

DIET-INDUCED ANIMAL MODELS TO GENERATE INSULIN RESISTANCE AND TYPE 2 DIABETES

Objectives

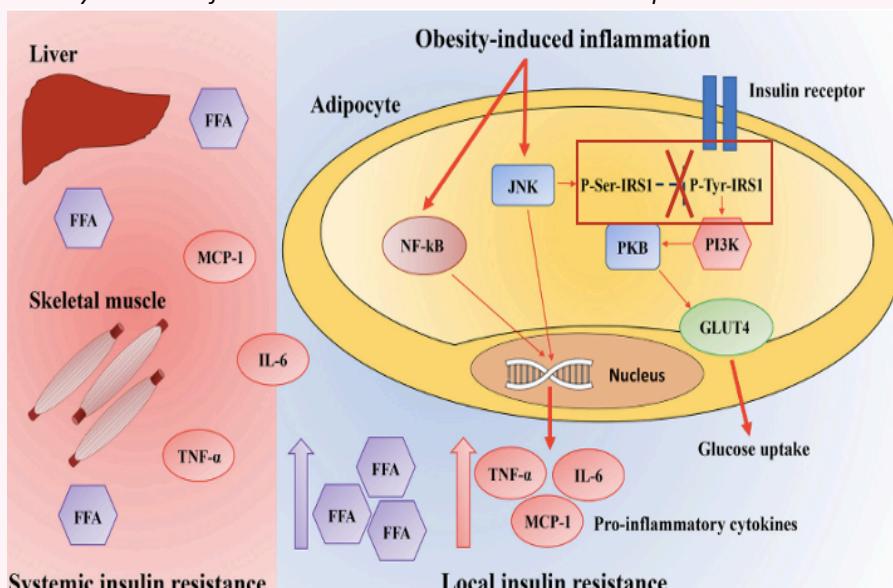
1. To review the main diets used to obtain diet-induced type 2 diabetes and insulin resistance rodent models.
2. To explain the molecular mechanisms of these diets that cause this pathology.
3. To compare the different diets and identify their benefits and disadvantages.

Table 1. Comparison of the main diets used to induce insulin resistance and type 2 diabetes in rodents

DIET	CHARACTERISTICS	ADVANTAGES	DISADVANTAGES	T2D
High-fat diet	High-fat diet Increase in dietary fat by approximately 45%	- High levels of obesity and insulin resistance - Accurate control of animal intake - Progressive development of type 2 diabetes	- Lack of standardization of fat type and fat percentage	4/5
	Very high-fat diet Increase in dietary fat by approximately 60%	- Higher and faster obesity and insulin resistance than in the high-fat diet model - Accurate control of animal intake	- Lack of standardization of fat type and fat percentage - Faster development of obesity and insulin resistance than in humans - Possible ketogenic effects that can cause opposite molecular mechanisms	3/5
High-carbohydrate diet	Isocaloric diet Replacement of dietary complex carbohydrates by simple carbohydrates (sucrose/fructose)	- Easy administration and low cost - High availability of fructose - Accurate control of animal intake	- Lower incidence of obesity and insulin resistance than the other diet models	1/5
	Hypercaloric diet Incorporation of an excess of simple carbohydrates (sucrose/fructose) into the drinking water	- Easier administration and lower cost than the isocaloric diet model - High availability of fructose - Accurate control of animal intake	- Low levels of obesity and insulin resistance	2/5
High-carbohydrate-fat diet	Cafeteria Diet <i>Ad libitum</i> diet based on ultra-processed food high in sodium, saturated fats and refined carbohydrates	- Higher incidence of obesity and insulin resistance than the other diet models - Simulates the human "Western Diet" - Hedonic hyperphagia - Development of type 2 diabetes similar to humans	- Low proteins, minerals and vitamins levels - Lack of uniformity and control of animal intake difficult to replicate and experimentally compare this diet effects	5/5

Figure 1

Obesity-induced inflammation and insulin resistance development



Note. Modified from Zatterale, F., Longo, M., Naderi, J., Raciti, G. A., Desiderio, A., Miele, C. & Beguinot, F. (2020). Chronic adipose tissue inflammation linking obesity to insulin resistance and type 2 diabetes. *Frontiers in physiology*, 10, 1607.

Conclusions

- There are specific diets that induce obesity in rodents and end up causing insulin resistance and type 2 diabetes through specific molecular mechanisms.

- Each of these diets has advantages and disadvantages, where high-fat diet is the most widely used diet and cafeteria diet is the one that best reflects human obesity and type 2 diabetes.

- These animal models are essential to study the pathophysiology of complications associated with obesity, like type 2 diabetes, and further studies are needed.