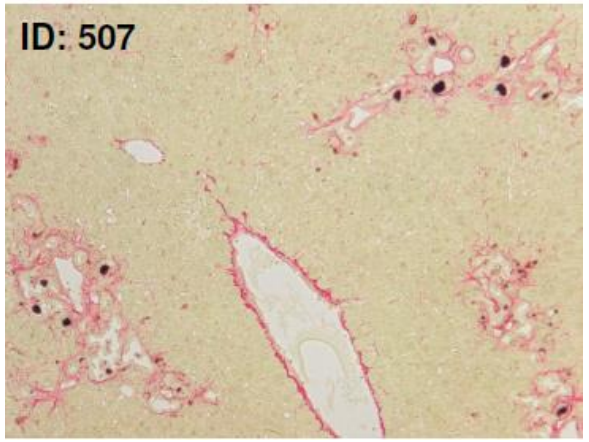
No DDC

DDC-feeding leads to formation of intraductal porphyrin plugs

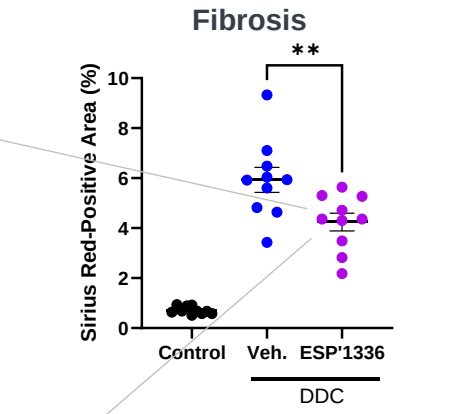


+DDC: accumulation of toxic bile acid; inflammation, necrosis immune cell recruitment & fibrosis

ESP-1336+DDC



ESP-1336 treatment attenuated elevation of liver enzymes and reduced fibrosis



N=10; One-way ANOVA vs. Vehicle **; p<0.01

ACLYi: ATP citrate lyase; DDC: 3,5-diethoxycarbonyl-1, 4-dihydrocollidine; AST: aspartate aminotransferase; ALT: alanine aminotransferase

