

Discovering Novel Interactions Between Thrombosis, Diabetes, and Obesity



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BACKGROUND

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Problem: Patients with obesity and type 2 diabetes (T2D) experience increased blood clots, the cause of which remains unclear.

Abbreviations

CD248: a type I transmembrane protein Insulin Receptor (IR): a transmembrane receptor

Tissue Factor (TF): major trigger of the clotting cascade

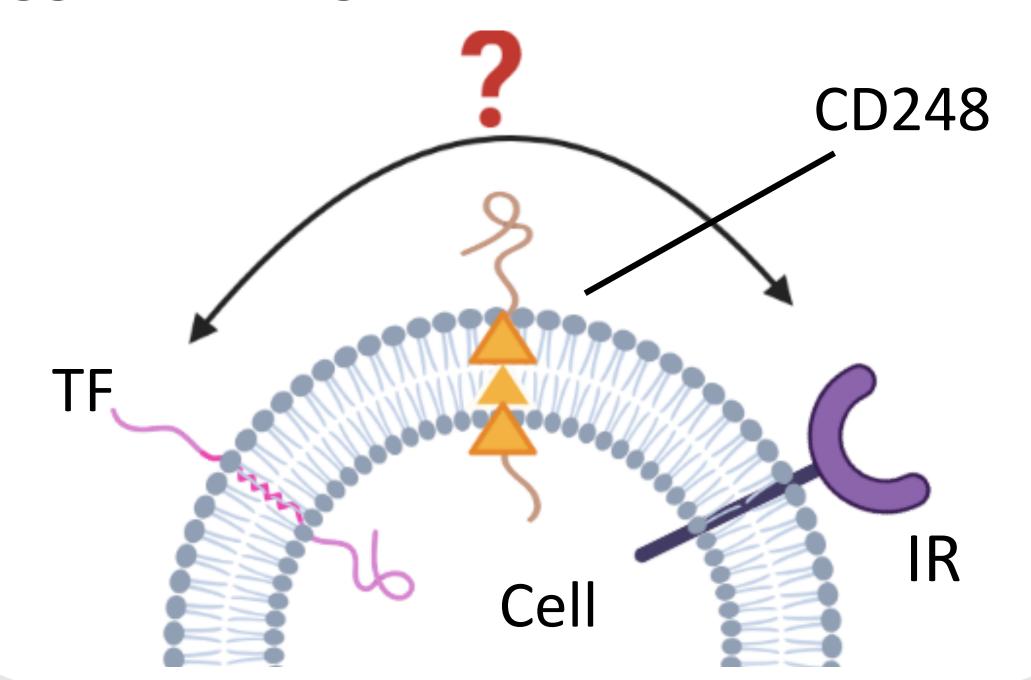
Previous Research

- High levels of adipocyte CD248 correlate with obesity & T2D
 - CD248 binds to IR and causes insulin resistance
- High levels of vascular smooth muscle cell CD248 associated with increased blood clot formation
 - CD248 interacts with TF and increases its activity
- ❖ Does an IR-CD248-TF complex link insulin signaling + coagulation and explain excess clots in T2D?

OBJECTIVE

Using in vitro systems, goal is to test whether:

