

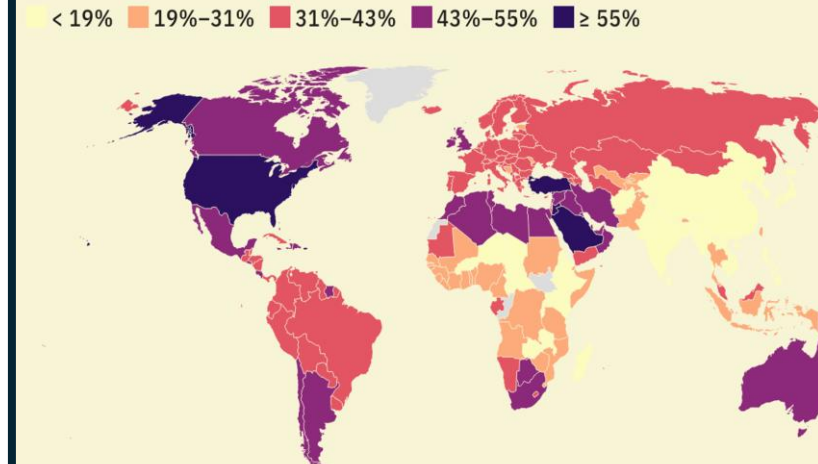
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Investigating BACE1 as a Novel Regulator of Lipid in Cardiometabolic Disease

