

The FATZO Mouse Model of Type 2 Diabetes Develops Non-Alcoholic Fatty Liver Disease (NAFLD)

Van Jackson¹, and Sandeep Sinha²,
¹PreClinOmics Inc., a Crown Bioscience Company, Indianapolis, IN; ²Crown Bioscience Inc., Santa Clara, CA

INTRODUCTION

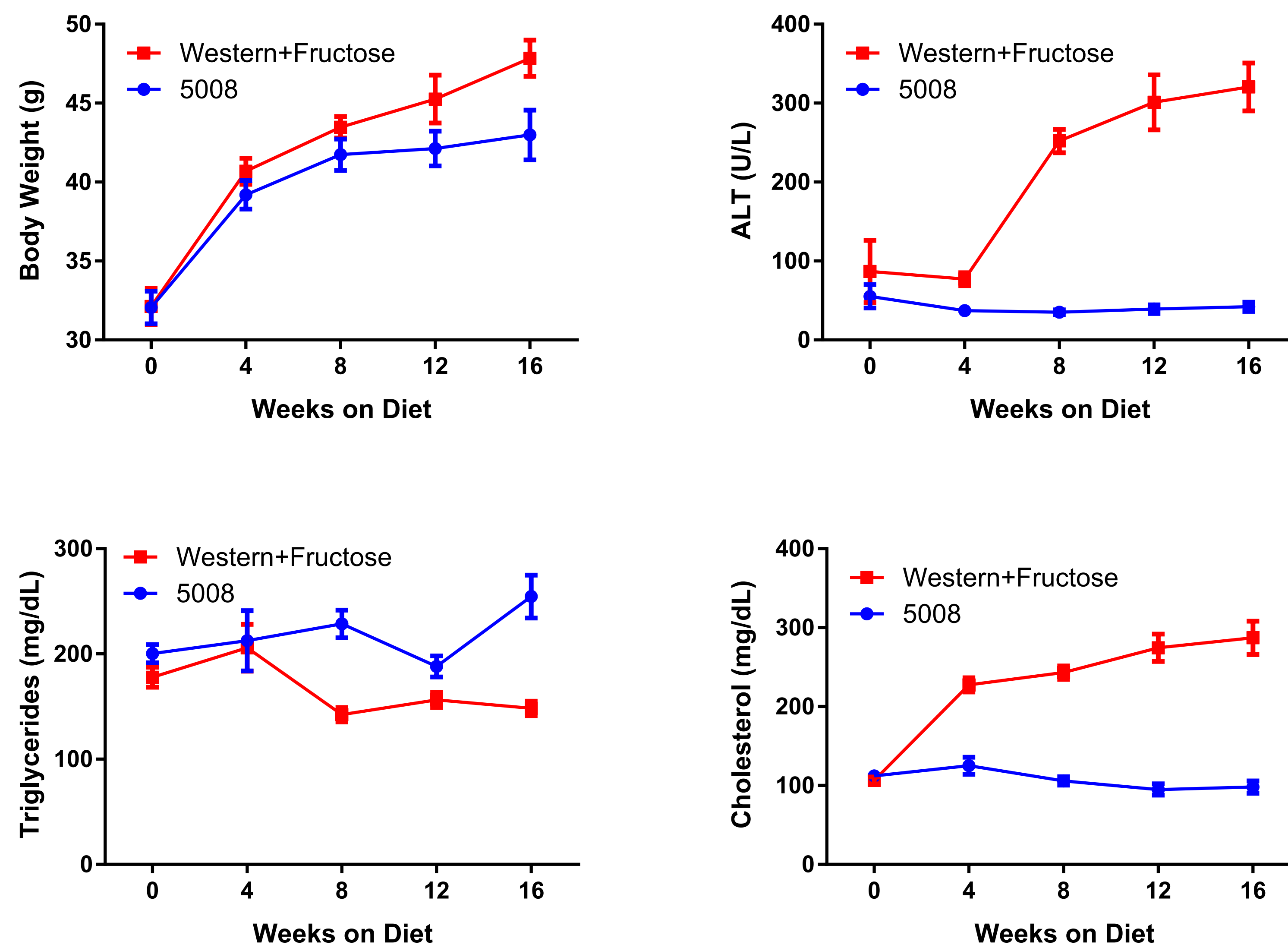
Non-alcoholic fatty liver disease (NAFLD) develops at a higher rate in obese, Type 2 diabetic individuals. There are no approved pharmacotherapies for the treatment of NAFLD or of its exacerbated form called non-alcoholic fatty liver disease (NASH). The FATZO mouse has been developed at PreClinOmics Inc., a Crown Bioscience Company, as a model of Type 2 diabetes, that spontaneously develops obesity, hyperglycemia, glucose intolerance, and insulin resistance. The purpose of this investigation was to characterize the FATZO mouse fed a Western diet supplemented with fructose in the drinking water as a potential model for NAFLD and NASH.