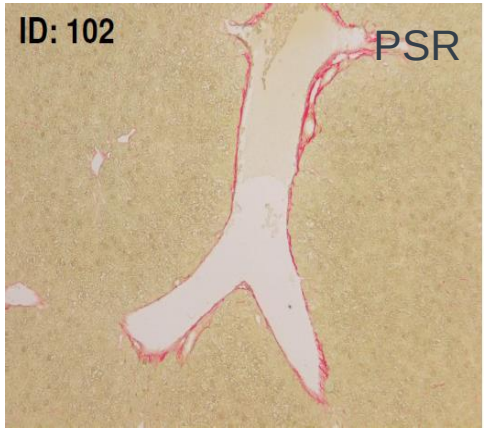
ESPERION

ESP-1336 Improves Liver Injury and Fibrosis in a Model of Hepatic Inflammation

Cholestasis & Injury
of bile and liver ducts

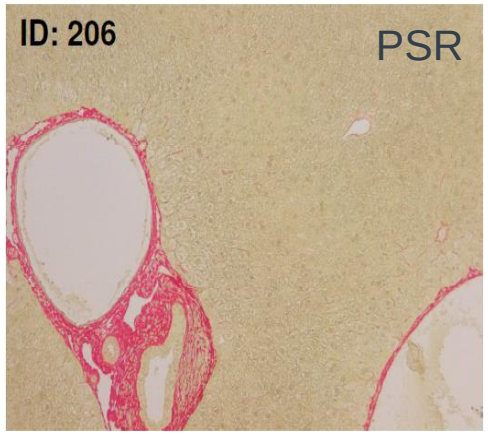
Fibrosis
in bile and liver ducts

Control



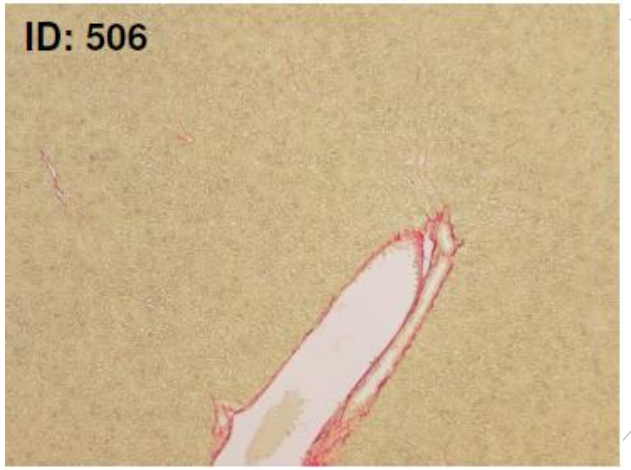
No ANIT

ANIT-Induced Liver Injury

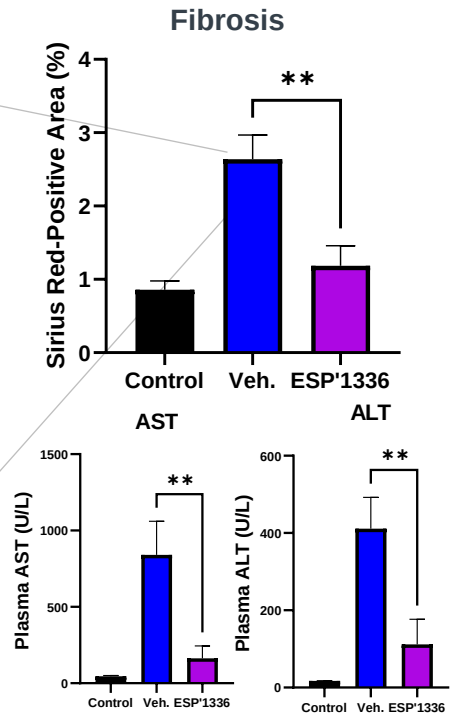


Pilot study shows rapid induction of fibrosis with ANIT treatment

ESP-1336+ANIT



ESP-1336 reduces fibrosis and markers of liver injury in pilot study



**One-way ANOVA vs. Vehicle p<0.01

ACLYi: ATP citrate lyase inhibitor; ANIT: alpha-naphthylisothiocyanate; AST: aspartate aminotransferase; ALT: alanine aminotransferase

ESPERION

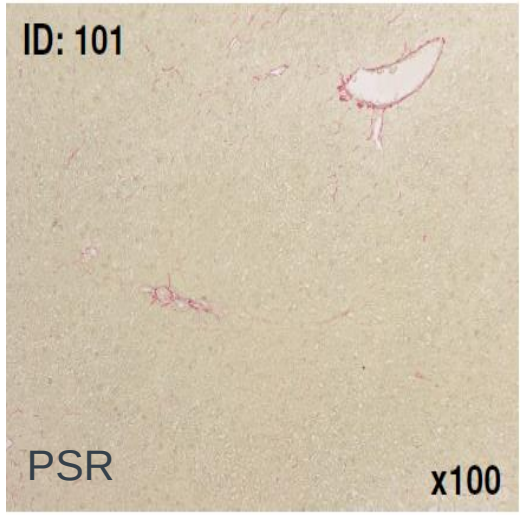
ESP-1336 Improves Liver Injury, Immune Cell Recruitment, and Fibrosis in a Severe Obstructive Model of Cholestasis