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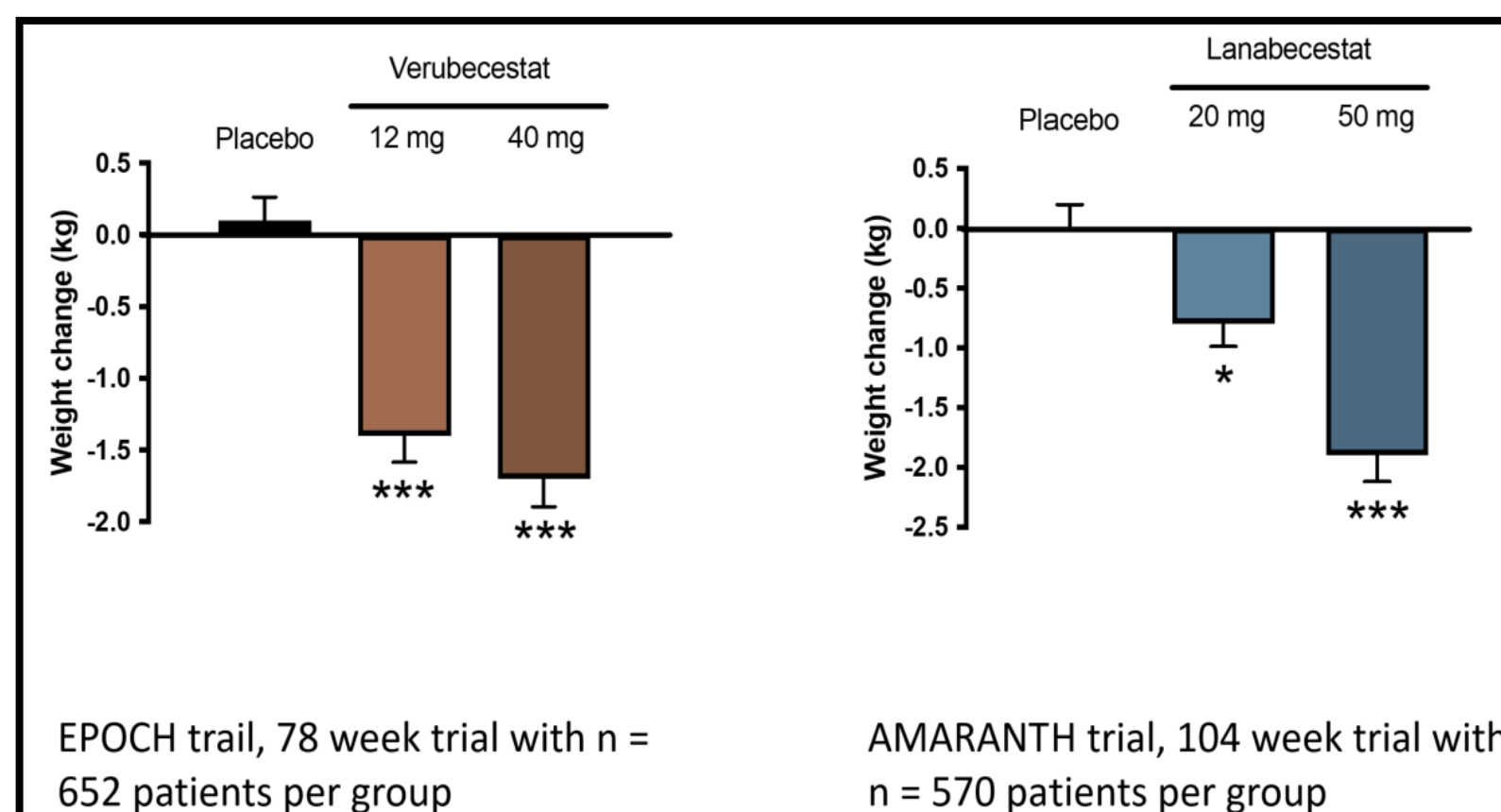
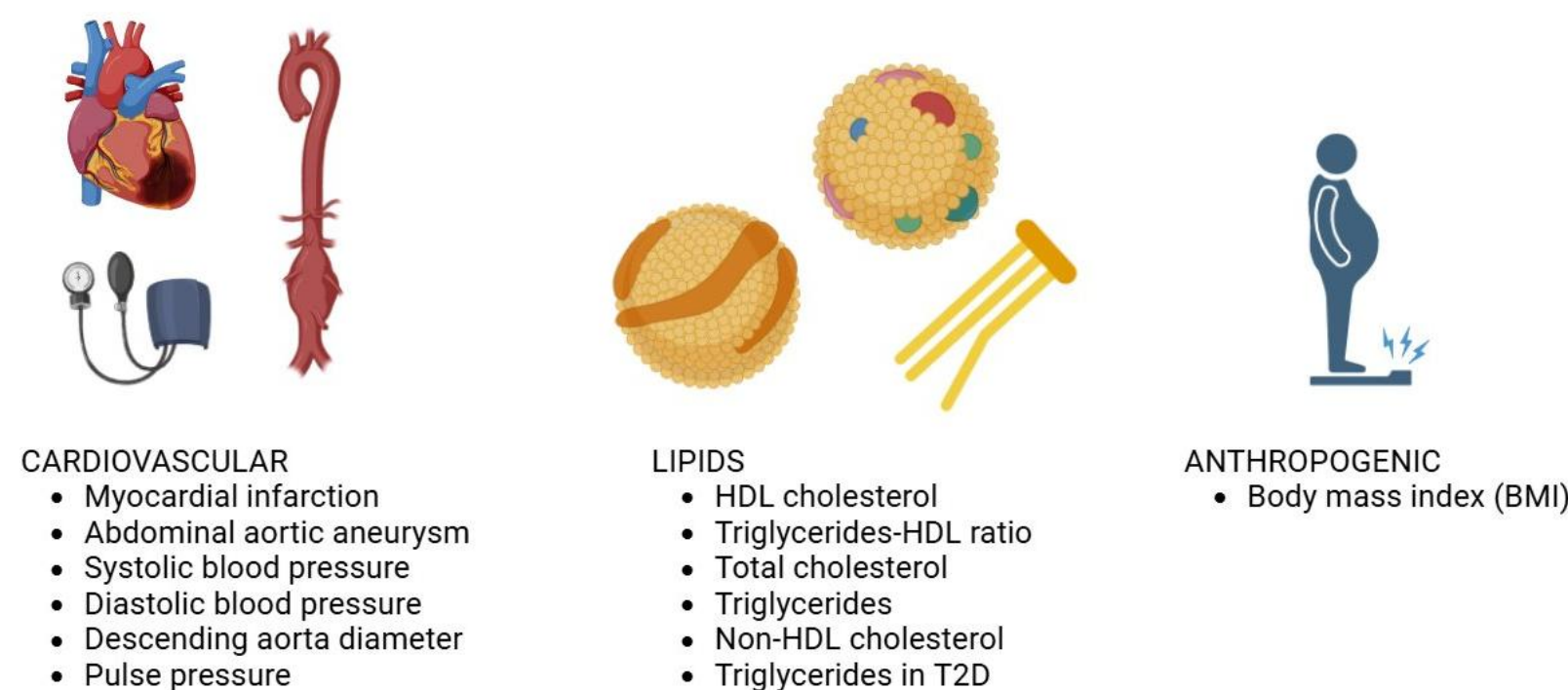
Obesity

Obesity rates are expected to rise
Percentage of the adult population projected to be obese by 2035.



