

Global ¹³C 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.

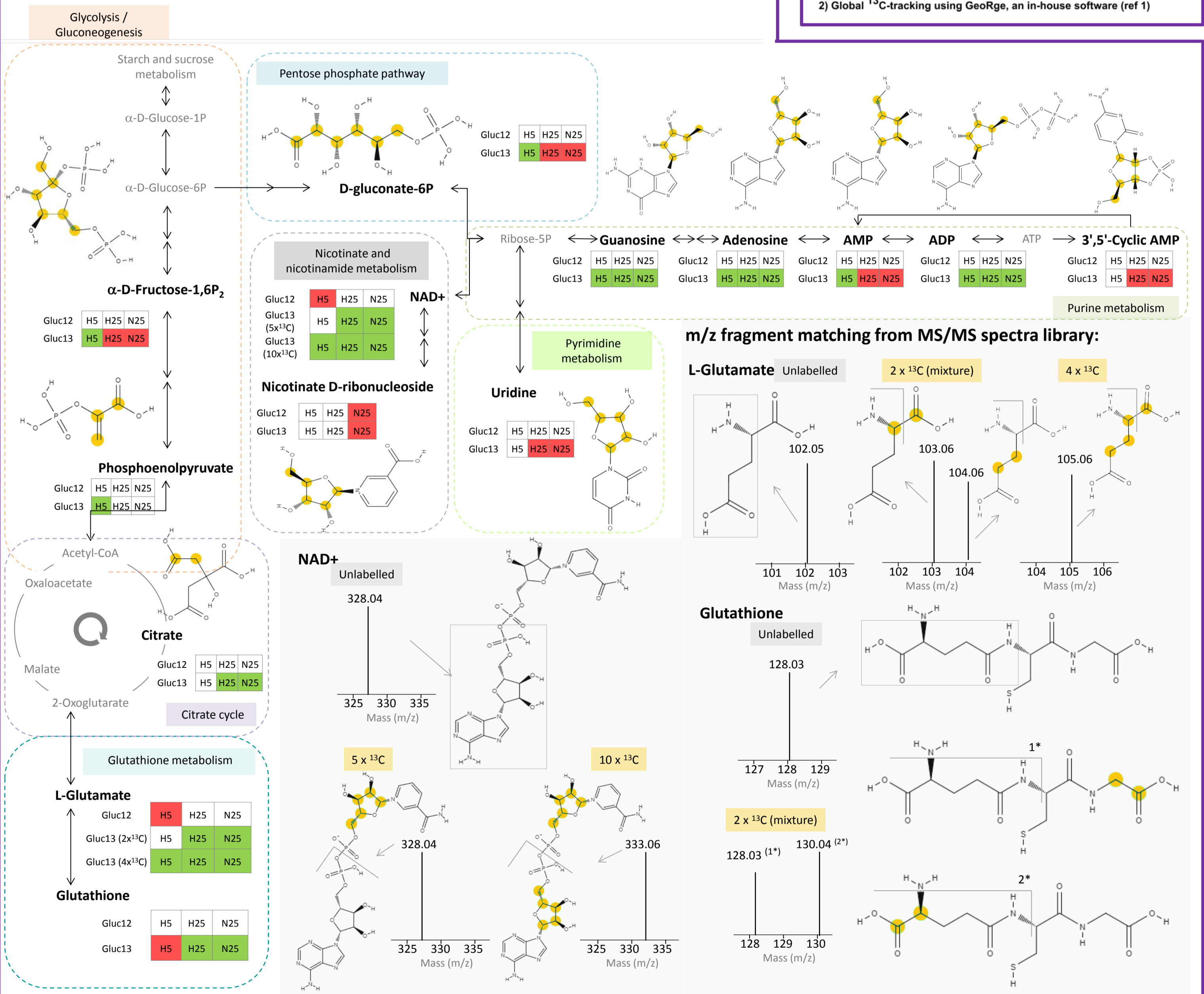
GOALS

- 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.

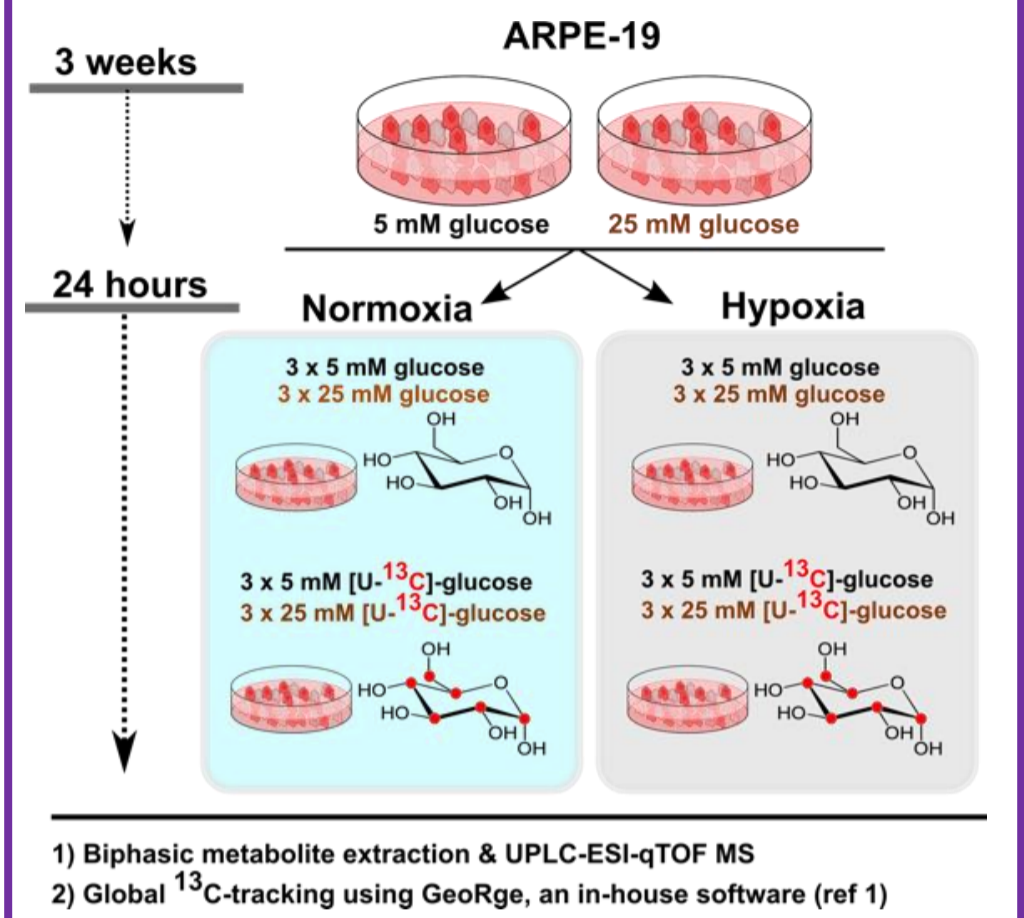
RESULTS

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

Increased versus N5 ■
 Decreased versus N5 ■



METHODS



CONCLUSIONS

- Metabolic flux analysis reveals changes in ¹³C incorporation levels in several metabolites while ¹²C 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 O₂ levels (H5).

REFERENCES

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