Cholestasis & Injury of bile and liver ducts

Inflammation & immune cell recruitment

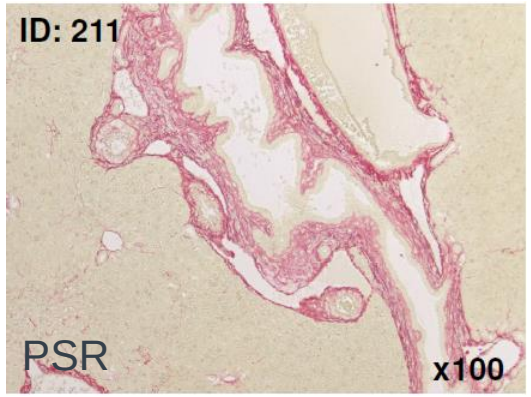
Fibrosis in bile and liver ducts

Control



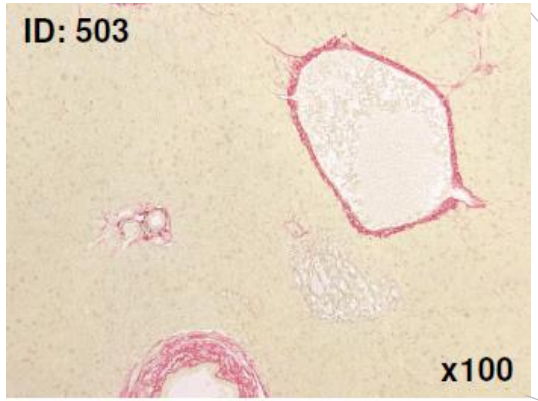
No Damage

Bile duct ligation (BDL): accumulation of toxic bile acid

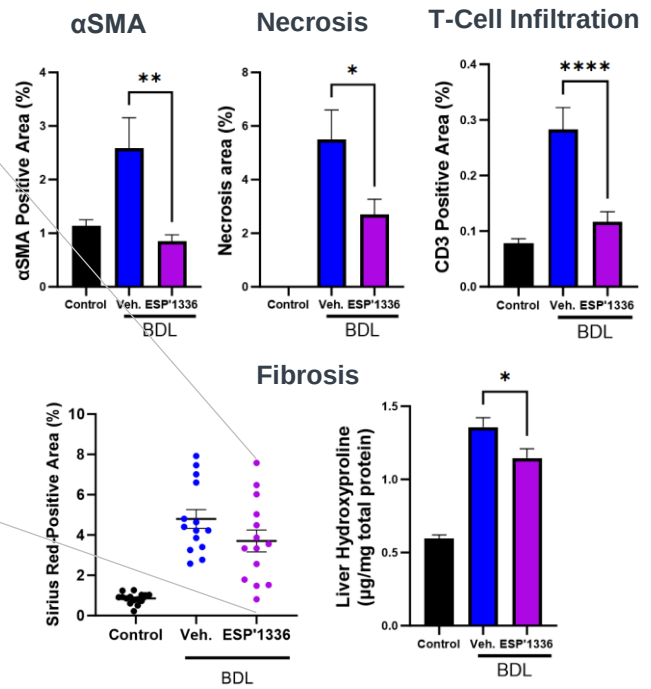


BDL induced inflammation, necrosis, immune cell recruitment & fibrosis

ESP-1336 + BDL



ESP-1336 reduces liver necrosis, T-cell infiltration, and markers of fibrosis/ myofibroblast formation



N=14-15; One-way ANOVA vs. Vehicle *; p<0.05, **; p<0.01, ****; p<0.0001

ACLYi: ATP citrate lyase inhibitor; CCl_4: carbon tetrachloride; αSMA: alpha-smooth muscle actin

