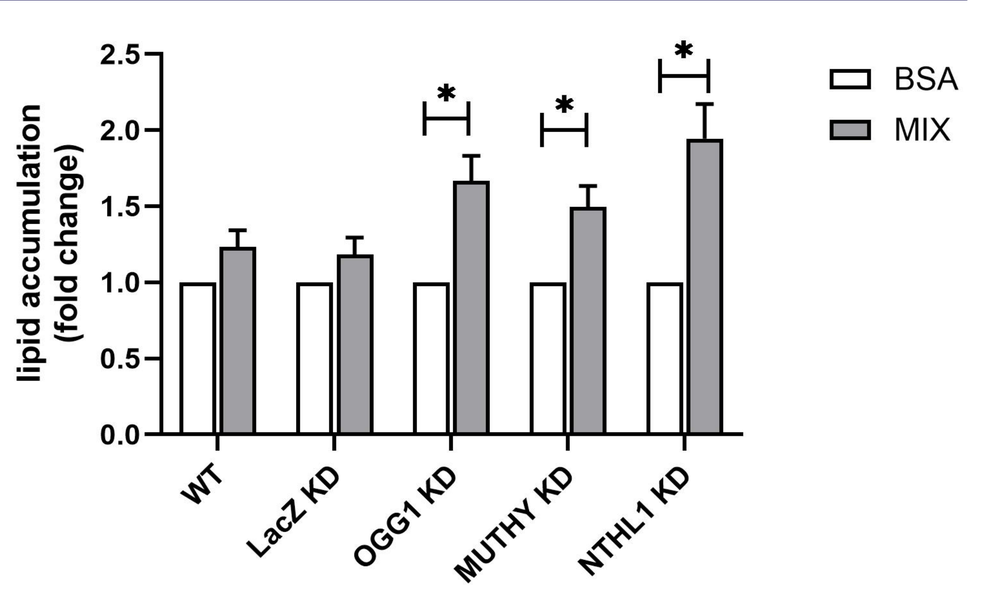
Impaired DNA repair (BER) activity leads to enhanced lipid accumulation via mitochondrial dysfunction



