

Spectrin Bio

Developed by the GW Cancer Center

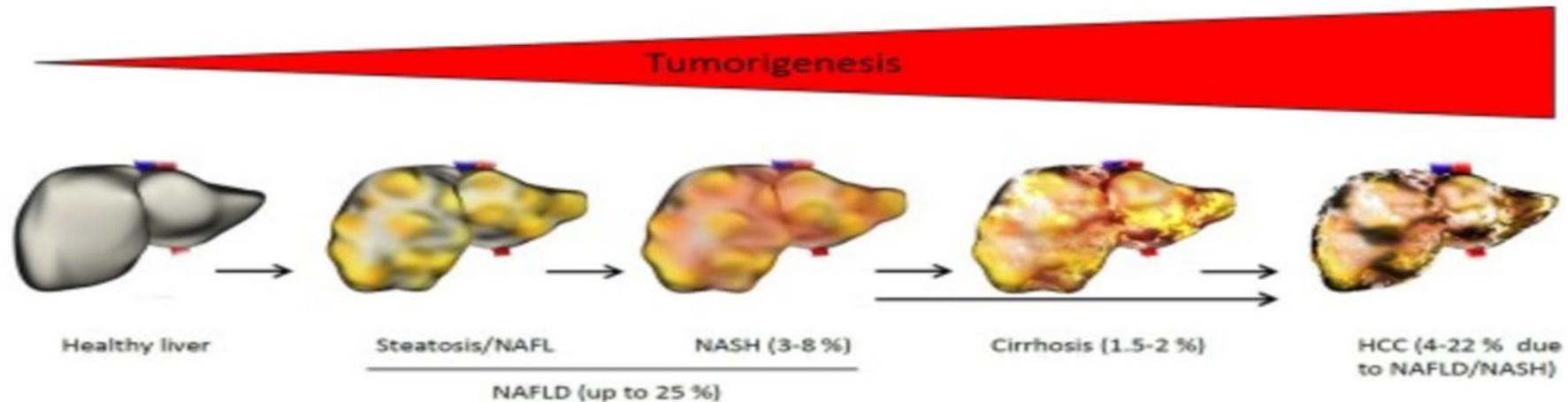
Technology Summary

- ▶ With the increase in obesity throughout the world, liver disease and obesity/nonalcoholic steatohepatitis (NASH)-related cancers are also increasing
- ▶ **Treatments are urgently needed** to prevent the progression from nonalcoholic fatty liver disease (NAFLD) to NASH and hepatocellular carcinoma (HCC)
- ▶ High fat diet (HFD) >> steatosis and fibrosis >> cancer
 - ▶ **New drug target: β -Spectrin (SPTBN1), a key player in both steatosis and fibrosis**
- ▶ Preclinical findings in mice (*in vivo*) and human 3D culture NASH model system
- ▶ siRNA therapies are already approved for diseases of the liver
 - ▶ **Trail is blazed for regulatory approval**