ESPERION

Innovative ACLY Inhibitor Discovery Program Designed for PSC

Optimization for PSC-specific mechanisms

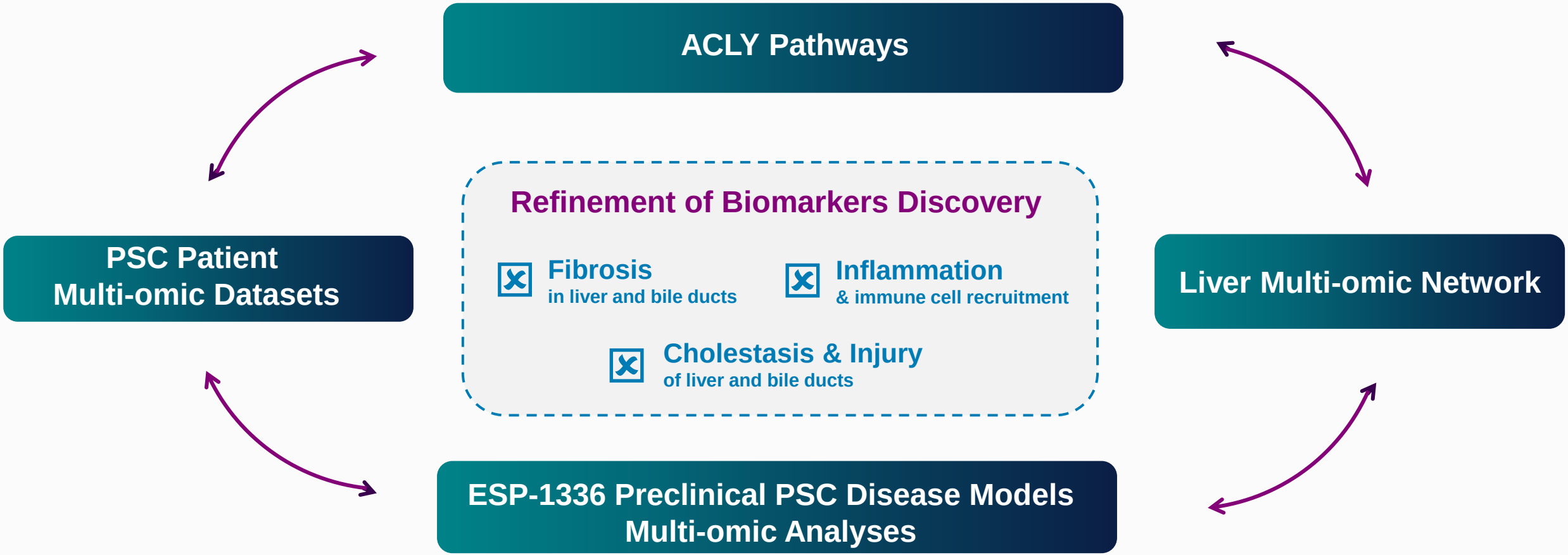
- Applied advanced discovery approaches and technology to design the next generation of differentiated ACLY inhibitors
- Leveraged multi-omic data and human genetics to identify novel ACLY pathways relevant to liver disease
- Developed a custom screening cascade to optimize compound activity for PSC-specific mechanisms

Strong Preclinical Profile

- De-risked, highly potent and specific allosteric ACLY inhibitor leads and backups selected
- Pharmacokinetic properties enable convenient once-daily oral dosing
- Compelling preclinical evidence confirm reductions in liver injury, inflammation and fibrosis in multiple PSC-relevant models, reinforcing therapeutic potential

ACLY: ATP citrate lyase; PSC: primary sclerosing cholangitis

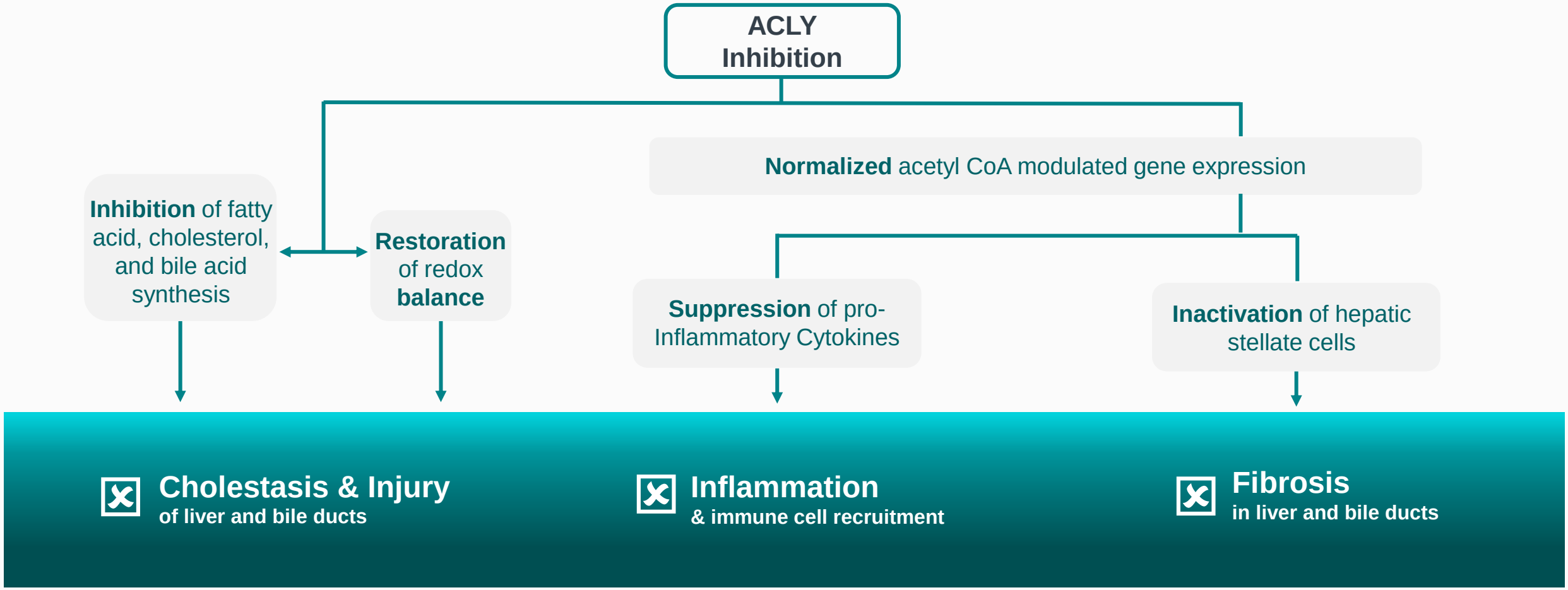
Ensuring Success: Utilizing Data Integration to Identify Early Biomarkers



