

Paniz Ghavimi, Kevin Gonzalez, Nooshin Safikhan, Patricia Benedet, Edward Conway

Centre for Blood Research, University of British Columbia Vancouver, BC

BACKGROUND

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

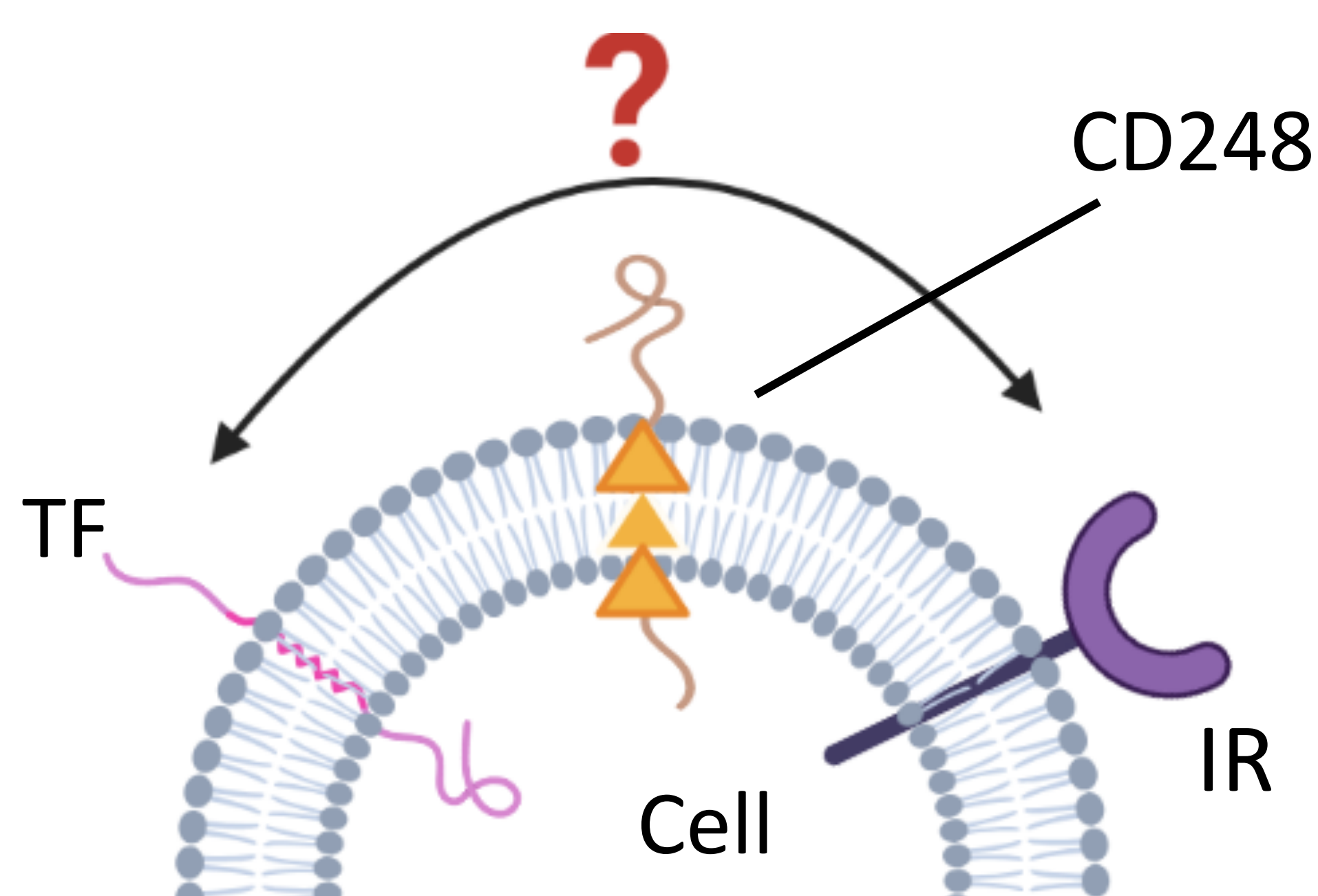
- High levels of adipocyte CD248 correlate with obesity & T2D
 - CD248 binds to IR and causes insulin resistance
- High levels of vascular smooth muscle cell CD248 associated with increased blood clot formation
 - CD248 interacts with TF and increases its activity

❖ Does an IR-CD248-TF complex link insulin signaling + coagulation and explain excess clots in T2D?

