

Amylin Liver NASH (AMLN)

A novel diet-induced mouse model of Nonalcoholic Fatty Liver Disease (NAFLD) and Nonalcoholic Steatohepatitis (NASH)



Animal model of human disease is a crucial part of translational research which provides deep understanding of the disease aetiology upon which new therapeutic candidates can be tested for use in the clinical populations. We at Aragen have validated diet induced mouse model similar to human like NASH. This model mimics the metabolic and pathological features like steatosis, liver inflammation, ballooning and fibrosis of human NASH diseases.

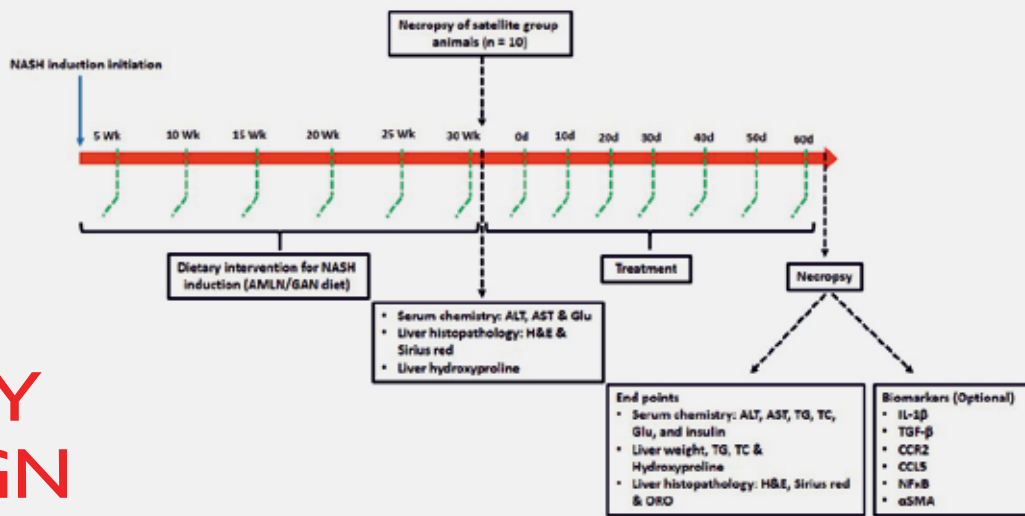
Capabilities of our AMLN/GAN NASH Model

- Model is validated with 3 reference compounds
- Ideal model to screen small and large molecule targeting NASH
- Our stringent selection criteria for NASH establishment is based on body weight, ALT, AST, blood glucose, liver hydroxyproline and histopathology
- Consistence disease induction with ≥ 6 NAS score across the studies
- Supporting global clients to screen NASH compounds
- Experienced and well-trained pathologist to support NASH studies
- Model is established in high quality Taconic SPF Animals
- To accelerate client NASH programs, Aragen offers multiple batches of animals which are fed on AMLN/GAN diet for NASH development