ACLY: ATP citrate lyase; PSC: primary sclerosing cholangitis; Acetyl CoA: acetyl coenzyme A

ESPERION

ACLY Inhibition is a Rational Therapeutic Target to Halt Multiple Mechanisms of PSC Progression



ACLY: ATP citrate lyase; PSC: primary sclerosing cholangitis; Acetyl CoA: acetyl coenzyme A

No Approved Therapy with Proven Efficacy to Halt PSC Progression

Esperion's oral next generation ACLY inhibitor has the potential to be the only agent to directly inhibit all 3 mechanisms of PSC disease progression

- **Cholestasis & Injury**
  of liver and bile ducts
- **Inflammation**
  & immune cell recruitment
- **Fibrosis**
  in liver and bile ducts

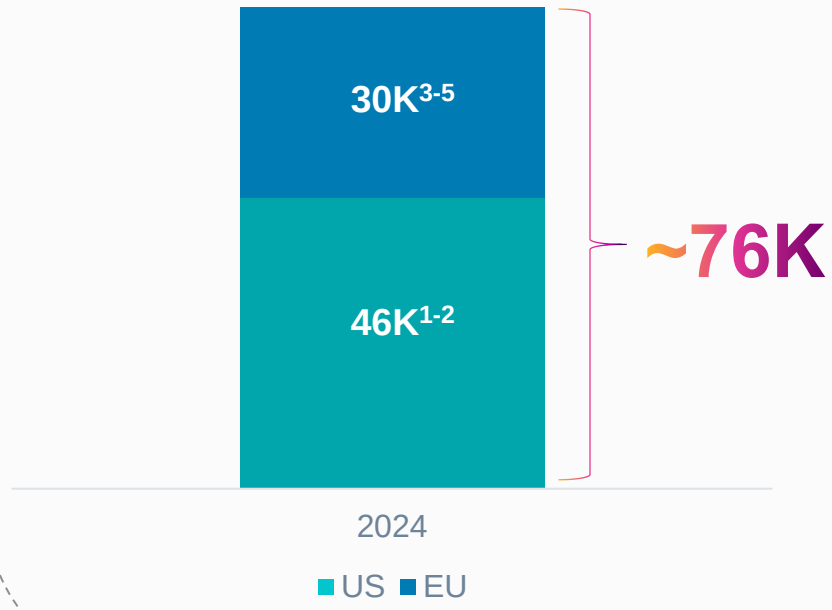
ACLY: ATP citrate lyase; PSC: primary sclerosing cholangitis