- Over 64% of adults in the UK are overweight or obese
- Obesity is a major risk factor for type 2 diabetes, heart disease and other metabolic diseases
- 67.5% of obesity related deaths are attributed to cardiovascular disease

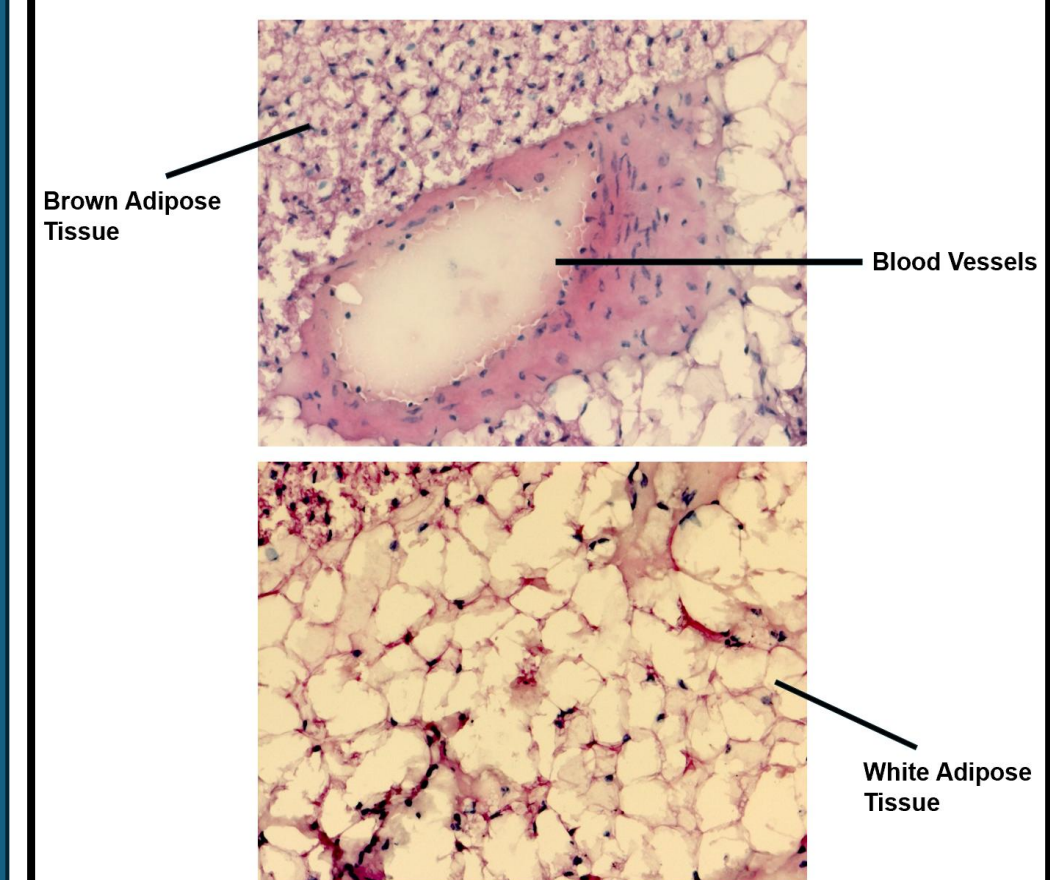
Why BACE1?



- BACE1 is a protein that acts like scissors and cuts other proteins.
- One of the proteins BACE1 cuts creates plaques in the brain which are a hallmark of Alzheimer's disease
- Human genetic data suggests that there is a link between BACE1 mutations, cardiovascular health and lipids.
- Clinical trial of BACE1 inhibitors used to treat Alzheimer's disease have been shown to have weight loss side effects.

