CIRCULATING ACE AND ACE2 ARE INCREASED IN THE NOD DIABETIC MICE

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INTRODUCTION

- It has been previously demonstrated that renin-angiotensin system (RAS) blockade delays chronic kidney disease progression and, thus, RAS is known to play a key role in diabetic nephropathy[1].
- In this sense, we work with the non-obese diabetic (NOD) mice, a strain which spontaneously develops autoimmune diabetes, mimicking type 1 diabetes in human[2,3].
- RAS in NOD mice remains not well described.

OBJECTIVE

- The aim of this study is to characterize the **enzymatic activities of angiotensin converting enzymes (ACE and ACE2) in the NOD strain** as compared to their respective control, the non obese resistant (NOR) strain.

METHODS

- At the end of the study, serum, kidney, lung, heart, liver and pancreas tissues were obtained from diabetic NOD mice (at 40 days of diabetes) and non diabetic NOR mice, and stored at -80ºC.
- Then sections of each tissue were homogenized using a buffer containing boric acid and HEPES for ACE and ACE2 extraction, respectively.
- Enzymatic activities of ACE and ACE2 were performed in mentioned samples of NOD and NOR mice, by using fluorimetric assays [4,5,6].
- Results are expressed in relative fluorescence units (RFU) related to micrograms of protein or microliters of serum, according to the studied tissue.

RESULTS

CHARACTERISTICS OF THE STUDIED GROUPS

	40days of diabetes	
	NOR	NOD
N of study	8	7
Blood glucose (mg/dL)	138.8 ± 4.82	560.6 ± 32.9 *
Body weight (g)	28.67 ± 0.72	17.2 ± 0.49 *
Right kidney weight (g)	0.147 ± 0.01	0.136 ± 0.01
Kidney weight/body weight ratio	0.01 ± 0.0006	0.015 ± 0.009 *
Albumin/creatinin ratio (ug/mg)	22.03 ± 4.43	184.4 ± 49.9 *

Table1.- Blood glucose (mg/dL), right kidney/body weight ratio (%) and albumin/creatinin ratio (µg/mg) were increased in NOD diabetic mice as compared to NOR. Body weight (g) was decreased in NOD as compared to NOR (p≤0.05)

ACE AND ACE2 ACTIVITIES IN SERUM

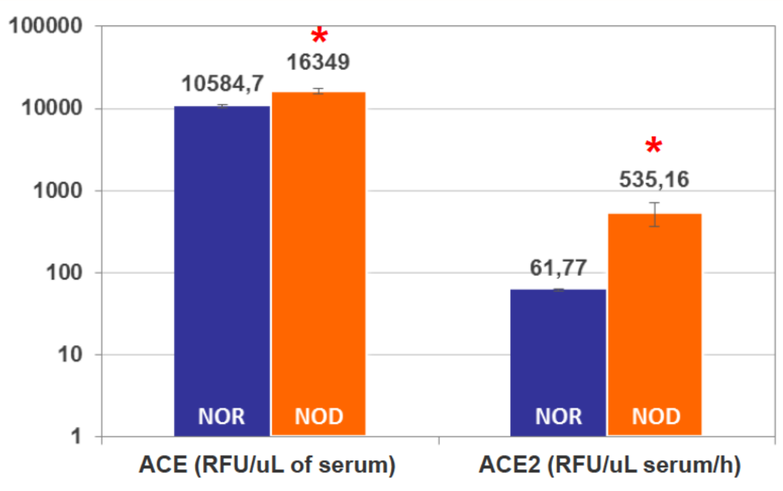

Figure 1.- Circulating ACE and ACE2 activities were increased in serum from NOD mice as compared to NOR (p≤0.05)