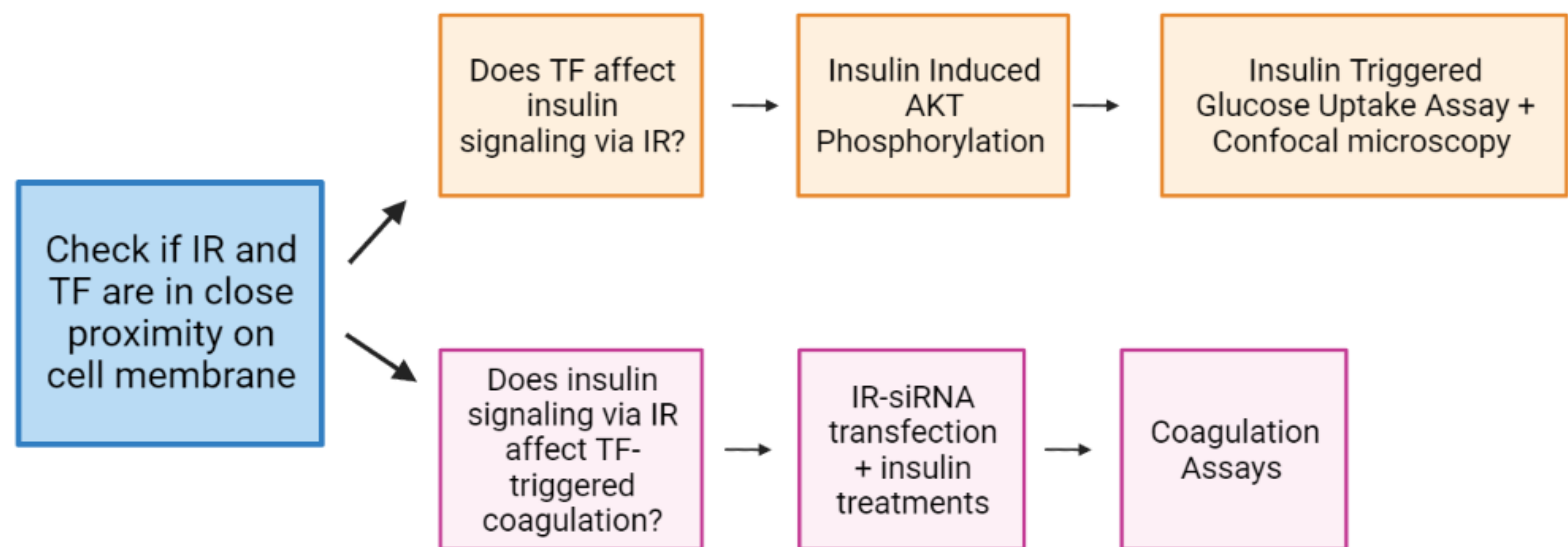
OBJECTIVE

Using in vitro systems, goal is to test whether:

- TF alters insulin-signaling via the IR
- insulin-signaling via the IR affects TF-triggered coagulation