Adipose Thermogenesis

- There are 2 main types of fat: White and Brown
- White fat has low ability to create energy and primarily store fat in the form of lipid.
- Brown fat burns lipid instead of storing it.

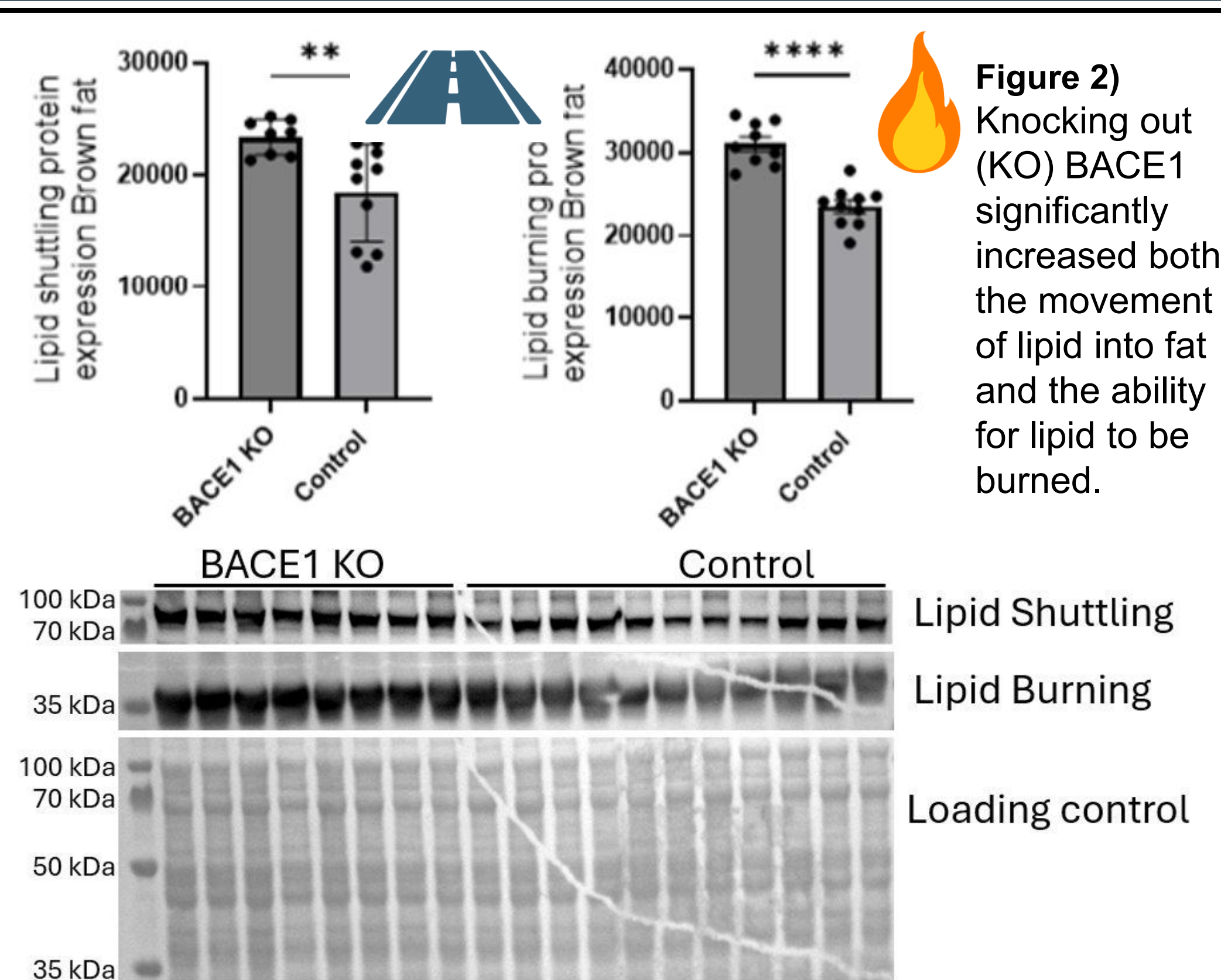
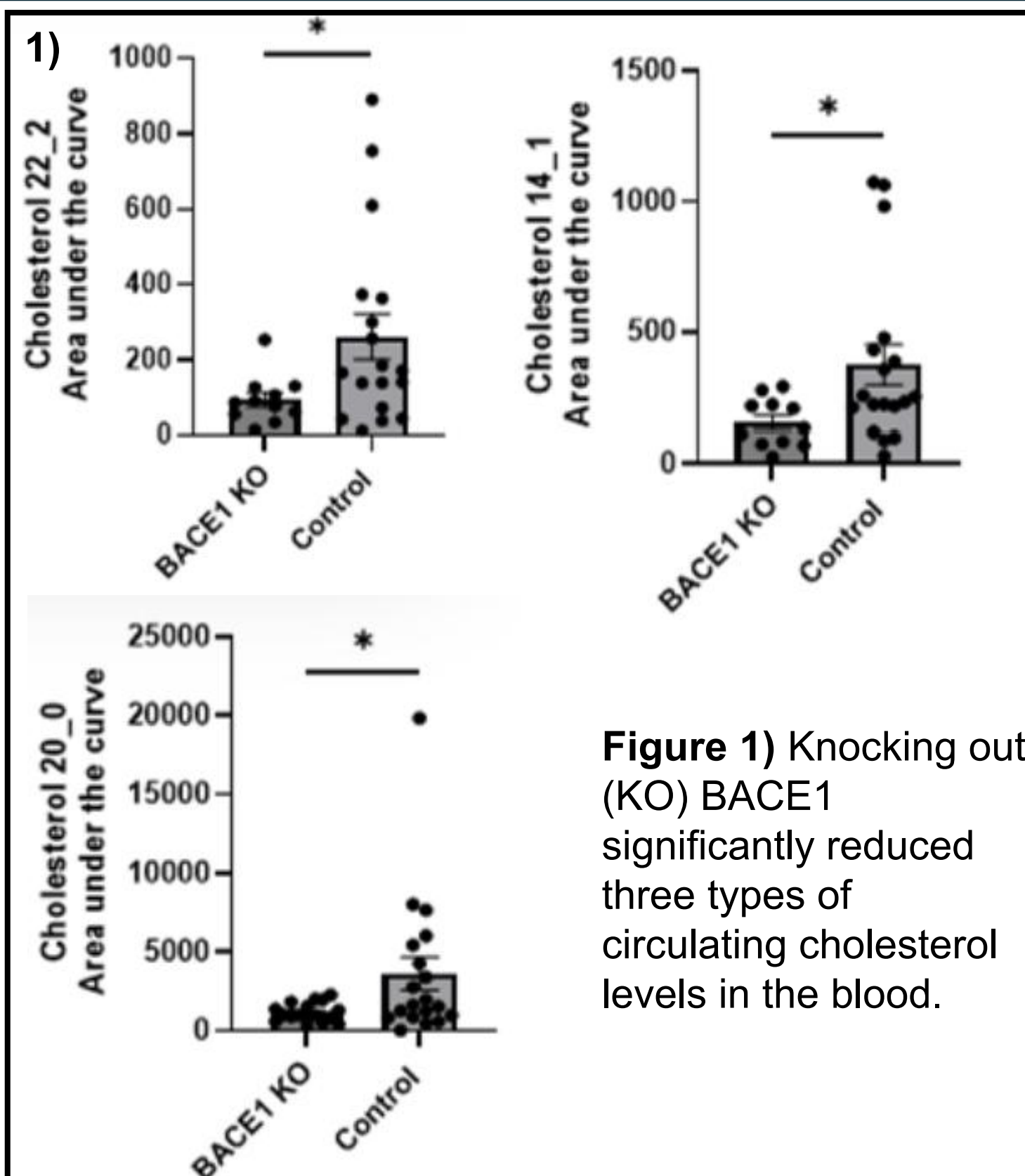