ESPERION

High Unmet Need Driving Significant Market Opportunity

PSC: A Rare and Progressive Liver Disease

Diagnosed Prevalence of PSC



>$1B Annual Market Opportunity Estimate

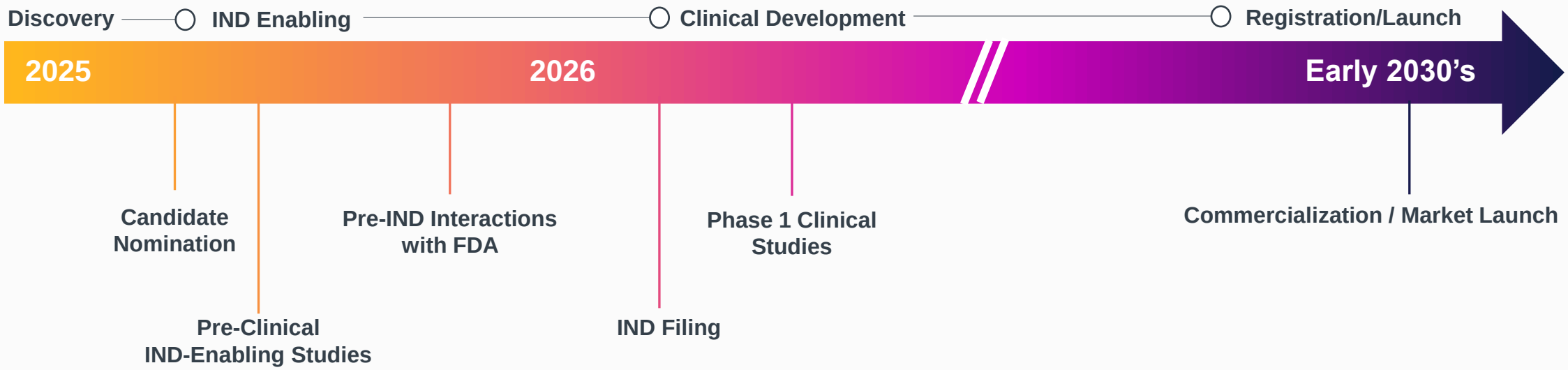
- **No approved therapies** with proven efficacy to cure or halt PSC progression
- **High healthcare burden** from hospitalization, transplants, and long-term management costs
- **Death or liver transplantation expected** within 1-2 decades after diagnosis
- Potential **Orphan Drug Designation & Fast Track** Approval
- Discovery program is **internally developed and wholly-owned globally**

PSC: primary sclerosing cholangitis

1. Bakhshi Z, et al. *J Gastroenterol*. 2020 May;55(5):523-532.; 2. Nguyen A, et al. *Front Gastroenterol (Lausanne)*. 2022;1:1076788.; 3. Liang H, et al. *Medicine (Baltimore)*. 2017;96(24):e7116.; 4. Boonstra K, et al. *Hepatology*. 2013;58(6):2045-55.; 5. Krampe, J, et al. Poster presented at: ISPOR 2024; Nov 2, 2024; Barcelona, Spain

ESPERION

We’re Off to a Strong Start



IND: Investigational New Drug; FDA: Food and Drug Administration

ESPERION®

KOL Discussion

ESPERION®

Q&A Session

ESPERION®

Closing

Why Esperion Will Succeed

Patient-Focused Strategy

- Targeting a disease with **no approved therapies** to slow progression
- Committed to delivering real therapeutic impact in an area of **profound unmet need**
- **Strengthened ties** with **PSC patients** by working closely with PSC-focused advocacy groups
- Potential for **rare and orphan drug designation**, proving opportunities to deliver the therapy to patients sooner

Scientific Edge

- **Deep expertise** in ACLY biology and inhibition
- **Novel and differentiated** mechanism of action with broad liver disease application
- Targeting **multiple mechanisms of PSC progression**: injury, inflammation and fibrosis
- **Strong partnerships** and **research collaborations** enhancing execution

Experienced Leadership

- **First to discover**, develop, and globally commercialize ACLYi therapy
- Decades of **end-to-end drug discovery, development, and commercialization experience**, including in orphan and rare diseases
- **Fully built organization** with all core functions in place

PSC: primary sclerosing cholangitis; ACLY: ATP-citrate lyase; ACLYi: ATP-citrate lyase inhibitor

ESPERION

ESPERION®

Thank You