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Annexin A1 deficiency increases liver damage and metabolic alterations in mice with type I diabetes

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INTRODUCTION & AIM

Diabetes mellitus (DM) is a global public health issue causing systemic dysregulations, including severe liver complications. Type 2 diabetes (DM2) patients show elevated annexin A1 (AnxA1) levels, and in murine DM2 models, AnxA1 mitigates insulin resistance effects like hepatosteatosis. However, its role in DM1 is underexplored. This study investigates AnxA1's role in hepatocyte biology in a streptozotocin (STZ)-induced DM mouse model.

METHOD

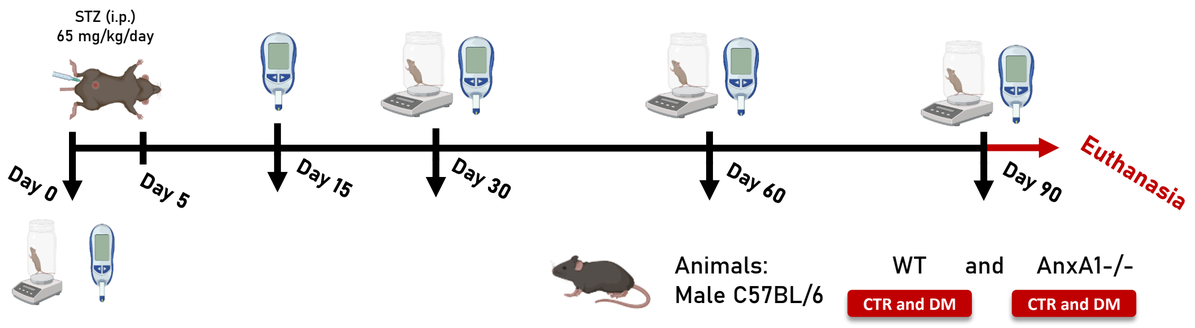


Figure 1. Experimental model of induction of type I diabetes mellitus by STZ in wild-type and AnxA1 knockout mice (Figure by the author).

RESULTS & DISCUSSION

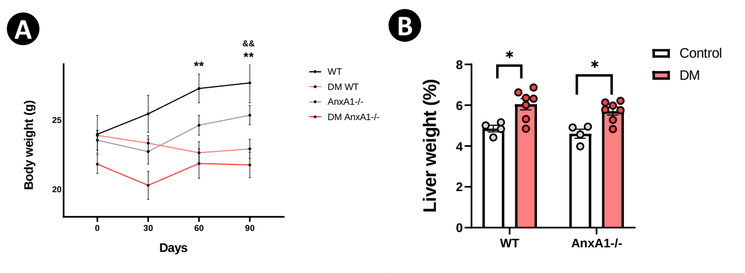
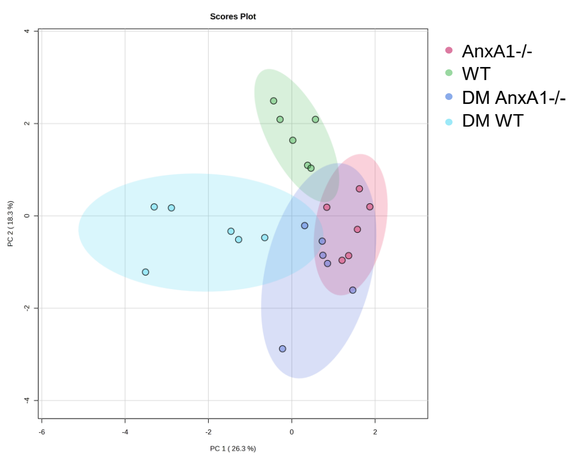


Figure 2 Analytical patterns of the animals and liver in the experimental diabetes model. Scale bars: A. 1cm. A-C: Data represent the mean ± SEM of liver weight (%), body weight (g) and glycemic levels (mg/dL). The dots in the bar graphs represent individual animals (n = 6-7/group). (*p< 0,05; **p< 0,01; ****p< 0,001 vs CTR WT; &&&& p< 0,0001 vs CTR AnxA1-/-; #### p< 0,0001 vs DM AnxA1-/-. Two-way ANOVA with Bonferroni post-test in A-C).



