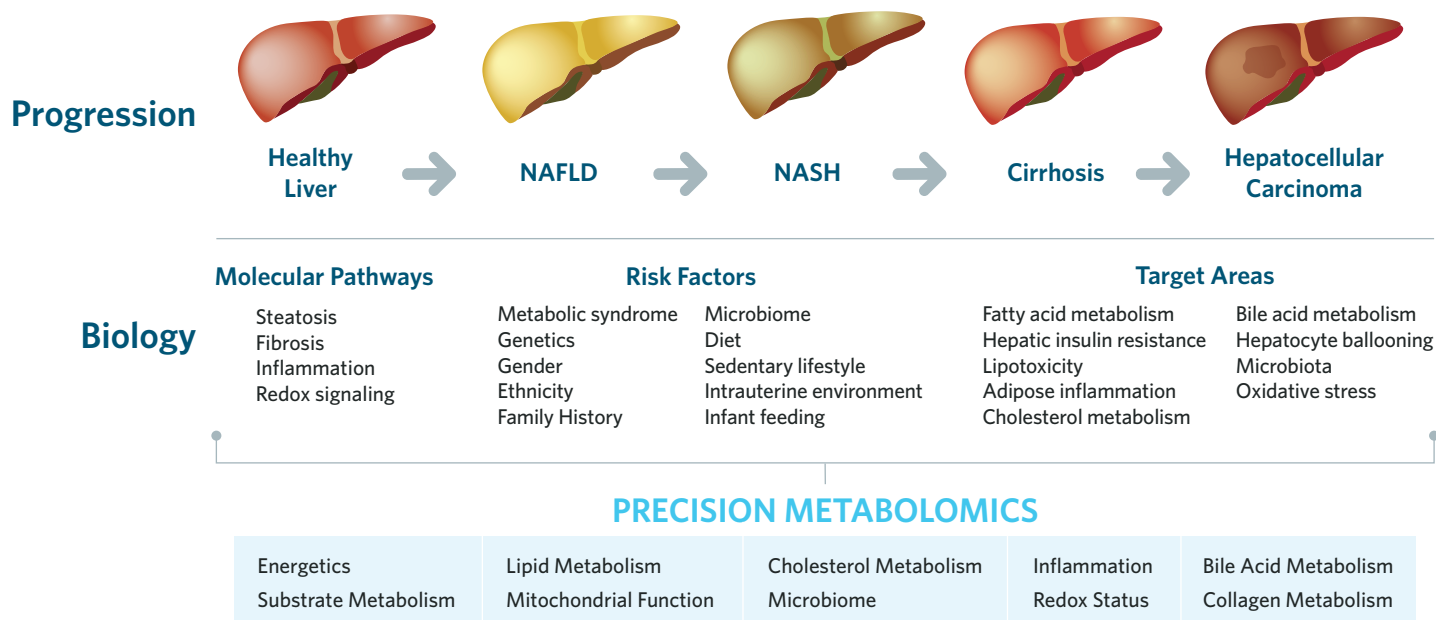


PRECISION METABOLOMICS™ FOR NASH R&D

A COMPLEX DISEASE WITH MANY OPEN QUESTIONS AND DEVELOPMENT HURDLES

NAFLD encompasses a spectrum of diseases that range from simple steatosis to NASH, cirrhosis and hepatocellular carcinoma. As the disease progresses, hepatic lipid accumulation is accompanied by excessive inflammation and oxidative stress. Eventually, fibrosis, the primary clinical predictor of risk, can be detected and used to stage NASH. Diagnostic and therapeutic options are starkly limited.



