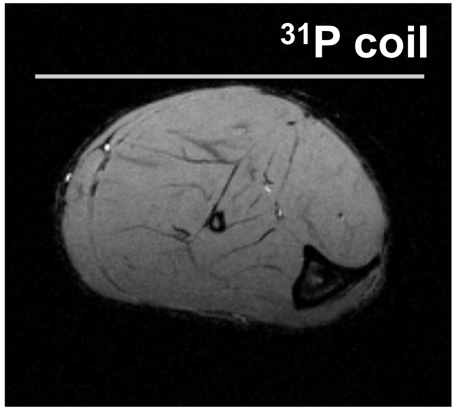


$$\mathrm{ADP} + \mathrm{P_i} \underset{k_r}{\overset{k_f}{\rightleftarrows}} \mathrm{ATP}$$

$$V_{ATP} = k_f * [\,P_i\,]$$

$$\text{saturation-transfer} \Rightarrow k_f \;\alpha\; \Delta P_i / T_1'(P_i)$$

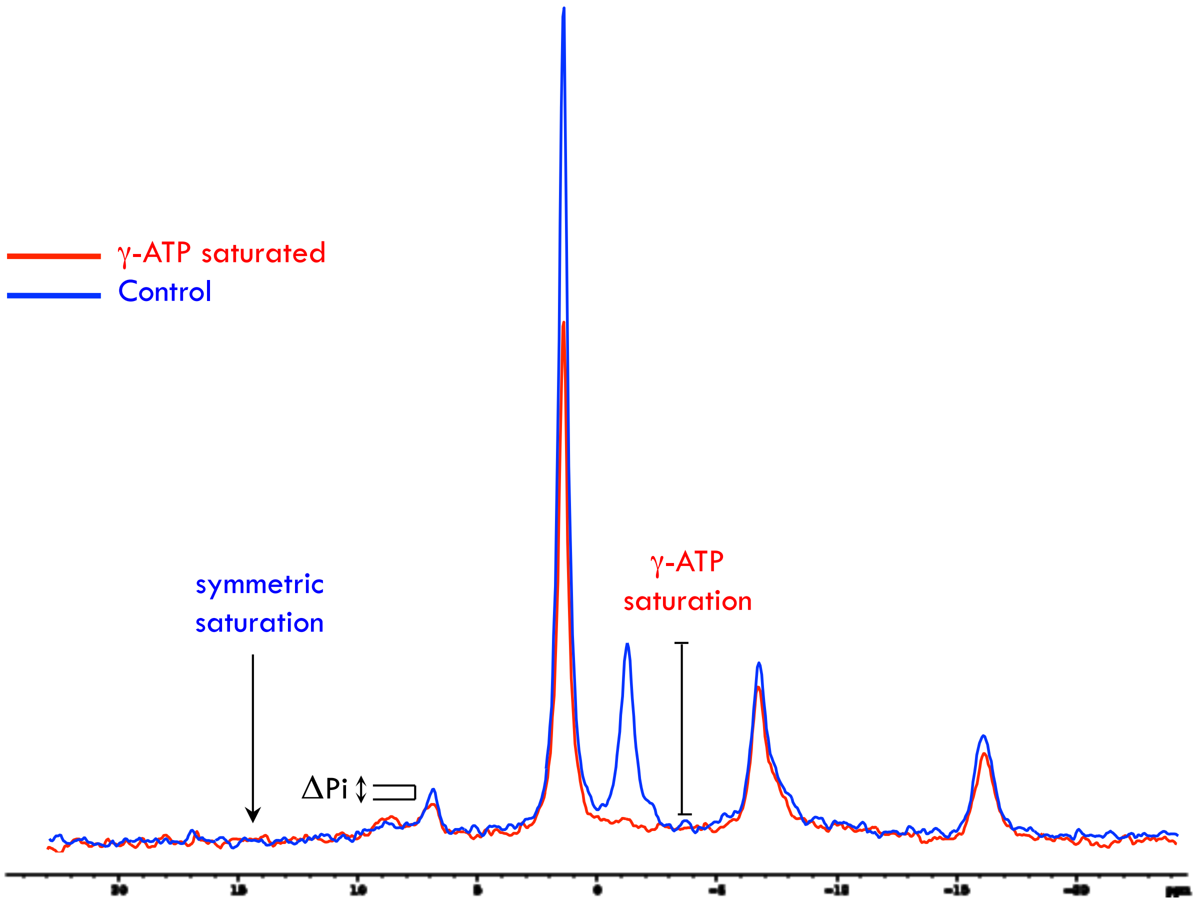


Fig. 1 Principle of ATP synthesis rate measurement by ^{31}P MR saturation transfer applied to exchange between Pi and ATP. In blue, the symmetric saturation spectrum: the saturation pulse is applied symmetrically to the γ-ATP, but on the downfield side of the Pi. In red, spectrum with the selective γ-ATP irradiation (NS=128). Subtraction of the spectra gives the fraction of Pi involved in the synthesis of ATP by the reaction:

ADP + Pi → ATP.