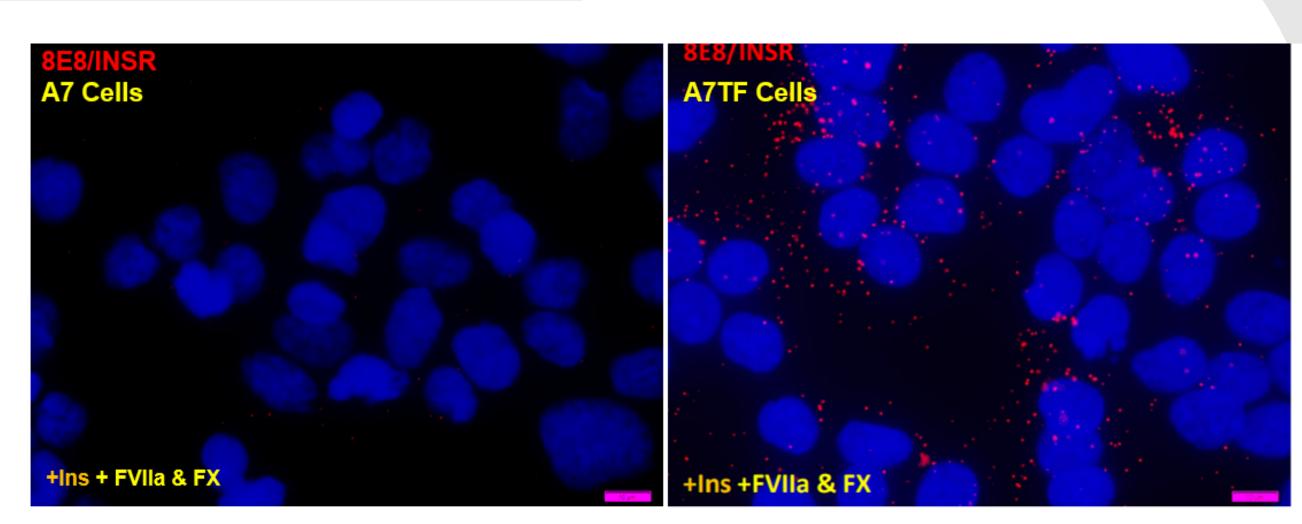
- 1) TF alters insulin-signaling via the IR
- 2) insulin-signaling via the IR affects TF-triggered coagulation



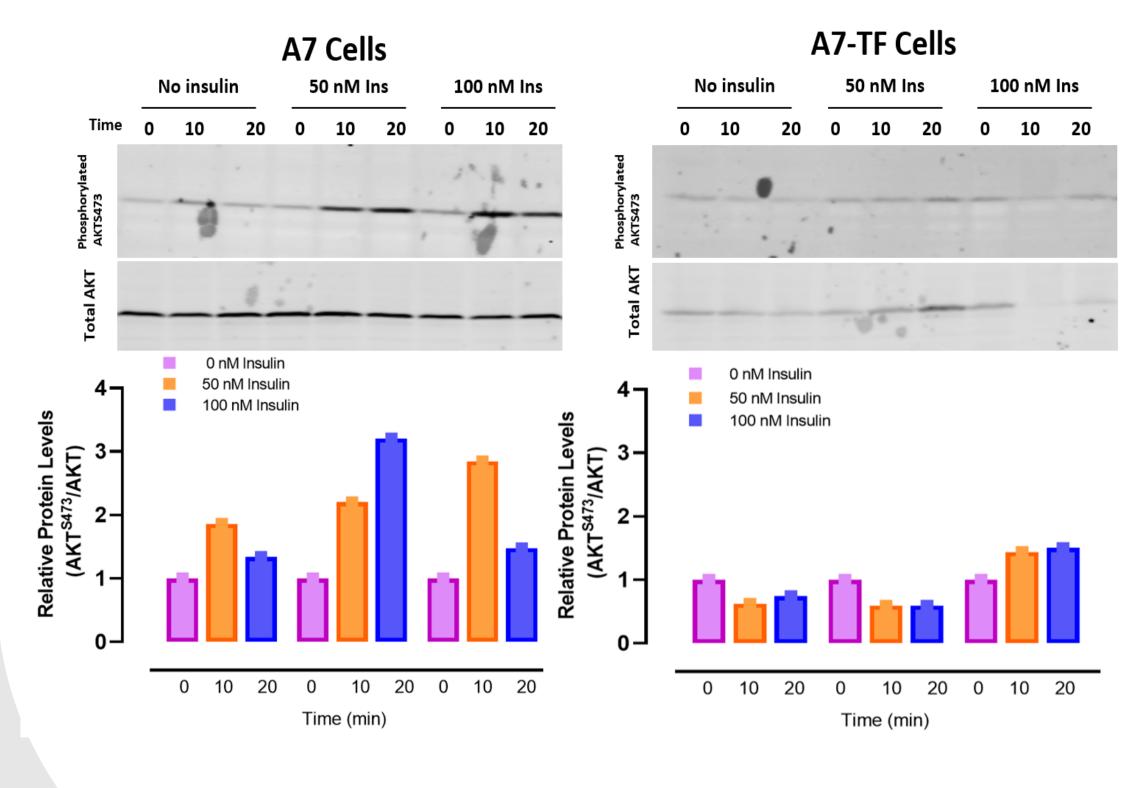
METHODS Does TF affect Insulin Induced Insulin Triggered Glucose Uptake Assay + insulin AKT Confocal microscopy signaling via IR? Phosphorylation Check if IR and TF are in close proximity on cell membrane Does insulin IR-siRNA signaling via IR transfection Coagulation affect TF-+ insulin Assays triggered treatments coagulation?