Value Proposition

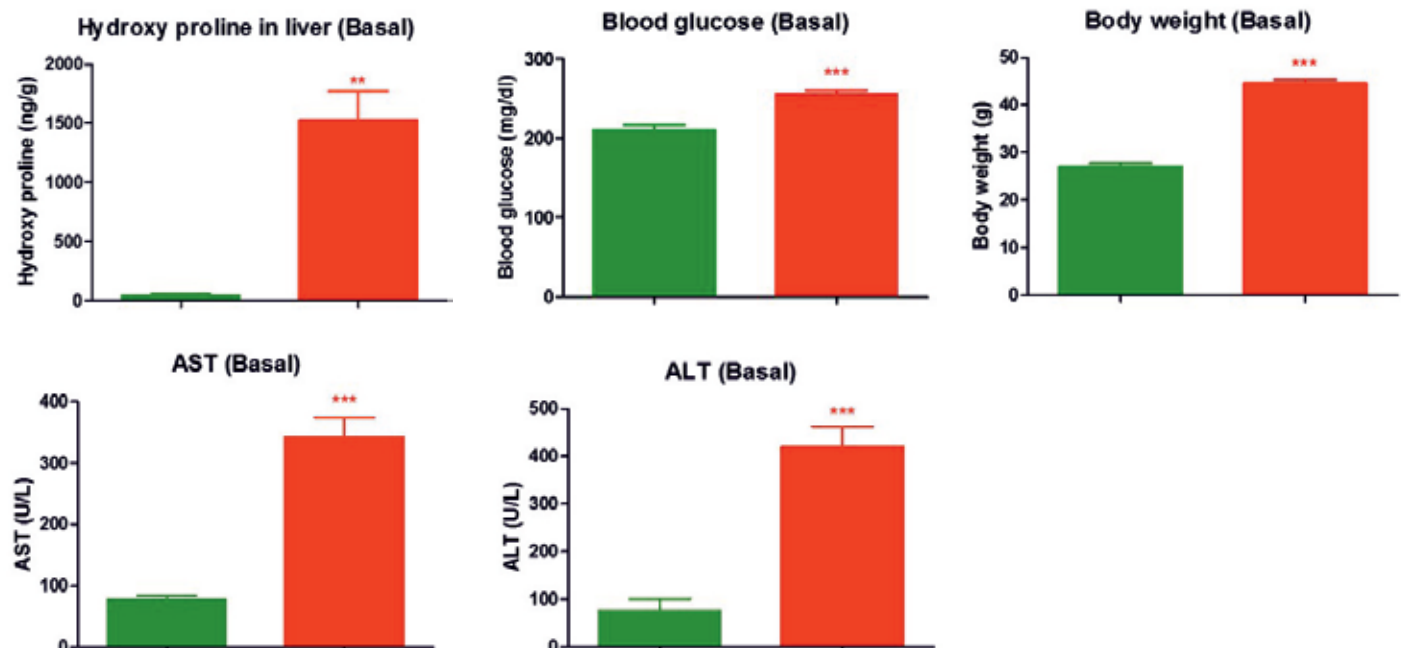
- Accelerating your research timeline from 9 months to 4 months
- Customized existing models to meet specific client needs or develop novel, fit-for-purpose models
- Easy Access to quality animals from Taconic and Charles River facilities in Hyderabad, India
- AAALAC accredited vivarium. Over 50 validated animal models in oncology, pain, inflammation, CVMD and fibrosis