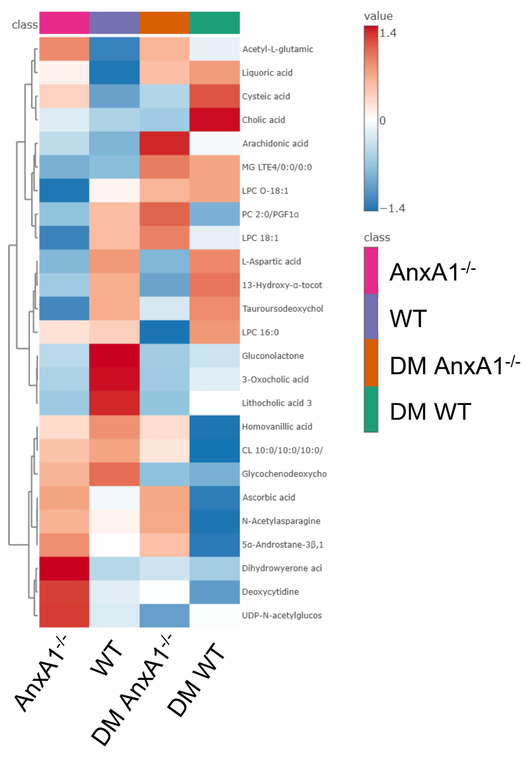
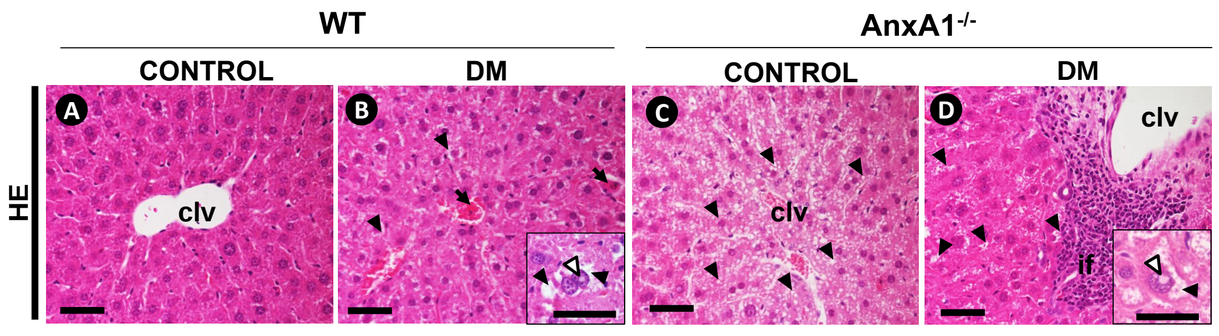


Figure 3. Metabolomic analysis, showing a change in the profile of diabetic animals. PCA analysis, indicating a reduction in the dimensionality of the data; and heatmap of the metabolic profile, indicating a change between the control and diabetic groups, of both genotypes (p<0,05, One-Way ANOVA with Tukey post-test).



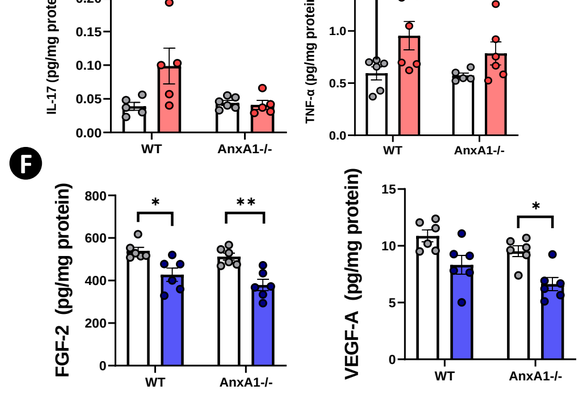


Figure 4. Morphology, cytokine profile and fibrotic markers in the liver. A-D. Morphology of liver; E. Levels of the cytokines IL-10, IL-17, TNF-a and MCP-1. F Levels of FGF-2, VEGF-A and the isoforms of TGFβ1 and 3. Data represent the mean ± SEM of pg/mg of protein (*p < 0.05; **p < 0.01; two-way ANOVA with Bonferroni post-test).