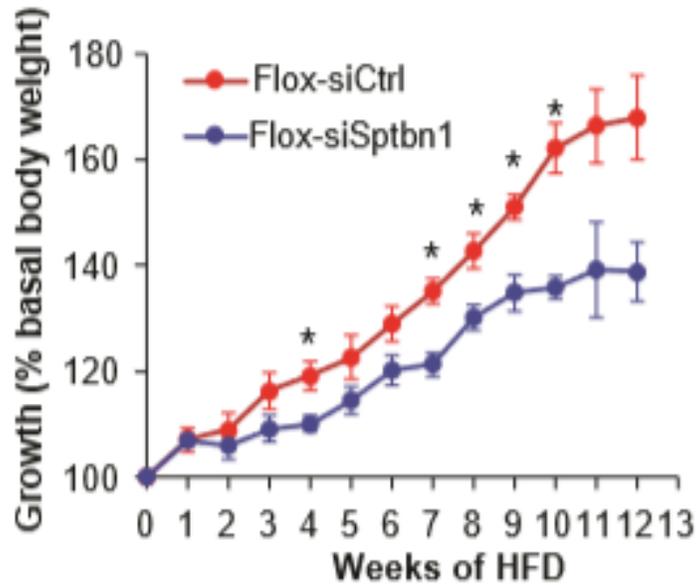
Lack of current therapies

There are no FDA-approved treatments for NAFLD or NASH

Few pipeline therapies correct both steatosis and fibrosis

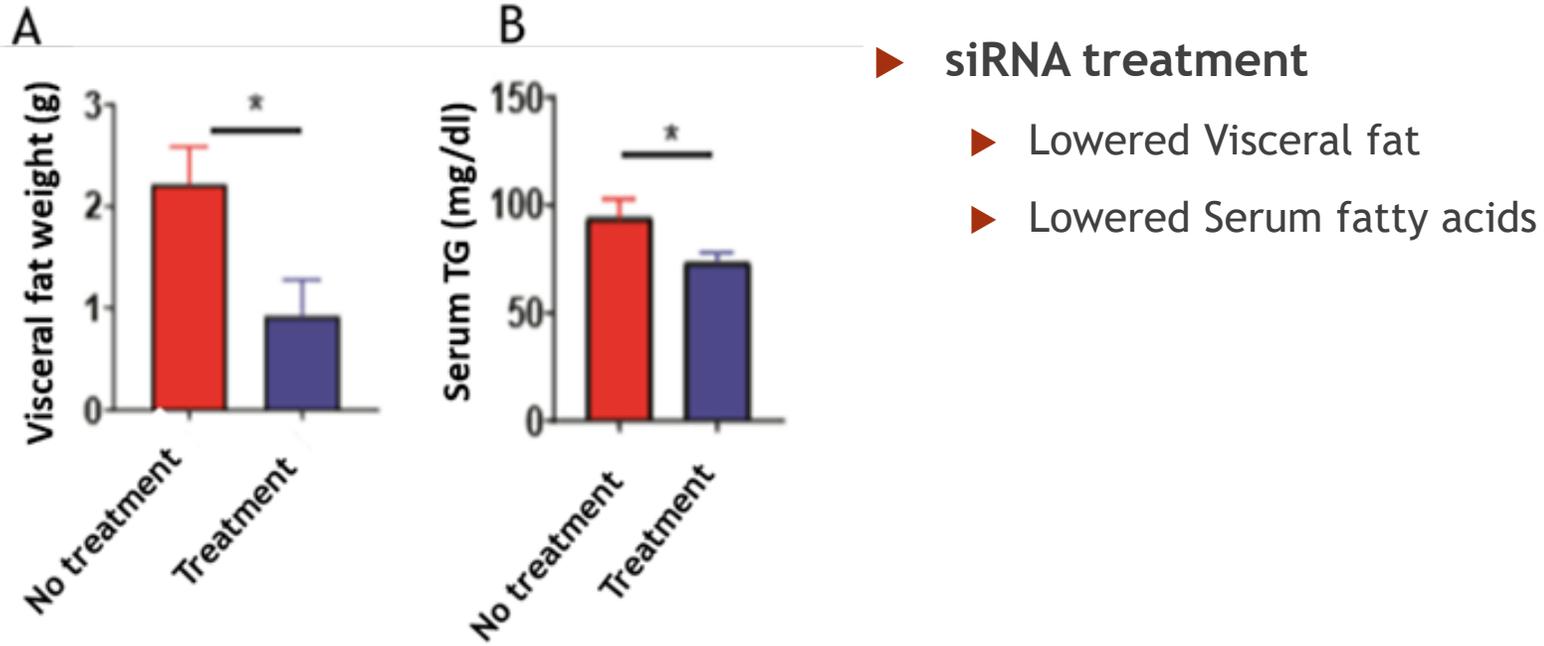


siRNA-mediated therapy protected mice from HFD-induced obesity



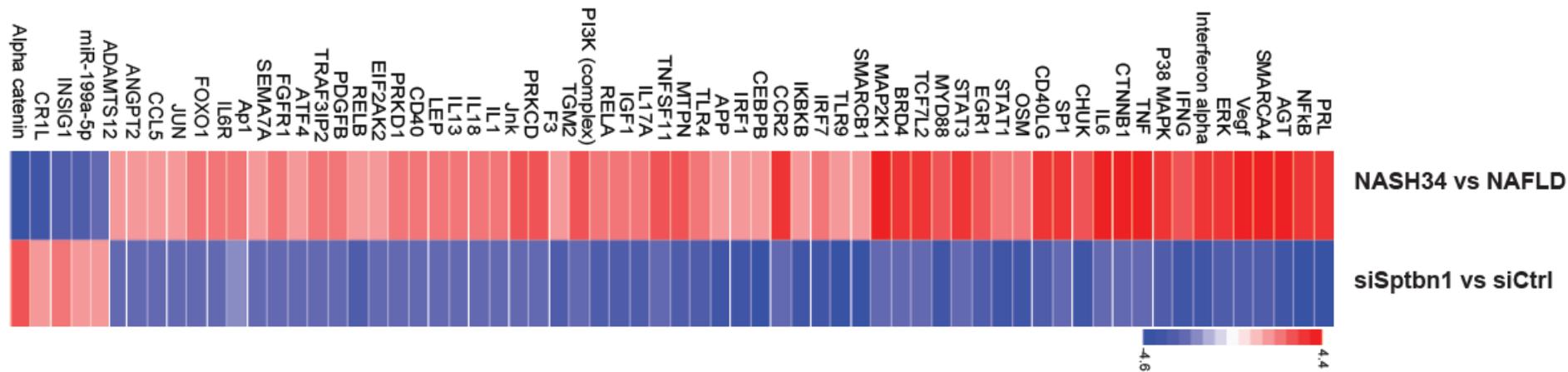
- ▶ High fat diet increased body weight
- ▶ siSptbn1 treatment reduced body weight increase

siRNA treatment during HFD lowers mouse body fat and blood triacyl glycerol (TG)



siRNA treatment of 3D human cultures reverses NASH signaling

- ▶ Regulatory gene expression profiles are different for NASH vs NAFLD
- ▶ Expression reversed with siRNA treatment
- ▶ Metabolism and inflammatory gene expression also improved



Competition

- ▶ First-line therapy for patients with NASH
 - ▶ Dietary changes and lifestyle modifications to reduce body weight
 - ▶ Body weight reduction cannot be achieved in many patients
- ▶ Drugs in Clinical trials
 - ▶ Obeticholic acid
 - ▶ Cenicriviroc

Drug Name	Outcome	Drawbacks
Elafibranor	Phase III study terminated	Not effective in NASH
Obeticholic acid (OCA)	Phase III intermediate results don't show clear benefit (accelerated NDA rejected)	Dose-dependent pruritis
Selonsertib	Phase III results not more effective than placebo	Headache, nausea and sinusitis