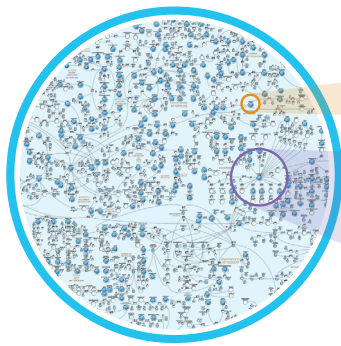
Leveraging Precision Metabolomics to Decipher NAFLD Complexity

A diverse set of disease drivers; including genetics, environmental cues, microbiota metabolism and lifestyle influences, come together resulting in an uncertain natural history of NAFLD/NASH. The constellation of risk factors for NASH has spawned a remarkable array of targets. Metabolic pathways underlie the biology of NAFLD/NASH, risk factors and the targets being pursued. By simultaneously surveying diverse metabolic pathways in a single sample, Precision Metabolomics provides a holistic assessment of NAFLD/NASH complexity.

Notable insights assessed by Precision Metabolomics are:

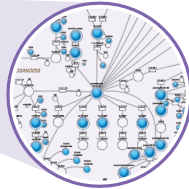
- **Lipid metabolism** (*de novo* synthesis and oxidation)
- **Inflammatory pathways**
- **Redox balance** (antioxidant defenses such as glutathione and markers of oxidative stress)
- **Microbiota metabolism** (bacterial and host metabolites at the intersection of this relationship)

HARNESS THE POWER OF METABOLOMICS



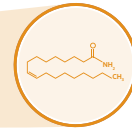
GLOBAL METABOLOMICS

Cast a wide research net with our global metabolomics technology (1,000+ metabolites/sample)



COMPLEX LIPID PANEL™

Our insightful lipidomics approach comprehensively quantitates up to 1,100 lipids/sample



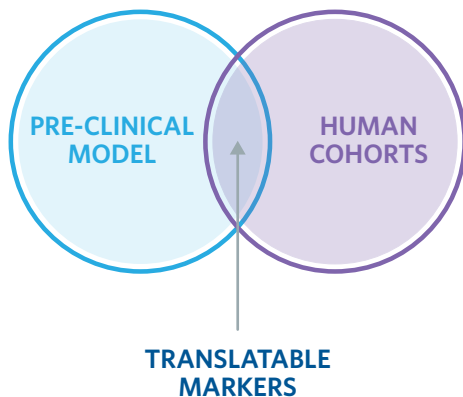
TARGETED ASSAYS

Narrow your focus to specific pathways, themes or metabolites with custom or pre-developed assays

Metabolon is prepared to work with you at every step of the development of your NASH program. Global metabolomics combined with our Complex Lipid Panel allows you to survey the entire metabolome. Metabolon also offers continuous optimization programs that incorporate your strategic aims. These can include the development of targeted metabolomic approaches or the use of validated targeted metabolomic assays. Please ask about the targeted assays currently available.

A Translational Resource

Metabolon has performed analysis on multiple human cohorts, revealing established and less appreciated metabolic signatures. These datasets can be used to evaluate the translatability of your model and build confidence in biomarker programs.



Metabolon is a leader in Precision Metabolomics in the NAFLD/NASH space with publications including:

Clinical

Puri, P et al. *Hepatology* **46**, 1081-1090 (2007)
Puri, P. et al. *Hepatology* **50**, 1827-1838 (2009)
Kalhan, S.C. et al. *Metabolism* **60**, 404-413 (2011)
Cheng, J. et al. *PLoS ONE* **7**, (2012)
Loomba, R. et al. *Cell Metabolism* **25**, 1054-1062 (2017)
Sookoian, S. et al, *Liver International* **37**, 611-619 (2017)

Pre-Clinical

Depner C.M. et al. *PLoS ONE* **8**, (2013)
Pierce, A.A. et al. *BMC Gastroenterology*, **15** (2015)
Garcie-Heredia A., et al. *J. Proteome Res*, **12**, 1946-1955 (2013)
Rull A., et al. *J. Proteome Res*, **13**, 1731-43 (2014)

In Vitro

Villanueva, C.J. et al. *Hepatology*, **50**, 434-442 (2009)
Brown M.V. et al. *Obesity*, **000**, 1-10 (2013)
Min H. et al., *Am J Physiol Gastrointest Liver Physiol*, **307**, G66-G76 (2014)

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CORPORATE HEADQUARTERS

Research Triangle Park, North Carolina
+1.919.572.1711

www.metabolon.com

info@metabolon.com