Hypothesis!

BACE1 Deletion reduces circulating cholesterol by increasing the amount of lipid burned in fat.

Research Objectives

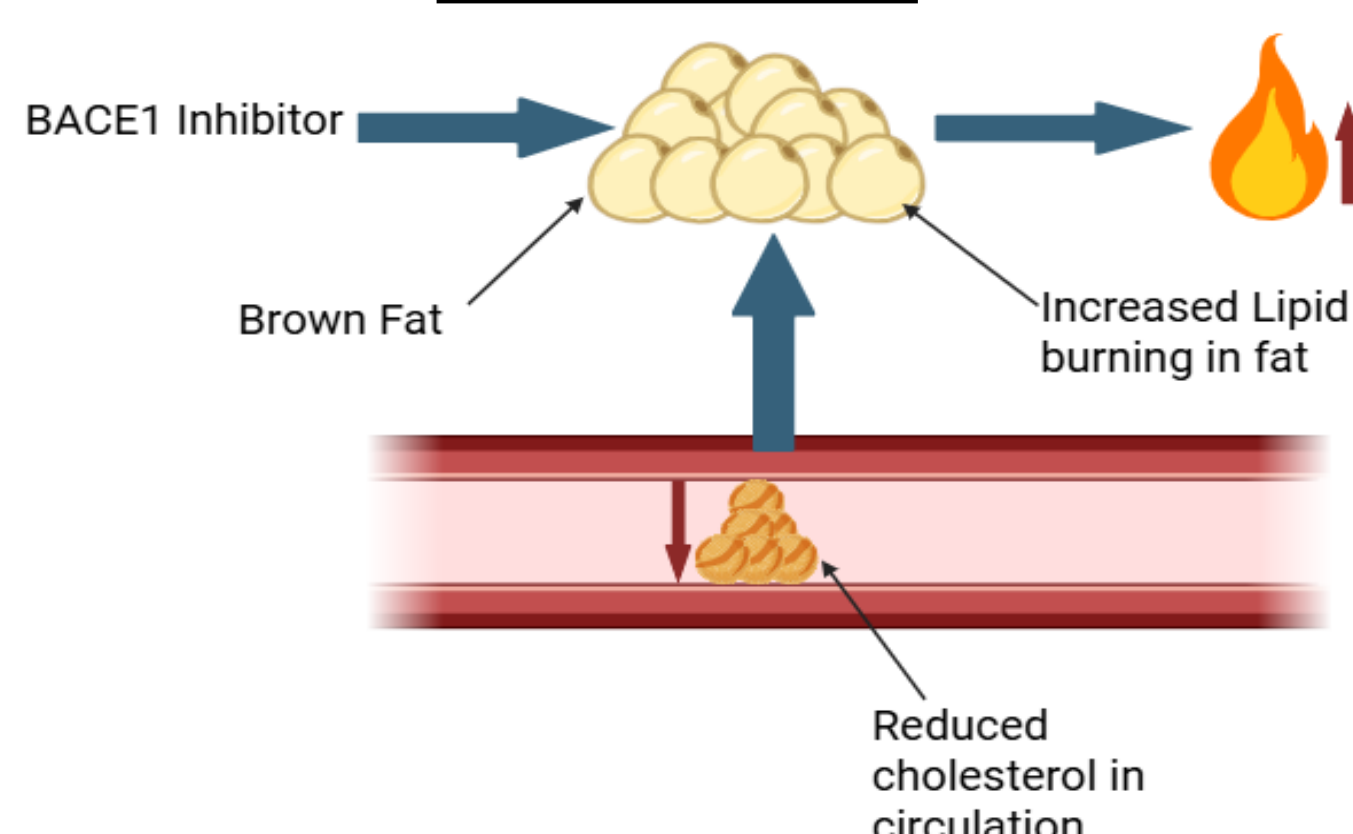
- Determine level of circulating cholesterol in mice that do and don't have BACE1 in their fat
- Measure proteins in fat that move and burn lipid



Key Findings

- BACE1 inhibition significantly reduced three types of circulating cholesterol levels.
- CPT1A expression in BAT showed a modest upward trend.
- Further investigation with larger sample sizes is required to determine whether these observed trends represent biologically meaningful effects.

Interpretation



Future Direction

- Investigate the mechanism of what BACE1 Cleaves to increase lipid shuttling and burning
- Asses whole animal energy expenditure and thermogenic capacity

Limitations

- Short 6-week project duration.
- Limited sample size.
- Protein expression changes may not reflect functional thermogenic activity.
- Findings should be considered preliminary.

References



BACE1 inhibition significantly reduced circulating cholesterol and produced modest changes in adipose thermogenic markers, suggesting a potential role for BACE1 in cardiometabolic regulation.