DELETION OF ACE2 GENE IMPAIRS GLUCOSE HOMEOSTASIS IN NOD MICE

Heleia Roca Ho[1]; Marta Riera[1]; Marta Rebull[1]; Julio Pascual[1,2]; MªJosé Soler[1,2]

[1]IMIM (Hospital del Mar Medical Research Institute), Barcelona. [2]Department of Nephrology, Hospital del Mar, Barcelona.

INTRODUCTION

- Angiotensin converting enzyme 2 (ACE2) acts as a negative regulator enzyme of renin angiotensin system (RAS) activation[1].
- ACE2 has been shown to play an important role in diabetic nephropathy [2].
- The non-obese diabetic (NOD) mice is a strain which spontaneously develops autoimmune diabetes, mimicking type 1 diabetes (DM1) in human[3].
- We have crossed in our lab C57BL/6 mice carrying an ACE2 deletion (ACE2ko) with NOD mice for generating the new NODACE2ko mouse strain.

OBJECTIVE

- The aim of this study is to determine **ACE2 knockout effects on glucose homeostasis in animals of NOD strain** as compared to wild-type NOD mice.

METHODS

- To asses glucose homeostasis intraperitoneal glucose tolerance test (IPGTT) was performed in female mice at 12 and 16 weeks of age. Animals were fasted overnight and glucose dose of 2g/kg of body weight was injected intraperitoneally. Tail blood glucose was then analysed at 0, 15, 30, 60 and 120 minutes after injection using glucometer (Accu-check, Roche). Results are expressed as mg of glucose/dL of blood (mg/dL).
- Intraperitoneal insulin tolerance test (IPITT) was also performed in same mice. Animals were also fasted 5h the day after and insulin dose of 0.75U/kg of body weight was injected intraperitoneally. Tail blood glucose was measured at 0, 15, 30, 60 and 120 minutes after injection using a glucometer. Results are expressed as percentage of glucose at time 0.

CONCLUSIONS

- **Female NODACE2ko mice exhibit impaired blood glucose tolerance, present lower body weight and higher insulin sensitivity** as compared to NODACE2wt control mice.
- Our results suggest that **deletion of *ace2* gene impairs glucose homeostasis** in the experimental model of DM1 NOD mice at 12 and 16 weeks of age.

RESULTS

IPGTT BODY WEIGHT

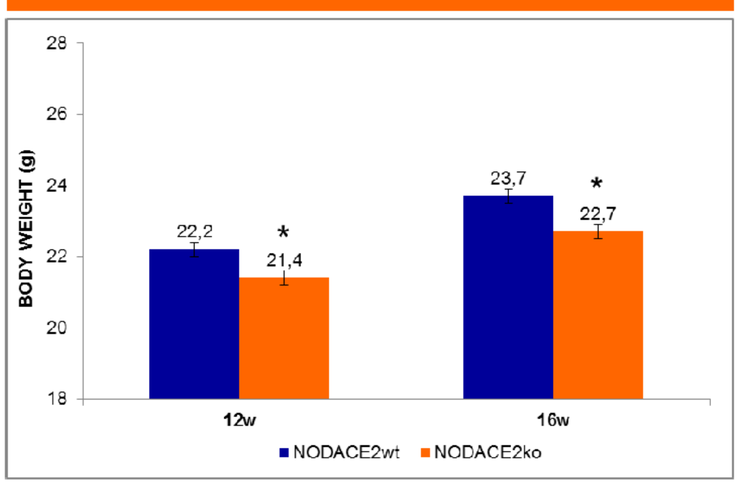

Figure 1.- Body weight in NODACE2wt and NODACE2ko after long fasting. After an overnight fasting, NODACE2ko mice showed significant lower body weight as compared to NODACE2wt mice at 12 and 16 weeks of age ($p<0.05$).