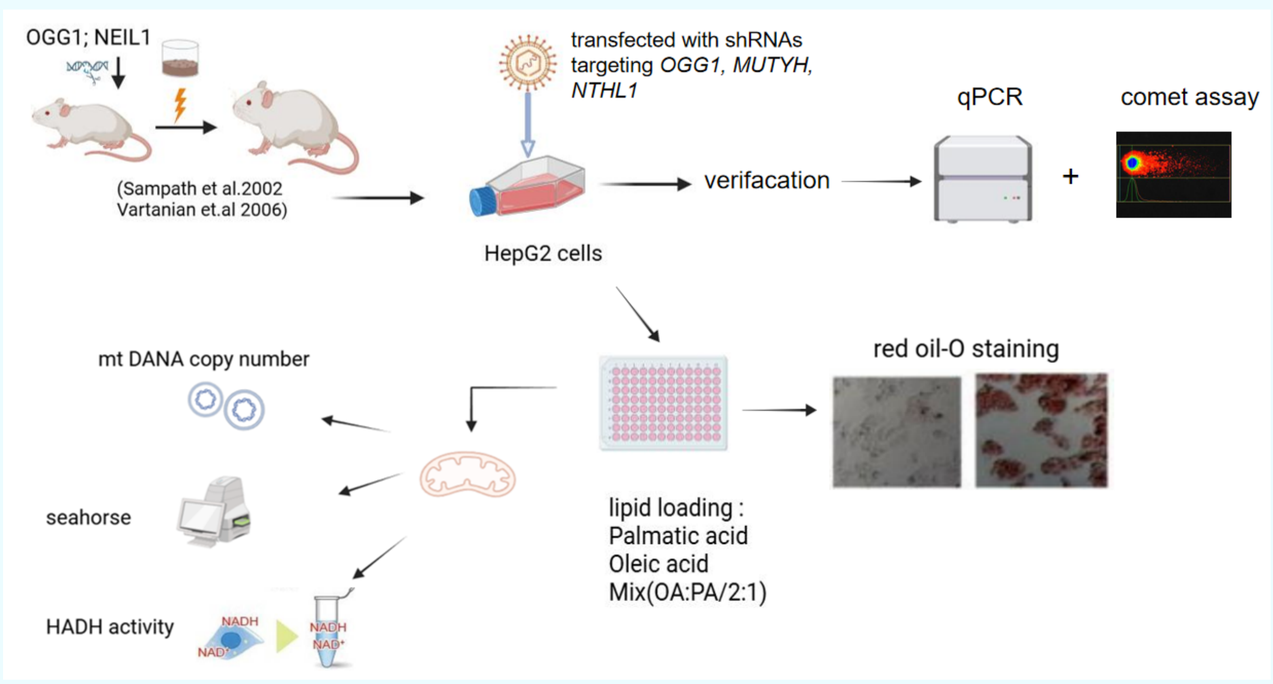
Background

- Lipid accumulation plays a role in the development of metabolic diseases like obesity
- Carriers of multiple variants in DNA repair genes are more prone to gain weight and develop obesity when exposed to an obesogenic environment (Himbert et al 2017, Langie et al 2010)
- Animal models indicated an association between BER (base excision repair) deficiency and increased risk of obesity and other metabolic disease

Objective

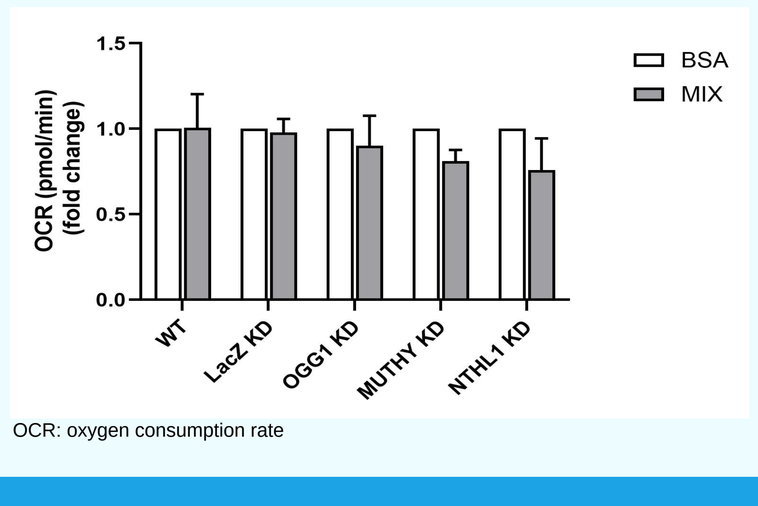
We hypothesize that BER deficiency could lead to enhanced intracellular lipid accumulation via reduced mitochondrial function .

