THE EFFECT OF GLUCAGON-LIKE-PEPTIDE-1 AND VITAMIN D ON JAK-STAT PATHWAY IN DB/DB MICE AND IN ENDOTHELIAL CELLS EXPOSED TO A DIABETIC-LIKE ENVIRONMENT

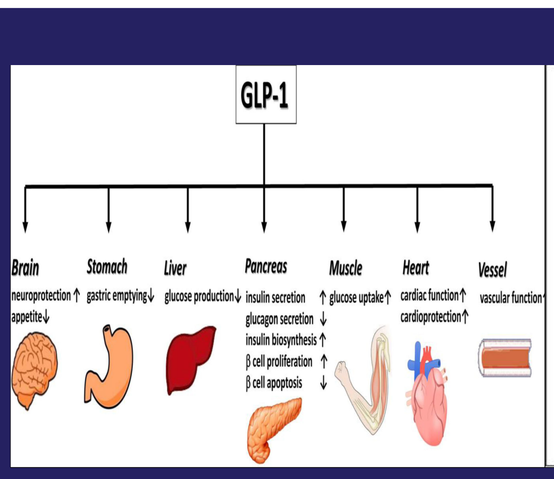
Tali Zitman-Gal[1], Nora Plotkin[1], Meital Ohana[1], Yael Einbinder[1], Sydney Benchetrit[1,2]

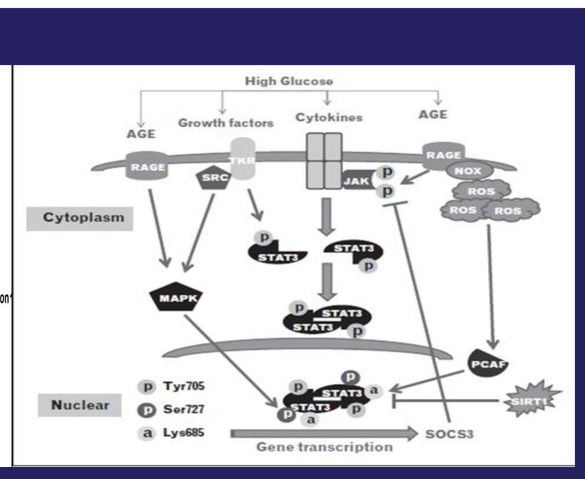
[1] Renal Physiology Laboratory, Department of Nephrology and Hypertension, Meir Medical Center, Kfar Saba, Israel

[2] Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

BACKGROUND

Diabetes mellitus is the rising cause worldwide of micro and macrovasculopathies. High levels of glucose and AGEs are involved in the pathogenesis of the vasculopathies. GLP-1, an incretin hormone improves glycemic control by increasing glucose-stimulated insulin release. The JAK/STAT proteins mediate the actions of many cytokines, hormones, and growth factors critical to cell proliferation, differentiation, migration, and apoptosis.

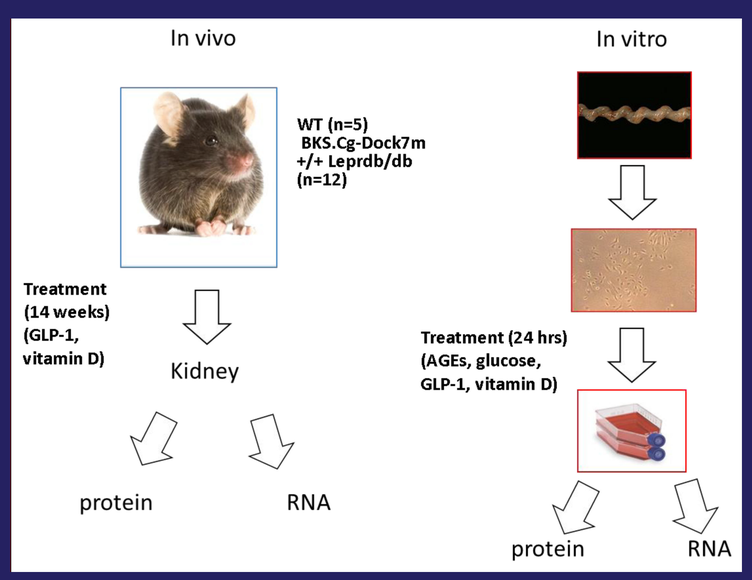




AIMS

- To determine in vitro in endothelial cells the effect of a diabetic-like environment on the JAK-STAT pathway, and to assess the involvement of the JAK-STAT in an animal model of diabetic nephropathy (db/db mice)
- To assess the potential effect of GLP-1 analogue and vitamin D on the JAK-STAT pathway.