STUDY DESIGN



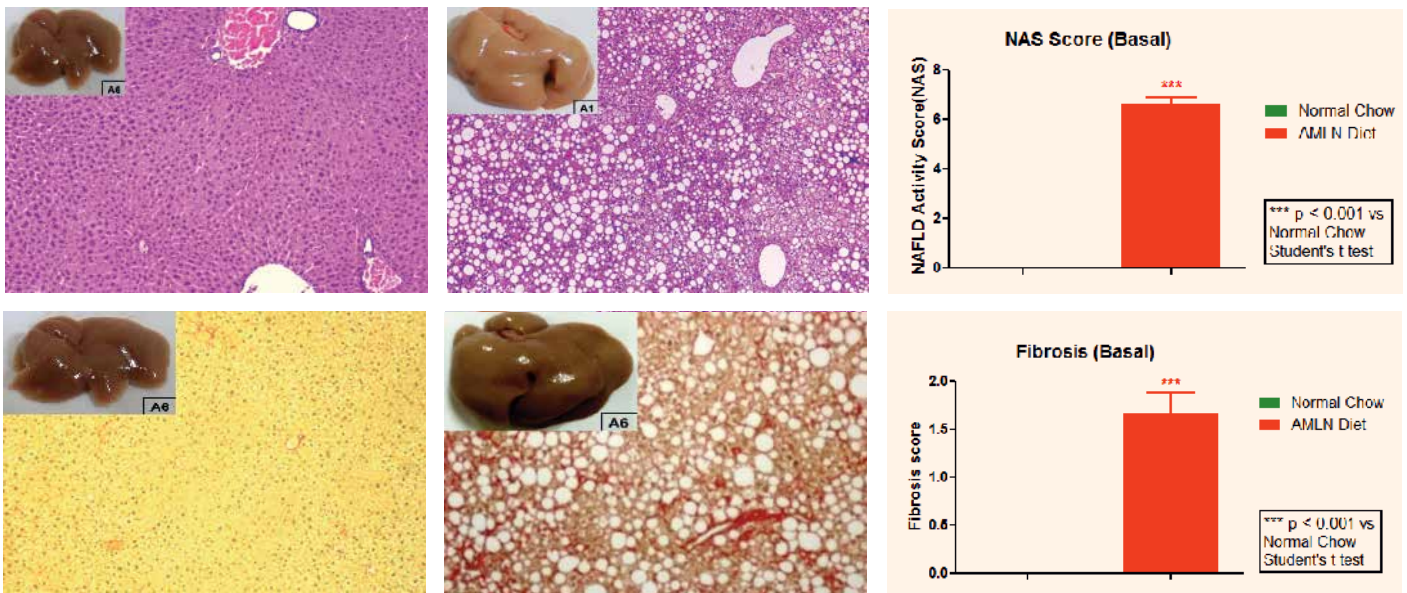
Metabolic and histopathological characterization of AMLN-NASH (Disease induction)

Increased body weight gain, Aminotransferase levels, Hyperglycemia and Hydroxy proline in liver collagen content



Histopathological assessment of NAFLD Activity Score (NAS) and fibrosis)

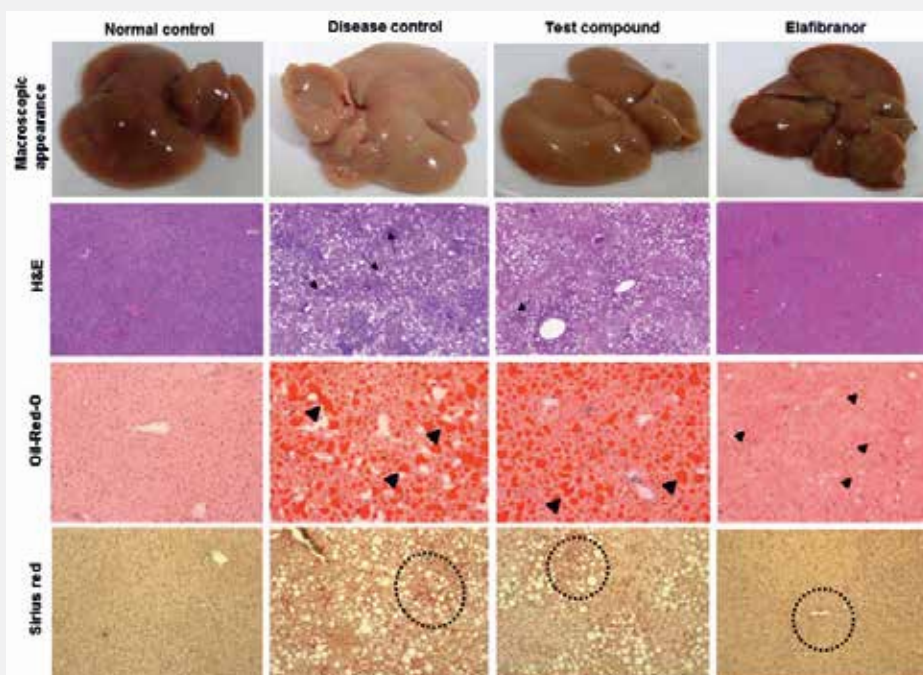
Statistical significant differences observed in liver fibrosis and NAS after 30 weeks of feeding with AMLN/GAN diet which depicts a clear disease onset.