Methods



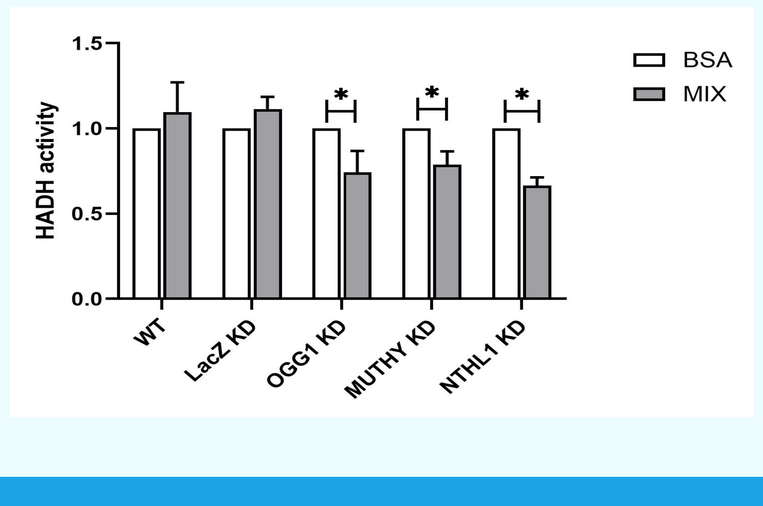
Main findings

BER gene deficiency leads to a slight decrease in mitochondrial respiration



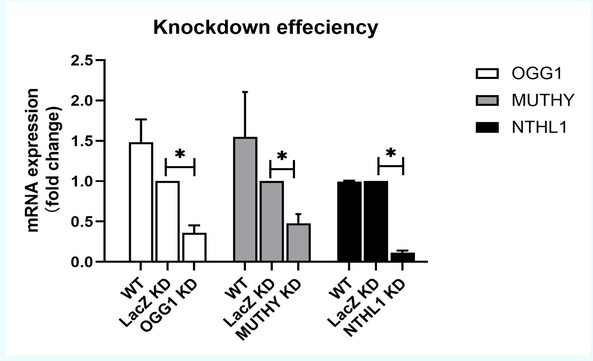
OCR: oxygen consumption rate

Decreased HADH activity was found in BER deficient HepG2 cells

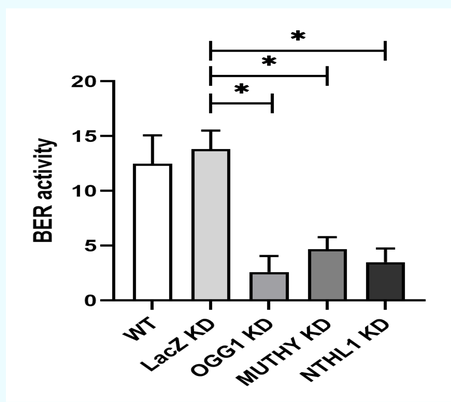


Extra results

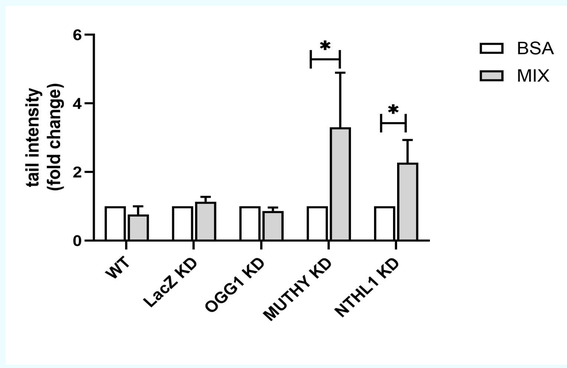
Lenti-virus transfected cells show lower gene expression level



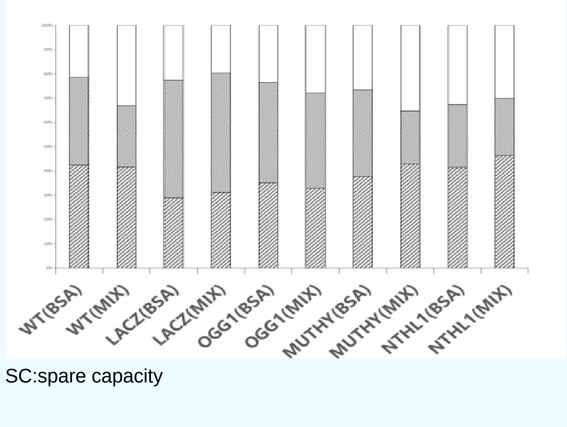
BER gene deficiency was found in transfected cells



Increased DNA oxidation was found in MUTHY KD and NTHL1 KD cells



Changes in mitochondrial respiration



SC:spare capacity

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