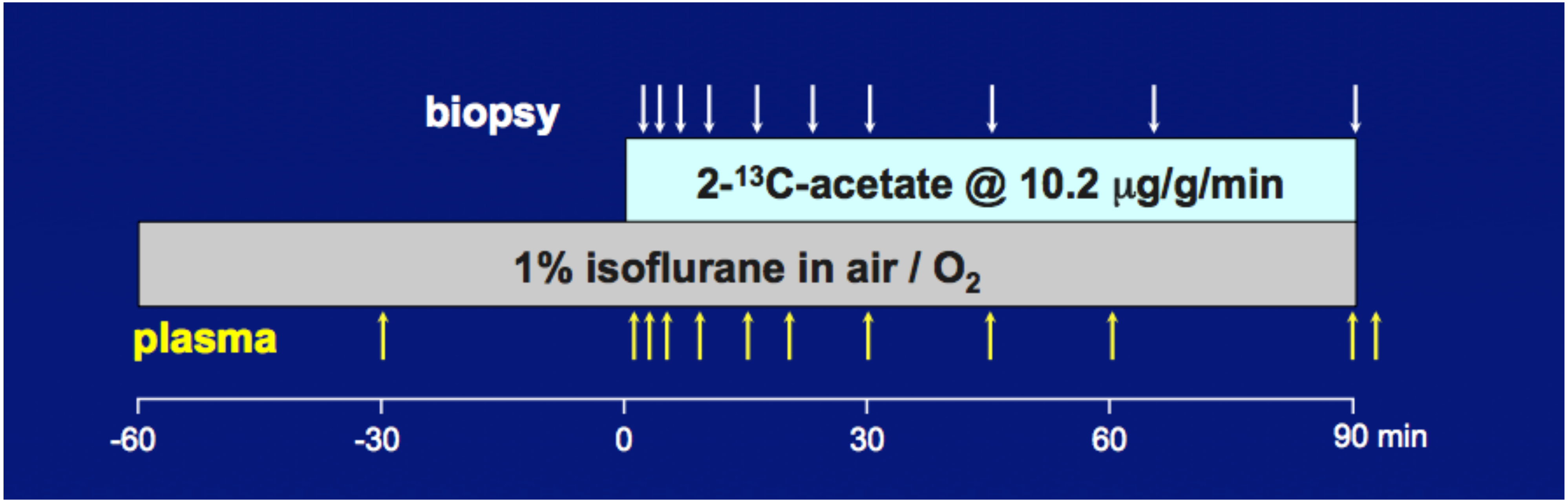


Fig. 2. A novel biopsy-based technique to determine substrate oxidation via the tricarboxylic acid cycle (V_{TCA}).