RESULTS

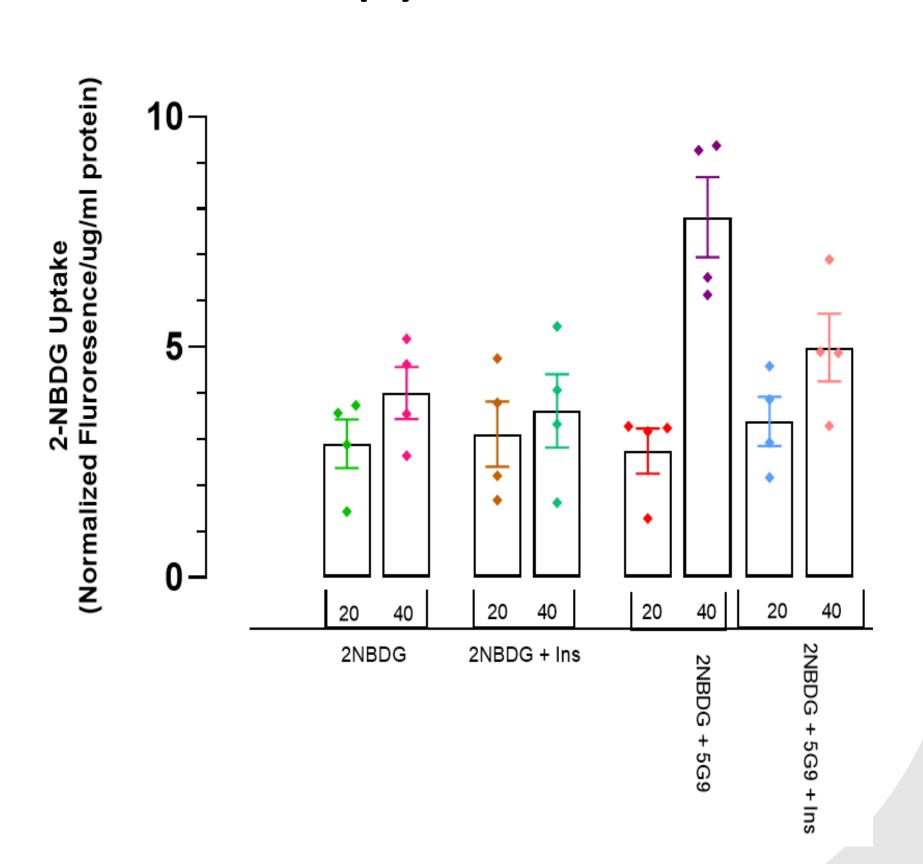
1. TF and IR are in close proximity on cell membrane showed by proximity ligation assay (PLA).



2. Insulin-induced AKT phosphorylation is more robust in A7TF cells as compared to A7 cells via Western blots



3. TF affects insulintriggered uptake of fluorescently labeled glucose into cells - confocal microscopy



CONCLUSION

- TF and IR are in close proximity on cell membrane suggesting a functional relationship
- TF alters the insulin signaling via IR

FUTURE PLANS

• Examine the role of IR on TF-triggered coagulation using cells expressing different levels of IR generated via IR-siRNA Knock down