METHODS



RESULTS IN VIVO

Figure 1: Effect of GLP-1 and vitamin D (vitD) on protein expression of p-STAT3 (ser 727) and p-STAT3 (tyr 705) in db/db mice kidney

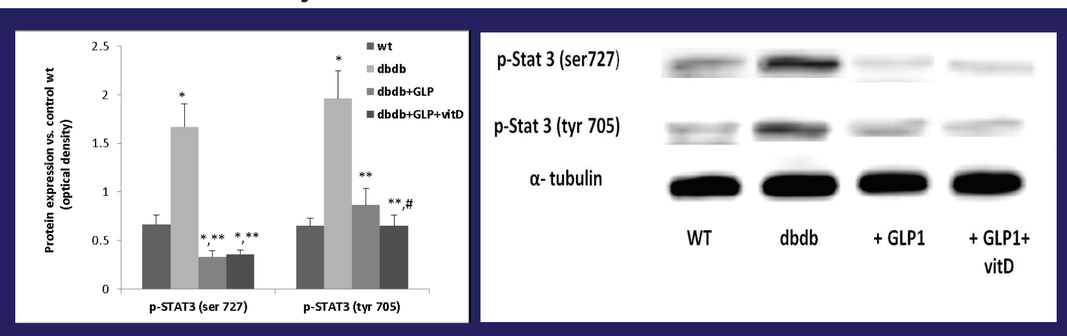


Fig. 1: (A) Densitometric analysis. Data are expressed as mean ± SE of 4 independent experiments. (B) western blot analysis. The level of α-tubulin is shown as a loading control. *p<0.05 compared with WT control group; **p<0.05 compared with db/db group; # p<0.05 compared with db/db + GLP group.

RESULTS IN VITRO

Figure 2: Effect of GLP-1 and vitamin D (vitD) on protein expression of p-STAT3 (ser 727) and p-STAT3 (tyr 705) HUVEC stimulated with diabetic like environment (250mg/dl glucose, 200µg/ml AGE-HSA)

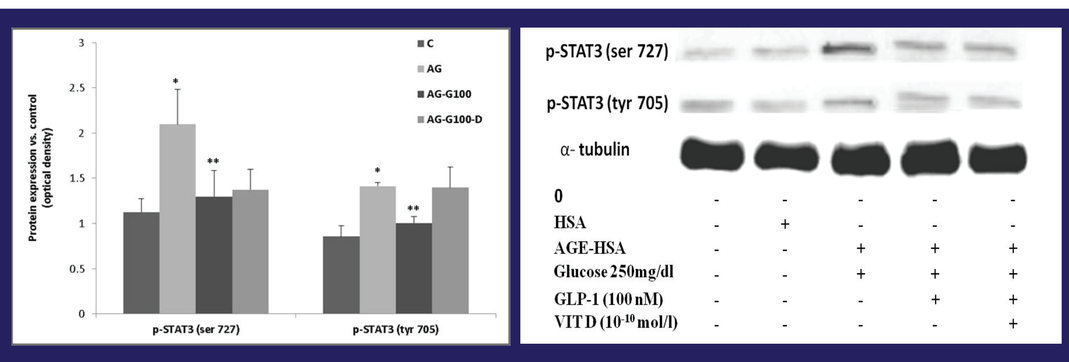


Fig. 2: (A) Densitometric analysis. Data are expressed as mean ± SE of 4-5 independent experiments. (B) Western blot analysis. The level of α-tubulin is shown as a loading control. *p<0.05 compared with C (control group -HSA); **p<0.05 compared with AG (AGE-glucose)

SUMMARY

- Activation of the JAK-STAT pathway appears to have a role in experimental models of diabetes mellitus.
- The GLP-1 analog inhibited STAT3 expression in db/db mice and in in vitro EC culture at the level of protein expression.
- Vitamin D supplementation provided additional benefit effect in db/db mice. No additional effect in vitro.

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Diabetes - Basic research.

Tali Zitman-Gal

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