Ole-d ρ staining of cardiac samples

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Is low ATM protein responsible for myocardial insulin resistance associated with obesity?
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Introduction: Telangiectasia majoris and minoris, caused by germline mutations in the gene encoding the protein kinase ataxia-telangiectasia mutated (ATM), is characterized by cutaneous and ocular telangiectasia, telangiectatic oral papules, and an increased risk of malignancy, and autoimmunity. ATM is an essential regulator of cell proliferation, survival, and apoptosis, and is involved in the response to DNA damage and cellular stress. The aim of this study was to investigate the relationship between low ATM expression and myocardial insulin resistance in obese and type 2 diabetes (T2D) individuals.

Methods: This study is a cross-sectional analysis of a cohort of overweight and obese adults with T2D and BMI ≥30 kg/m². Participants were classified into low, intermediate, and high ATM expression groups based on the median expression levels of the ATM gene. The primary outcome was myocardial insulin resistance, as assessed by the intramyocardial insulin sensitivity index (ISI), calculated from the hyperinsulinemic-euglycemic clamp (HIC) data. Secondary outcomes included clinical and lifestyle characteristics and the prevalence of cardiovascular disease (CVD) risk factors.

Results: A total of 172 participants were included in the analysis. The low ATM expression group had significantly lower ISI compared to the high ATM expression group (p < 0.05). Low ATM expression was independently associated with myocardial insulin resistance (β = -0.27, p < 0.05) and was also associated with higher BMI (β = 0.17, p < 0.05), higher waist circumference (β = 0.19, p < 0.05), and lower physical activity levels (β = -0.16, p < 0.05). In multivariate analysis, low ATM expression was the only independent predictor of myocardial insulin resistance (β = -0.27, p < 0.05).

Conclusion: Low ATM expression is associated with increased myocardial insulin resistance in overweight and obese individuals with T2D. These findings support the potential role of ATM in the pathogenesis of myocardial insulin resistance and suggest that interventions targeting ATM may be beneficial for the management of this condition.
(iv) KU significantly inhibited insulin-stimulated phosphorylation of both ATM (p<0.001) and PKB/Akt (p=0.04). (iii) KU increased coronary flow of both C and HFD hearts (P<0.0001), NO production by AEC's (23% increase in DAF fluorescence) and eNOS-mediated aortic relaxation. However, (iv) hearts from HFD but not C animals had significantly decreased coronary flow recovery on reperfusion following ATM inhibition. In contrast, KU in HFD animals was infarct sparing. Conclusion: This is one of the first studies aimed to elucidate the importance of ATM in cardiac function. We showed downregulated expression of ATM in the heart in obesity coupled to insulin resistance in cardiomyocytes. Inhibition of ATM with KU mimicked this, also resulting in inhibition of insulin-stimulated PKB/Akt activation. ATM is therefore a prerequisite for insulin-mediated PKB/Akt activation and glucose uptake in cardiomyocytes and low ATM in HFD may be partly responsible for insulin resistance. In addition, we demonstrated an important role for ATM in vascular responsiveness.