NAS score and hepatic fibrosis were significantly increased in AMLN- NASH mice after 30 weeks on AMLN diet compared to normal chow fed animals. Animals were included in the study based on pre-study metabolic permeates (body weight ≥ 40 g, ALT (≥ 250 U/L), AST (≥ 250 U/L), blood glucose (≥ 200 mg/dl), histological assessment of NAS (≥ 6) and fibrosis score (minimum 1) and subsequently randomized into treatment groups.

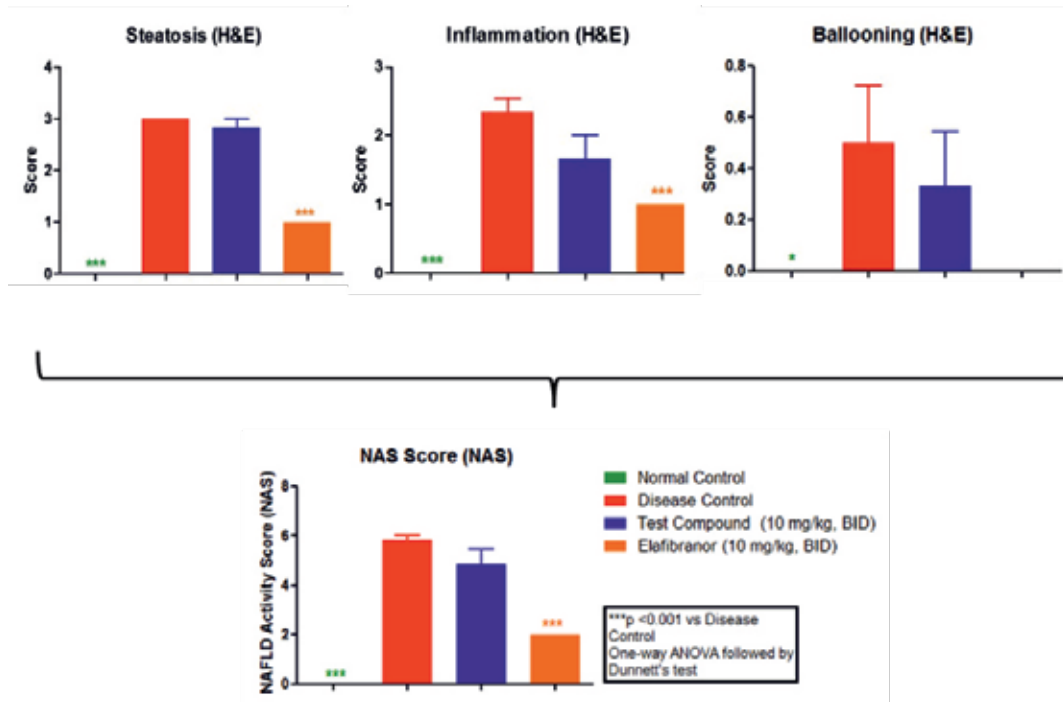
Histopathological characterization of NAS score (Treatment)

Arrow depicting inflammatory foci. Dotted circle represents fibrotic areas. Arrow head depicting Oil-Red-O stained lipid lobules



NAFLD Activity Score (NAS): Steatosis, Inflammation and Ballooning Degeneration

- Increased steatosis, lobular inflammation and ballooning were observed in disease Control group when compared with normal control.
- Elafibranor treatment significantly reduced steatosis, inflammation and a trend towards decreased ballooning, thus, exhibited reduced NAS.



Conclusion

- A special diet high in trans-fat, fructose and cholesterol induced a mouse phenotype exhibiting metabolic and histological characteristic of NAFLD and NASH.
- Pharmacological intervention with Elafibranor induced discrete metabolic and histological changes in AMLNNASH mice when compared with normal controls.
- Elafibranor significantly improved steatosis and inflammation in AMLN-NASH mice when evaluated by H&E and Oil-Red-O staining.

Let's begin the
Conversation

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