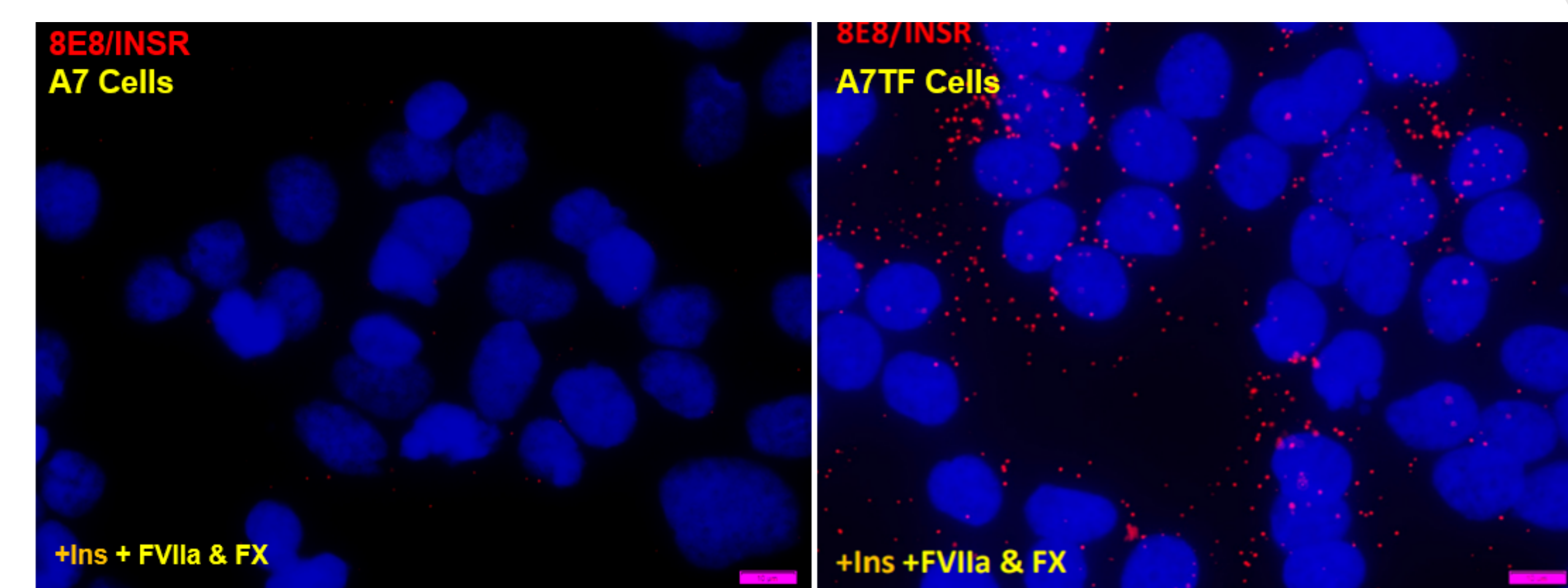


METHODS

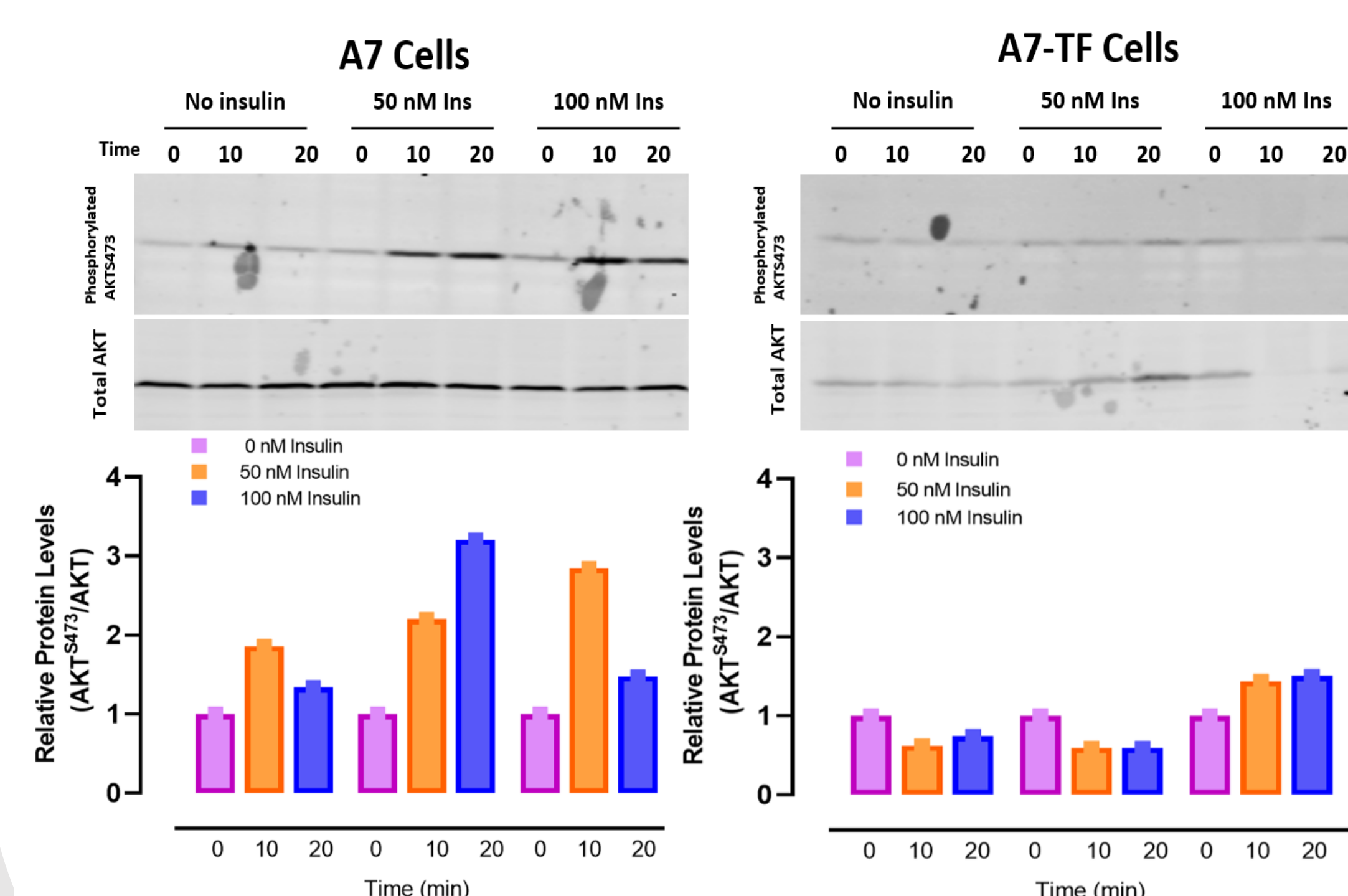


RESULTS

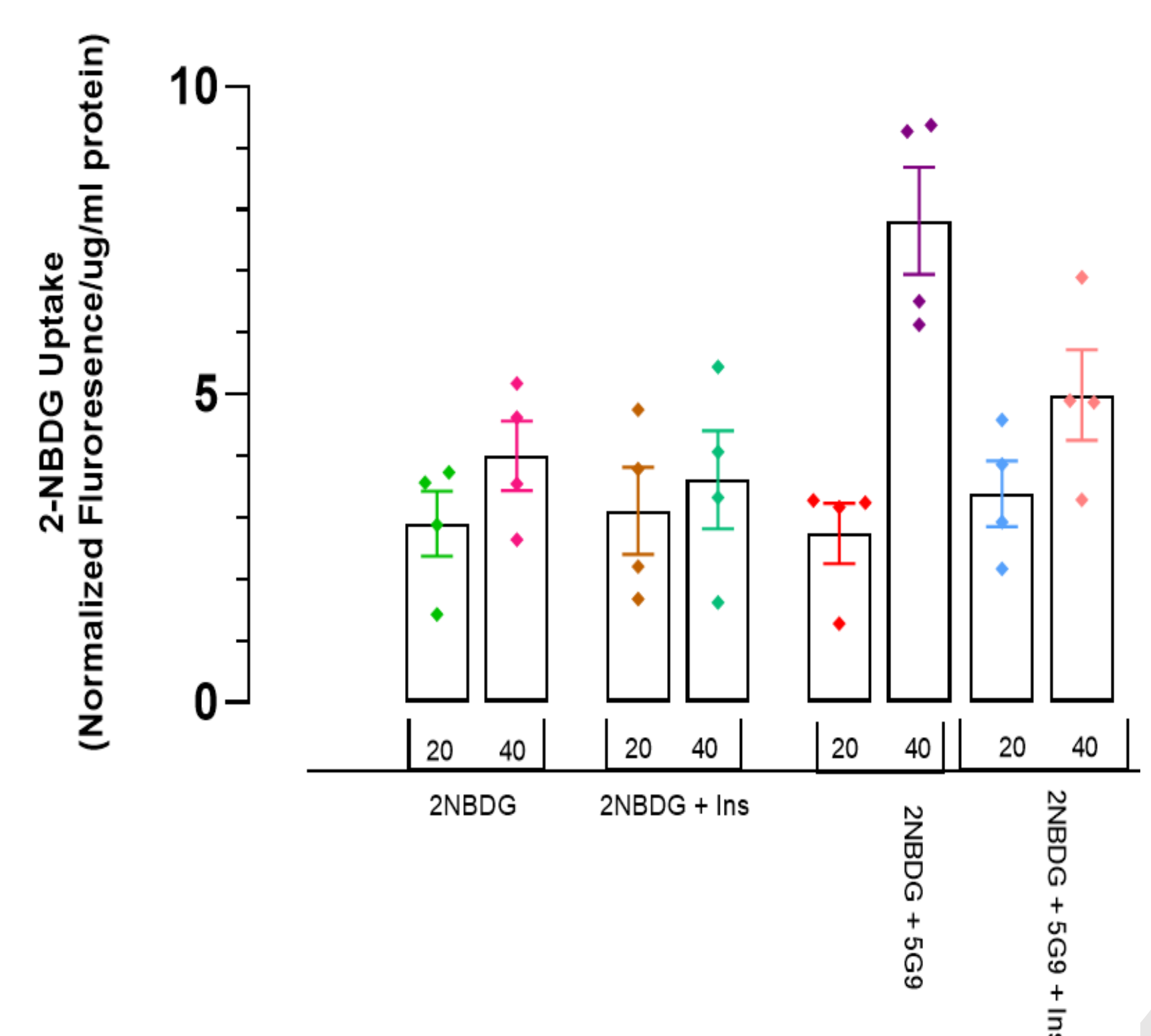
1. TF and IR are in close proximity on cell membrane showed by proximity ligation assay (PLA).



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



3. TF affects insulin-triggered 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