Study design factors to consider in diet-induced NAFLD rodent models

	High Fat Diets	High Fructose Diets	High Fat, Fructose & Cholesterol Diets	Choline Deficient High Fat Diets	Methionine and Choline Deficient Diets
Dietary modifications commonly used	• 30 – 60 kcal% fat, higher SFA increase ER stress, higher omega-6 PUFA increase oxidative stress, both increase NASH • More sucrose or fructose leads to NASH and mild fibrosis	• Usually 60 – 70 kcal% fructose drives steatosis, NASH; • The addition of sucrose (50% fructose) also effective for steatosis, NASH	• 40 kcal% fat (trans fat or SFA), 20 - 40 kcal% fructose, and 1 – 2% cholesterol • Fat type and cholesterol increases ER and oxidative stress / fibrosis • Fructose drives steatosis and inflammation	• Fat level (30 – 60 kcal% fat) • Lard commonly used; typically can drive steatosis, but prolonged feeding (6 months) can cause fibrosis	• Rapid onset of steatosis (1 week), NASH / fibrosis in 6 – 8 weeks • Addition of fat (up to 60 kcal% fat) • Fat type typically lard, butter (SFA) or corn oil (PUFA), addition of sucrose and/or cholesterol drive further NASH/fibrosis
Other metabolic effects	• Increases body weight • IR / glucose intolerance	• Increases body weight • IR / glucose intolerance • Increased plasma TG (typically rats and hamsters)	• Increases body weight • IR / glucose intolerance • Increases plasma lipids	• Increases body weight • Less IR than choline sufficient diet	• Reduces body weight but 0.1% methionine maintains weight • No IR, reduced plasma lipids
Matched Control Diet	• Low fat diet with matched level of sucrose or mostly corn starch	• Low fat diet with 60 – 70 kcal% as either glucose or corn starch	• Low fat diet with 60 – 70 kcal% as either glucose or corn starch	• Low fat diet with choline	• Methionine and choline sufficient diet