Global ^{13}C tracking reveals altered metabolic fluxes in retinal pigment epithelium under hyperglycemic and hypoxic conditions

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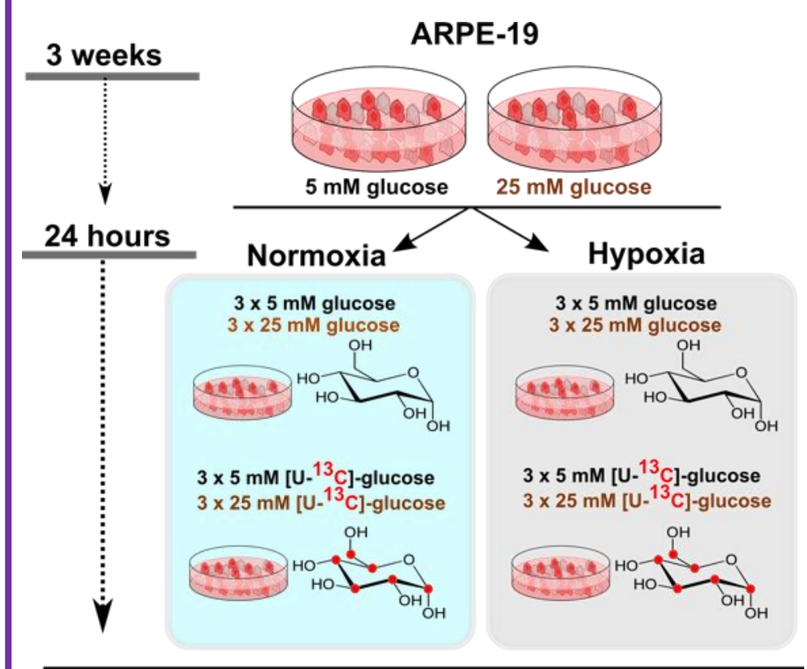
BACKGROUND

- Diabetic retinopathy (DR) is the commonest sight-threatening lesion in diabetics.
- Current treatments for DR are applicable only at advanced stages of the disease, when the blood vessels proliferate (PDR, Proliferative Diabetic Retinopathy) and they associate with significant adverse effects.
- DR therapy would greatly benefit from early stages disease diagnosis and intervention.

GOALS

- Identify deregulated metabolic pathways behind the hyperglycemic pseudohypoxic state leading to PDR
- Based on ARPE-19, a human retinal pigment epithelial cell line model, we studied metabolic imbalances resulting from hyperglycemia and hypoxia and their interaction.

METHODS

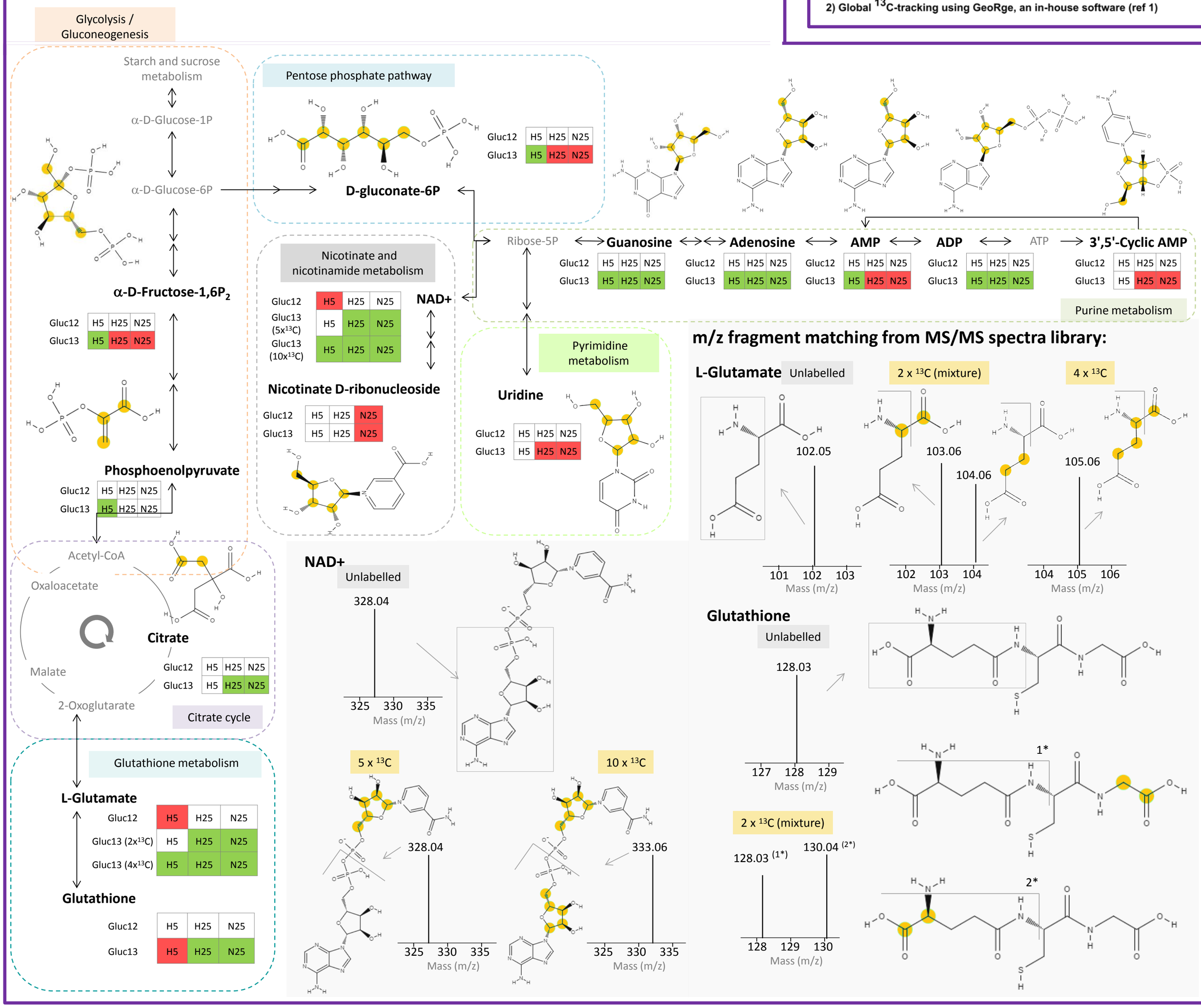


RESULTS

N5 (control) =5mM Glucose/Normoxia
H5=5mM Glucose/Hypoxia
H25= 25 mM Glucose /Hypoxia
N25=25mM Glucose/Normoxia

Increased versus N5

Decreased versus N5



CONCLUSIONS

- Metabolic flux analysis reveals changes in ^{13}C incorporation levels in several metabolites while ^{12}C pool levels keep constant (ref 2)
- Flux through glycolysis, pentose phosphate, pyrimidine and part of purine metabolism pathway are increased in hyperglycemia, while TCA cycle, glutamate and glutathione metabolism pathways are down regulated.
- In general, the major flux alterations are due to high glucose concentrations (N25 and H25) rather than low O_2 levels (H5).

REFERENCES

1. Capellades et al. *in preparation.*
2. Navarro et al. *in preparation*.