ACE AND ACE2 ACTIVITIES IN KIDNEY

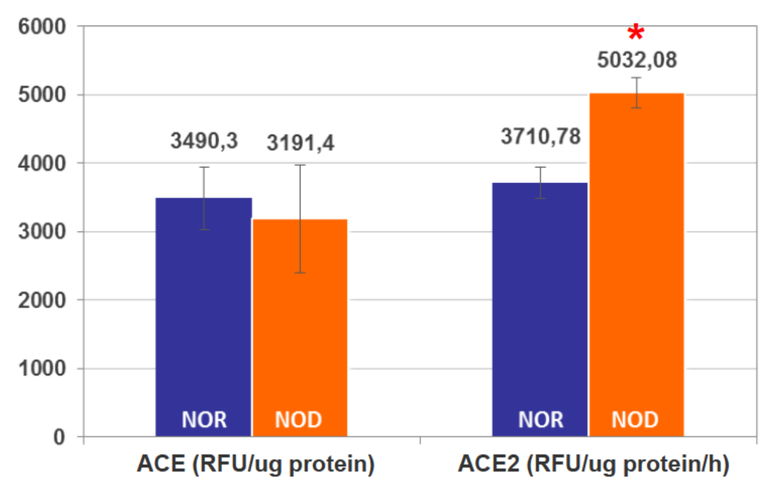

Figure 2.- Renal ACE2 activity was significantly increased in NOD mice as compared to NOR controls (p≤0.05)

ACE AND ACE2 ACTIVITIES IN LUNG

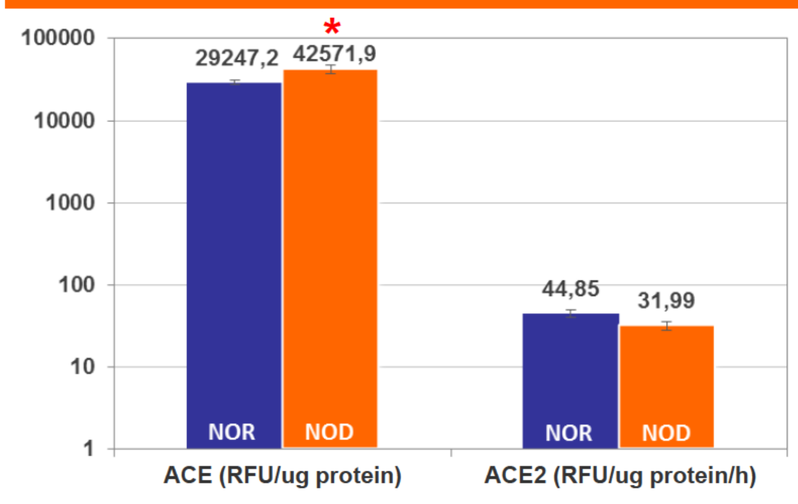

Figure 3.- Lung ACE activity was significantly increased in NOD diabetic mice as compared to NOR (p≤0.05)

ACE AND ACE2 ACTIVITIES IN HEART

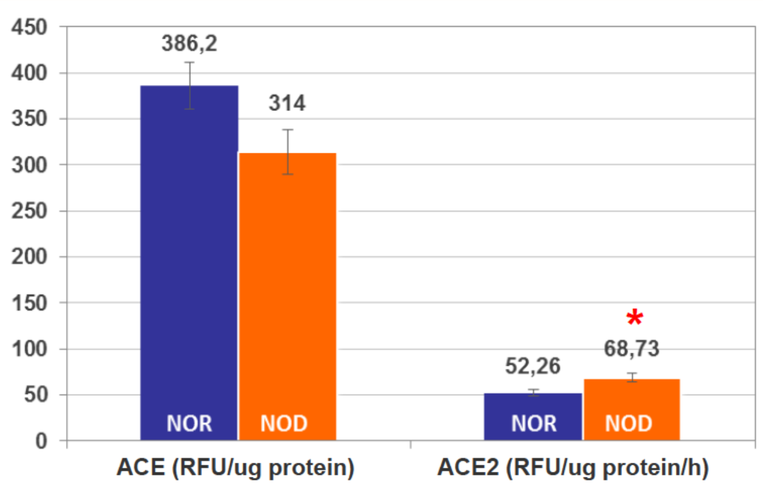

Figure 4.- Cardiac ACE2 activity was significantly increased in NOD mice as compared to NOR (p≤0.05)

