Understanding how our fat cells store and release energy

MAPPING THE ADIPOCYTE SUBCELLULAR PROTEOME IN RESPONSE TO FED AND FASTED STIMULI

Why are we interested in this?

- The role of our fat cells is to store energy after we’ve eaten, and release this energy when we haven’t eaten for a while.
- Proteins have to move between different compartments in fat cells in order for this to happen (e.g., a glucose transporter moves to the surface of fat cells in response to insulin to allow glucose to be taken up and stored).
- This movement has to be highly regulated to ensure our bodies have a constant energy supply, regardless of when we’ve last eaten.

What do we want to know?

- WHAT proteins move in response to a ‘fed’ or ‘fasted’ signal, and WHERE do they move?
- How does this movement of proteins allow our fat cells to switch between taking up and releasing energy?

How did we do this?

1. Treat the fat cells with drugs to mimic the “fed” or “fasted” state
   - + nothing (“baseline”)
   - + insulin (“fed”)
   - + noradrenaline (“fasted”)
2. Spin the cells at increasing speeds to separate cells into different compartments
3. Measure the proteins in each fraction
4. Assign proteins to cell compartments, and detect which proteins move compartments in a fed/fasted state

What did we find?

- c3orf18: a new insulin-responsive protein
- c3orf18 moves to the surface of fat cells in response to insulin – if it plays a role in glucose uptake it could be a new therapeutic target for type 2 diabetes

Why is this important?

- Research so far has focussed on individual proteins that move in response to a fed/fasted state.
- We don’t understand all the proteins that move to allow this shift between taking up and releasing energy, or how these are regulated.
- Protein movement in response to fed and fasted signals can be dysregulated in insulin resistance, a key feature of type 2 diabetes.
- Understanding what proteins move could provide new therapeutic targets for type 2 diabetes.

What have we found?

- We have identified a novel insulin-regulated protein in fat cells, and are now working to understand its function.
- We know it moves to the surface of fat cells in response to insulin – if it plays a role in glucose uptake it could be a new therapeutic target for type 2 diabetes.

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