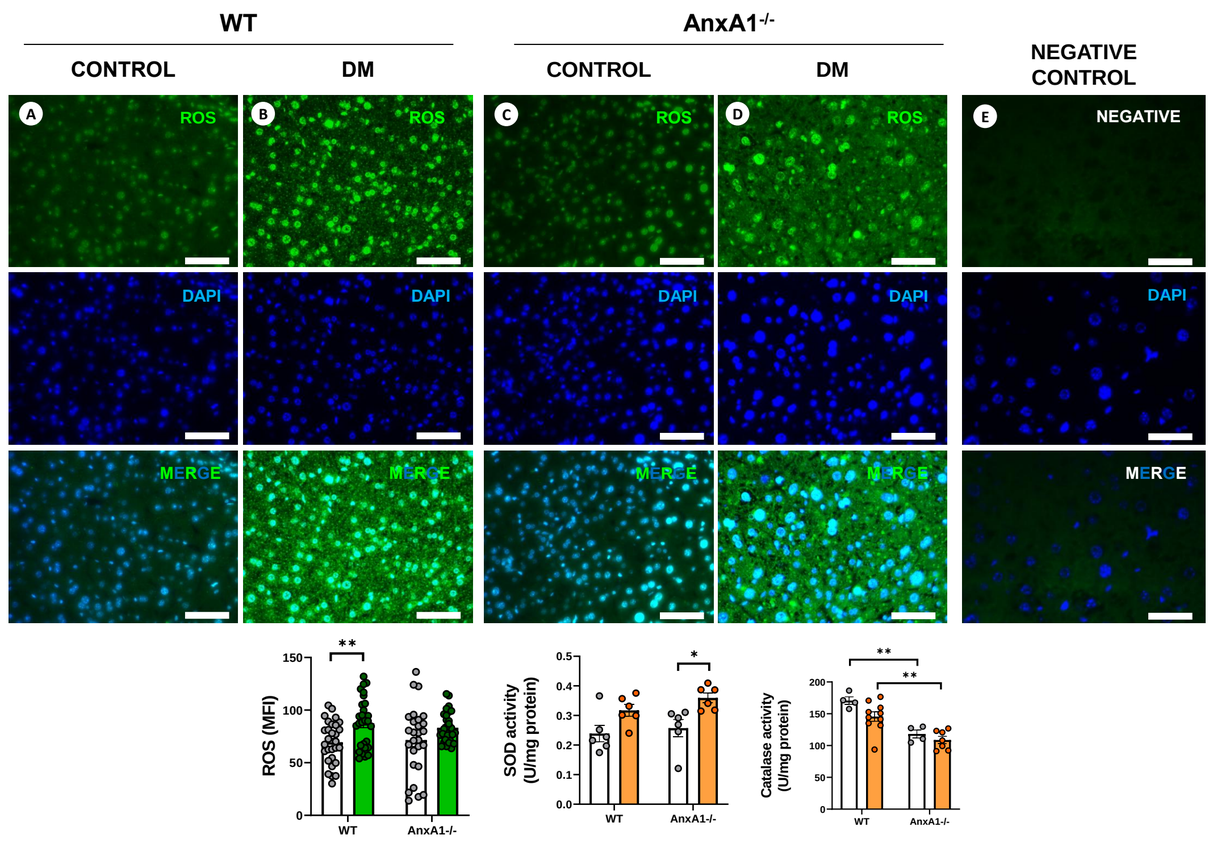


Figure 5. Analysis of oxidative stress in the liver. A-F: Increase in ROS fluorescence intensity is observed in the nuclei of hepatocytes from diabetic animals, both AnxA1+/+ and AnxA1-/-. G. SOD and Catalase activity of liver. Scale bar: 100µm. Data represent mean ± SEM of SOD and catalase activity (U/mg protein) (*p < 0,05; **p < 0,01; Two-Way ANOVA with Bonferroni's post-test).

CONCLUSION

AnxA1 seems to play a crucial role in the metabolic regulation of lipids and glucose, so it is possible to say that AnxA1 deficiency promotes an increase in the alterations caused by diabetes.

FUNDING

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