ACE AND ACE2 ACTIVITIES IN LIVER

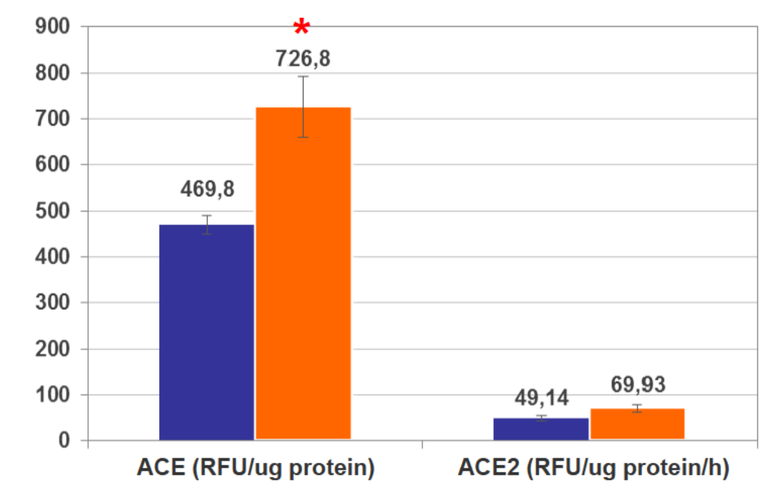

Figure 5.- Liver ACE activity was significantly increased in diabetic NOD mice as compared to NOR (p≤0.05)

ACE AND ACE2 ACTIVITIES IN PANCREAS

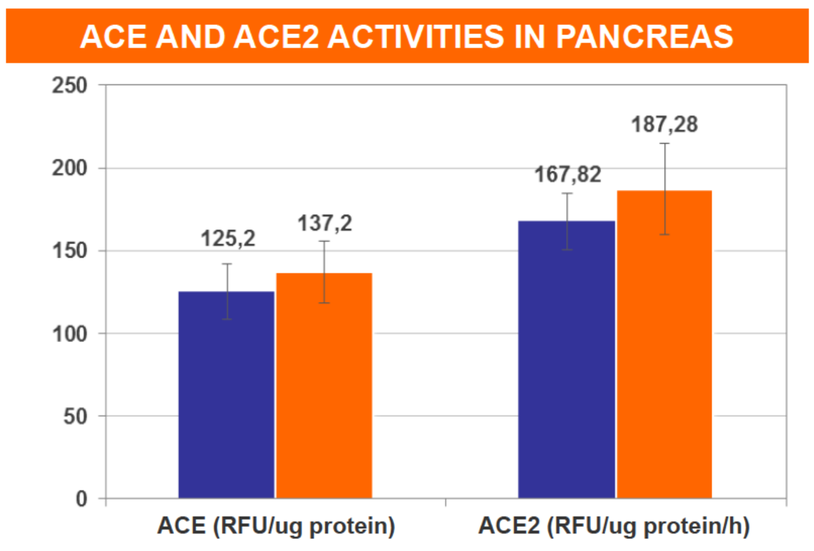

Figure 6.-No significant differences were observed in ACE neither ACE2 enzymatic activities in pancreas among the studied groups (p≤NS)

CONCLUSIONS

- **Circulating ACE and ACE2 activities are increased in NOD** diabetic mice.
- Whereas ACE2 is also increased in kidney and heart, ACE is increased in lung and liver.
- These results showed that **ACE and ACE2 are modulated in diabetic NOD mice**.
- In addition, our results suggest that **circulating ACE and ACE2 might be produced in different tissues**.

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