IPITT BODY WEIGHT

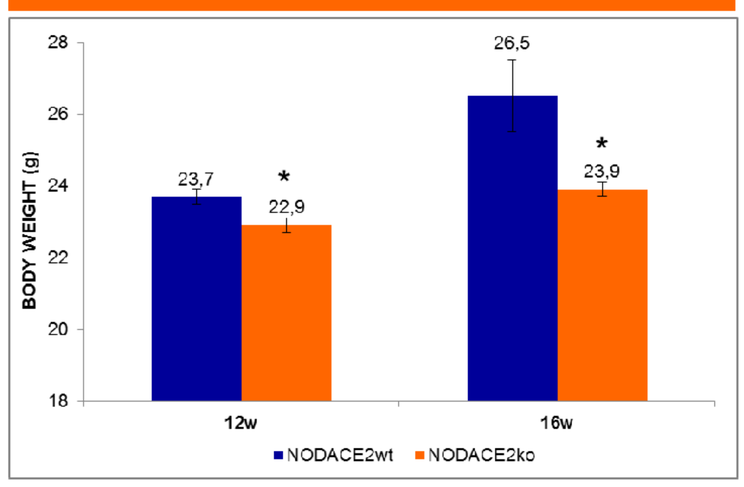

Figure 2.- Body weight in NODACE2wt and NODACE2ko after short fasting. After 5 hours fasting, NODACE2ko mice showed significant lower body weight as compared to NODACE2wt mice at 12 and 16 weeks of age ($p<0.05$).

IPGTT AT 12 WEEKS OF AGE

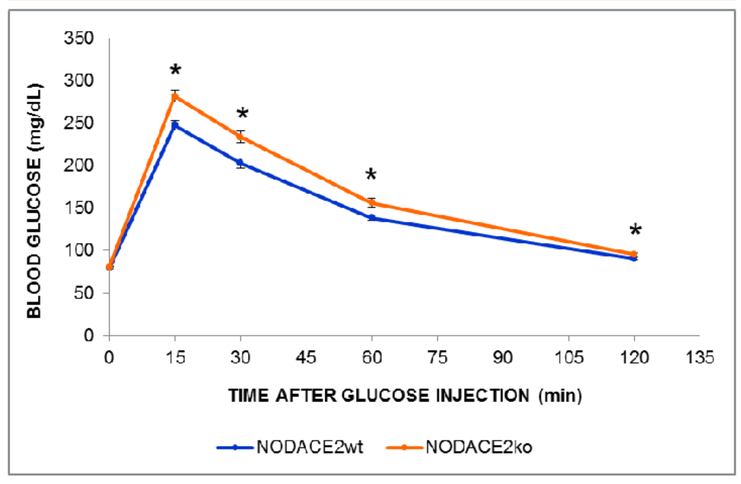

Figure 3.- IPGTT blood glucose curves at 12 weeks of age. NODACE2ko mice showed significant higher blood glucose as compared to NODACE2wt mice at 15, 30, 60 and 120 minutes after glucose injection at 12 weeks of age ($p<0.05$).

IPGTT AT 16 WEEKS OF AGE

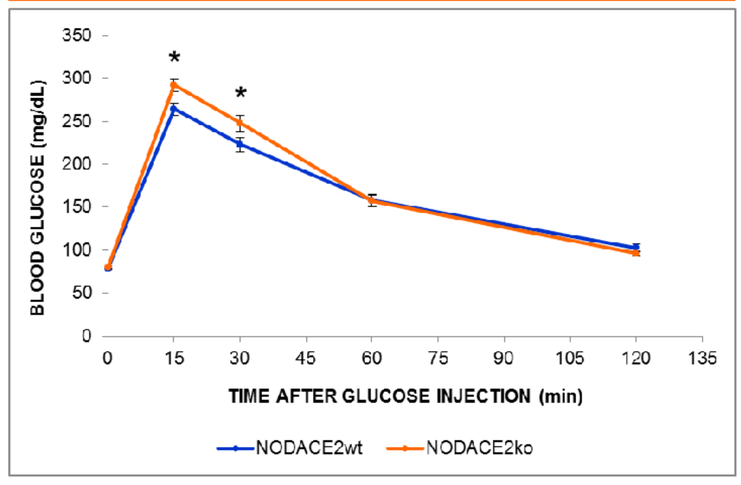

Figure 4.- IPGTT blood glucose curves at 16 weeks of age. NODACE2ko mice showed significant higher blood glucose as compared to NODACE2wt mice at 15 and 30 minutes after glucose injection at 16 weeks of age ($p<0.05$).