Cenicriviroc	Phase III active; Phase II showed antifibrotic effect, but no impact on steatohepatitis	Fatigue, diarrhea, nausea

U.S. Market Opportunity

- ▶ No current FDA-approved therapies for NAFLD and NASH
- ▶ Incidence in United States
 - ▶ NAFLD affects up to 30% to 40% of adults
 - ▶ NASH affects 3% to 12% of adults
 - ▶ Liver cancer 43,000 new cases/year
 - (5-year survival rate = 18%)
 - Portion due to hepatitis is falling due to HCV treatments
 - Portion due to obesity is increasing

The Scientist



- ▶ Lopa Mishra, M.D, Lead Scientist
- ▶ Director, Center for Translational Medicine
- ▶ Research Interest: TGF- β pathway, Liver Cancer

The ASK

- ▶ What we are looking for:
 - ▶ Serial entrepreneur with potential for CEO role
 - ▶ Investment / Financing
 - ▶ Corporate collaboration or licensing
- ▶ How far from evaluation of the technology in patients?
 - ▶ We generated a significant amount of pre-clinical *in vivo* data in mice and *in vitro* human data and human trials could begin within 1 year.

Closing

- ▶ siRNA against β -Spectrin is a promising therapeutic for obesity/NASH and related cancers
- ▶ Invention is protected by provisional patent application.
- ▶ *Mishra Bio.* team focused on translational medicine can help complete pre-clinical studies.