METHODS

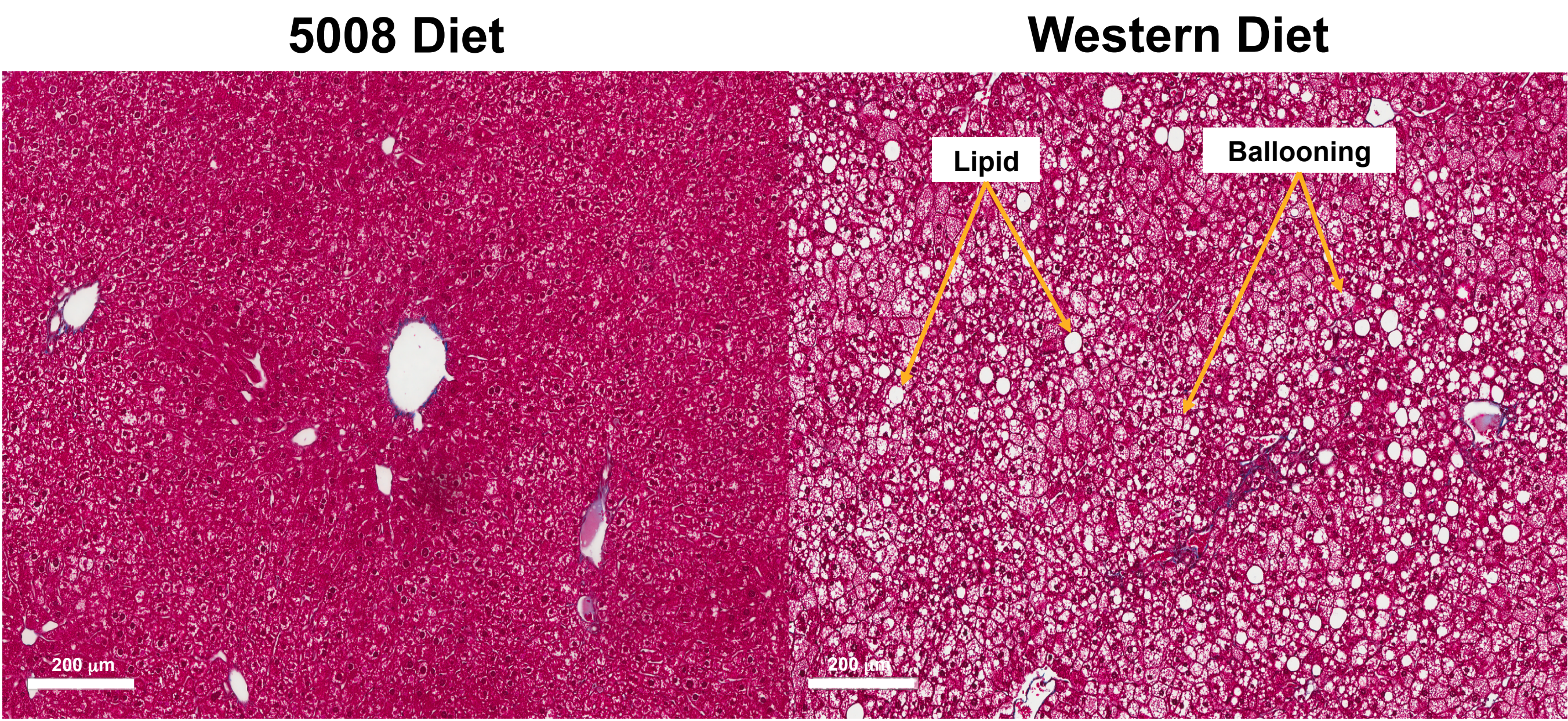
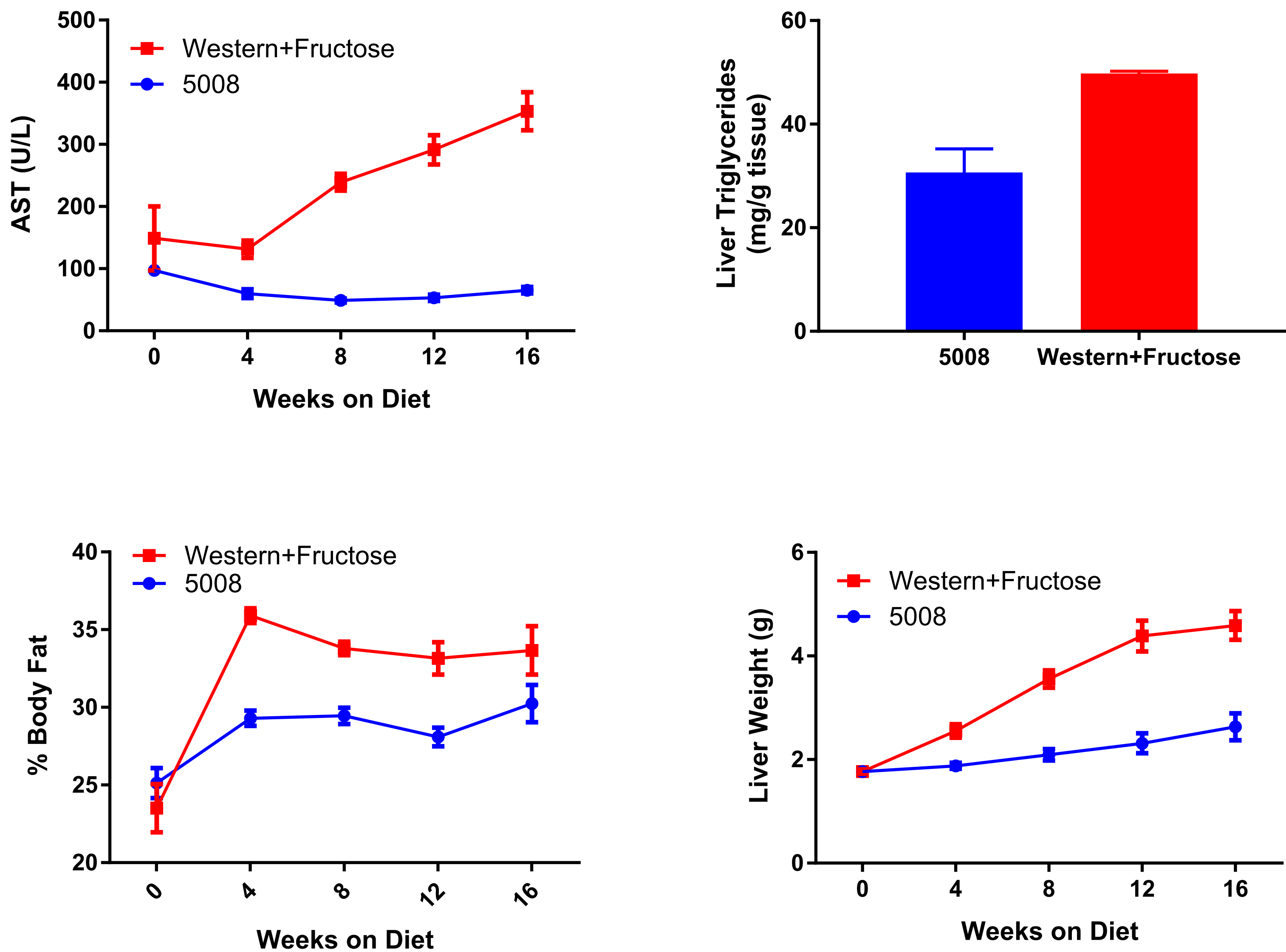
FATZO mice (n=104) at 8 weeks of age were randomized based on body weight and glucose levels into 2 groups of 48 animals each. The remaining eight animals were used to establish baseline parameters for the remainder of the study. One group was placed on a Western diet (Research Diets D12079B diet) + 5% fructose in their drinking water. The other group remained on regular Purina 5008 diet. Each month, 8 animals from each group were terminated and blood was collected via cardiac puncture for the plasma analysis of glucose, insulin, AST, ALT, cholesterol, and triglycerides. Livers were collected, weighed, and then split with one part fixed in 10% buffered formalin and the other part snap frozen in liquid nitrogen for histology and liver triglyceride determination.

All data are presented as the Mean±SEM, n=8.

RESULTS



RESULTS



4 Month Histology NASH Scoring

NASH Histology Scoring					
	Animal ID	Steatosis	Lob Inflamm	Balloon Degen	Fibrosis
5008	550345033	1	0	1	0
	550345034	2	1	3	0
	550345035	1	0	1	0
	550345036	1	0	1	0
	550345037	2	0	2	0
	550345038	2	1	3	1
	550345039	1	1	1	0
	550345040	1	0	0	0
Western	550345081	2	1	4	0
	550345082	2	1	4	0
	550345083	2	1	4	0
	550345084	2	1	4	0
	550345085	2	2	4	1
	550345086	2	1	4	1
	550345087	2	1	4	1
	550345088	2	2	4	1

SUMMARY

- The data demonstrate that the FATZO mouse develops NAFLD after 2 months on a Western diet supplemented with 5% fructose, which is maintained for up to 5 months.
- At 4 months, NASH histological scoring demonstrates steatosis, inflammation, ballooning, and early signs of fibrosis.
- Further research is needed to determine if the FATZO mouse will develop NASH and eventually hepatic cellular carcinoma.