IPITT AT 12 WEEKS OF AGE

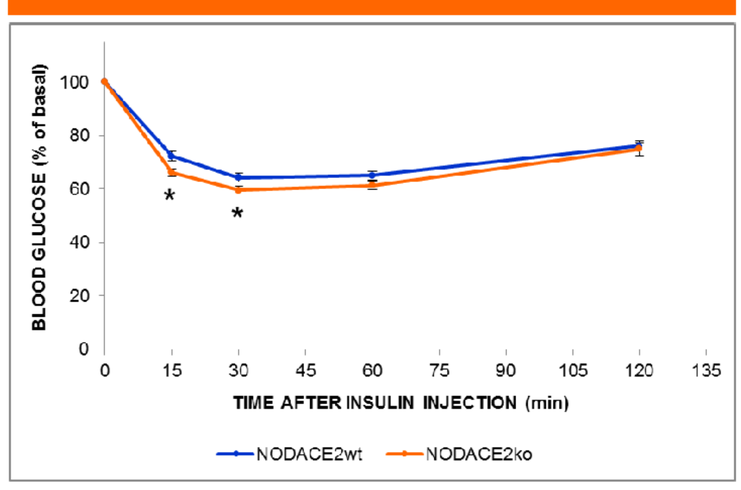

Figure 5.- IPITT blood glucose curves at 12 weeks of age. NODACE2ko mice showed significant lower blood glucose as compared to NODACE2wt mice at 15 and 30 minutes after insulin injection at 12 weeks of age ($p<0.05$).

IPITT AT 16 WEEKS OF AGE

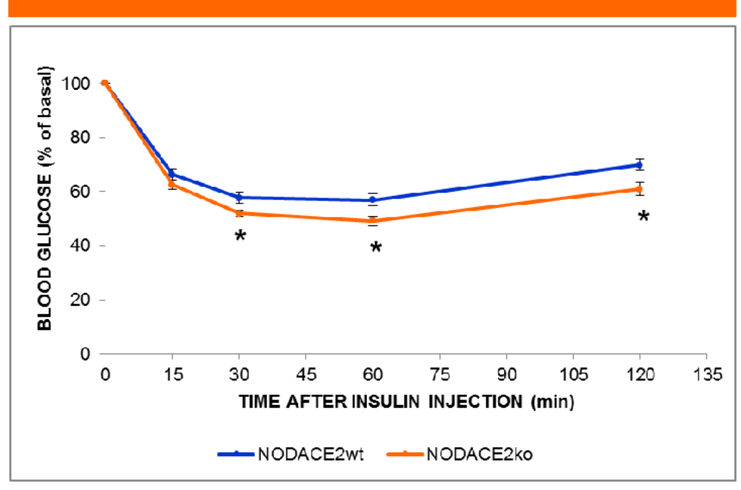

Figure 6.- IPITT blood glucose curves at 16 weeks of age. NODACE2ko mice showed significant lower blood glucose as compared to NODACE2wt mice at 30, 60 and 120 minutes after insulin injection at 16 weeks of age ($p<0.05$).

REFERENCES/BIBLIOGRAPHY

(1) Bindom SM , Lazartigues E . The sweeter side of ACE2: physiological evidence for a role in diabetes . Mol Cell Endocrinol . 2009 ; 302 : 193 – 202 .

(2) Oudit GY, Liu GC, Zhong J, Basu R, Chow FL, Zhou J, et al. Human recombinant ACE2 reduces the progression of diabetic nephropathy. Diabetes. 2010;59: 529–538.

(3) Makino S, Kunimoto K, Muraoka Y, *et al.* Breeding of a non-obese, diabetic strain of mice. Jikken Dobutsu 1980; 29: 1–13.

52 ERA

464--FP

K1) Diabetes - Basic research.

Heleia Roca-Ho

DOI: 10.3252/pso.eu.52era.2015

ePosters supported by F. Hoffmann- La Roche Ltd.