

# Establishment of a murine model of type II diabetes

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## Scientific Background:

Diabetes is the fourth leading cause of death induced by disease and its prevalence is increasing (Global prevalence: 382 millions or 8,3% of the world population in 2013 - 5,1 millions deaths per year linked to diabetes in 2013). As in most type II diabetic syndrome diseases, hyperglycemia and insulin-resistance are mainly involved. The development of hyperglycemic animal models with an insulin-resistance is an important step in the selection of new anti-diabetics therapeutics. The purpose of this study is to implement a murine model of type II diabetes to evaluate the efficacy of new anti-diabetic-therapeutics.



## Material and methods:

**Animals and nursing :** Male mice C57Bl/6Jrj

Table 1: Stain's choice.

	Benefits
Mice	Small size (cost, large numbers of animals, easy accommodation) Known genetics
C57Bl/6J	Obesity and type II diabetes easy to induce with high fat diet (HFD)
Male	Diabetes easy to induce No hormones influence

Nursing and suitable accommodation  
Bedding change twice a week (if polyuria)  
Group housing/ Enrichment  
Maintaining the health status -> ventilated unit, filtered water, manipulation under hood


## Establishment of the model:

### Induction of type II diabetes

Diet : High Fat 60% - SAFE 230HF (U8957 Version 1)

Several injections of Streptozotocin (STZ) by IP administration

Table 2: Randomization

Groups	Diet	Streptozotocin	Animal number
G1 - Control	A04 SAFE standard maintenance diet	/	4
G2 - HFD	SAFE 230HF (U8957 Version 1)	/	8
G3 - HFD-S1		3*40mg/kg	8
G4 - HFD-S2		5*40mg/kg	8



Picture 1: Weight difference between groups G1 and G2

## Clinical characterization of the model:

- General health, hydration – following 6 months
- Behavior
- Weight Monitoring – once a week

## Biochemical characterization of the model :

- Blood glucose and insulin levels
- Oral test glucose at D 179
- Last fasting during 6H
- IP administration at T0 – Glucose 30% - 2g/kg
- Blood glucose level : T-15min, T+15min, T+30min, T+1H, T+1H30, T+2H
- Confirm insulin-resistance

Table 3: Biochemical characterization of diabetes

Diabetes	Blood glucose level	Blood insulin level
Type II diabetes	Increased G > 250mg/dL	Normal or Increased
Type I diabetes	Increased G > 250 mg/dL	decreased
Compensated insulin-resistance	Normal	Increased

## Results:

Figure 1: Body weight (g)

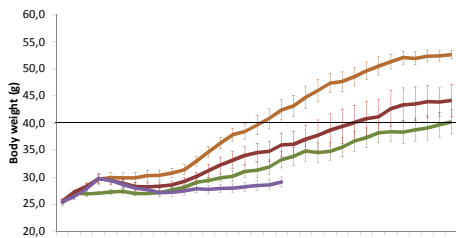


Figure 2: Blood glucose level (mg/dL)

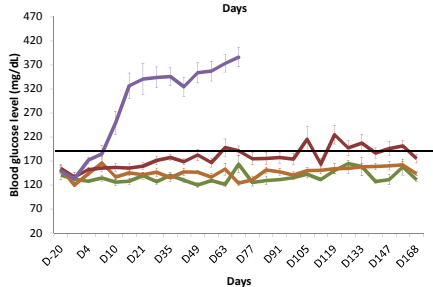


Figure 3: Blood insulin level (ng/mL)

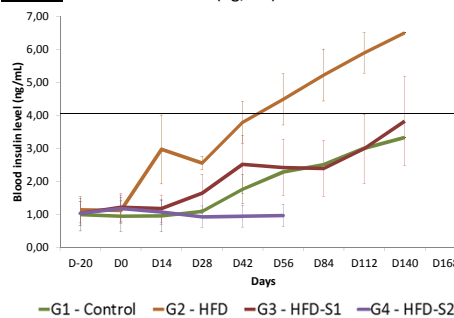
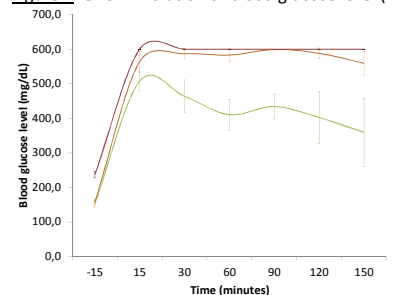


Figure 4: OTG – Evolution of blood glucose level (mg/dL)



## Discussion & Conclusion:

Feeding with High fat diet during 70 days induced obesity and insulin-resistance in all mice in the G2 group but no mice developed type II diabetes. However, obese mouse model with a stable insulin-resistance was developed without mortality or morbidity. This obesity and insulin-resistance are characteristics of a pre-diabetic stage in human type 2 diabetes. This new model could also be used to experiment several human therapies for this endocrinopathy condition.

Moreover, to experiment different treatments using human cells of the diabetic patient, a murine model of insulin-resistance with obese mouse is under development. Athymic nude mice (Strain C57BL/6J), prone to obesity and induction of type 2 diabetes, will be used to develop this new model.



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