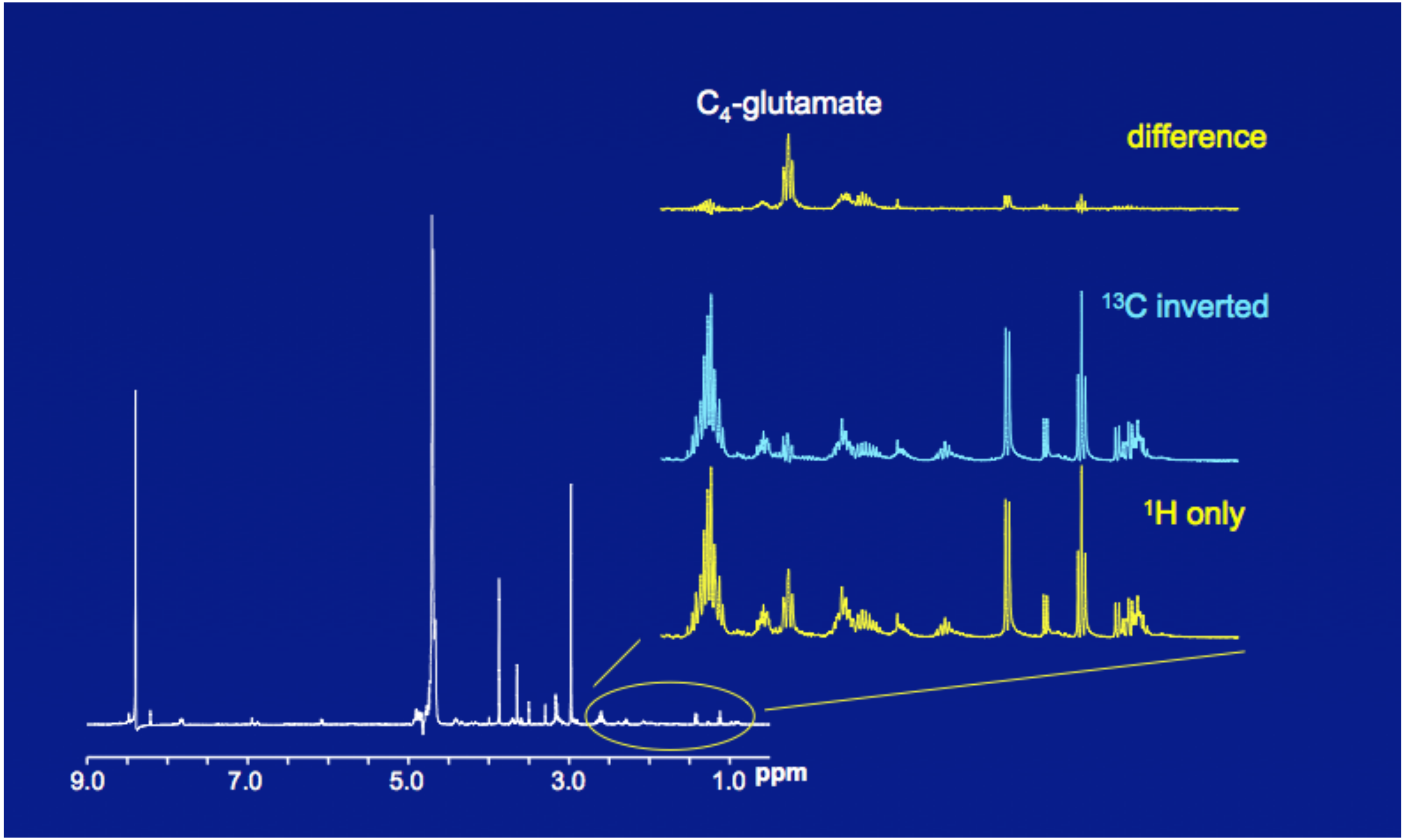


Fig. 3 *(details in the following slide)*

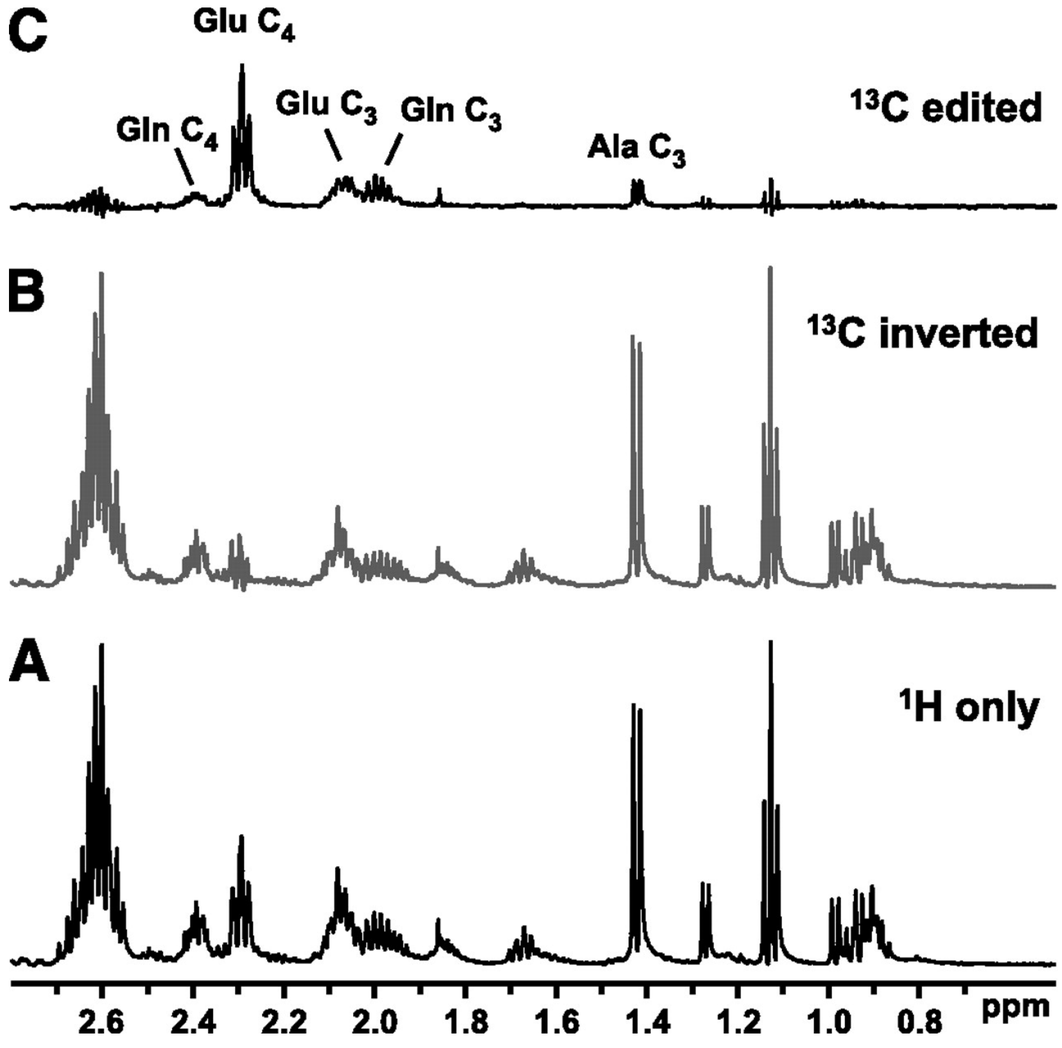
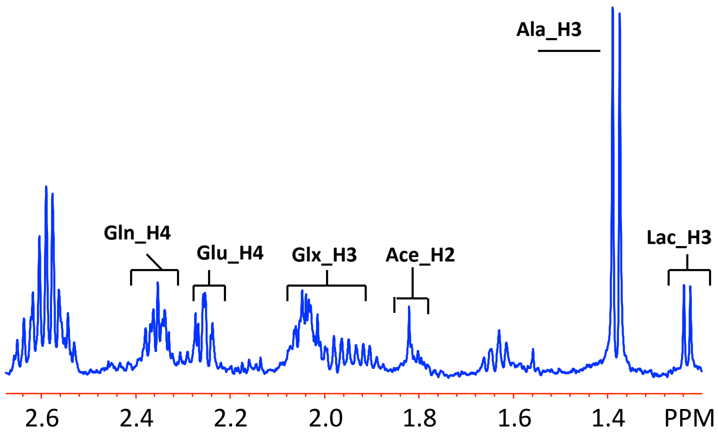
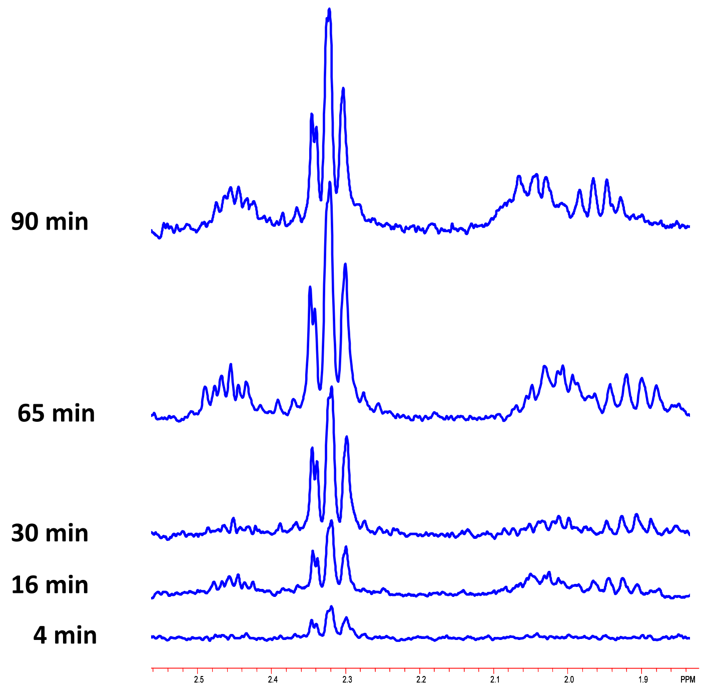


Fig. 3 *POCE MRS can be used to enhance the detection of ^{13}C-enriched metabolites.*
A: Standard ^{1}H acquisition. B: The incorporation of an additional ^{13}C pulse in the ^{1}H pulse sequence selectively inverts the signal of all ^{1}H bound to ^{13}C; ^{1}H bound to ^{12}C are unaffected. C: The difference spectrum (A minus B) yields only ^{13}C-enriched metabolites. Fractional enrichment can be calculated from the ratio of C-to-A. These UCP3 example spectra from a muscle extract show ^{13}C enrichment at multiple sites, including the C_4 and C_3 positions of glutamate (Glu) and glutamine (Gln) and C_3-alanine (Ala).



Typical POCE spectra at 500MHz from UCP3 mouse muscle extracts



High resolution POCE spectra depicting 13C-labelling timecourse of glutamate C4 in a tg-mouse

Fig. 4

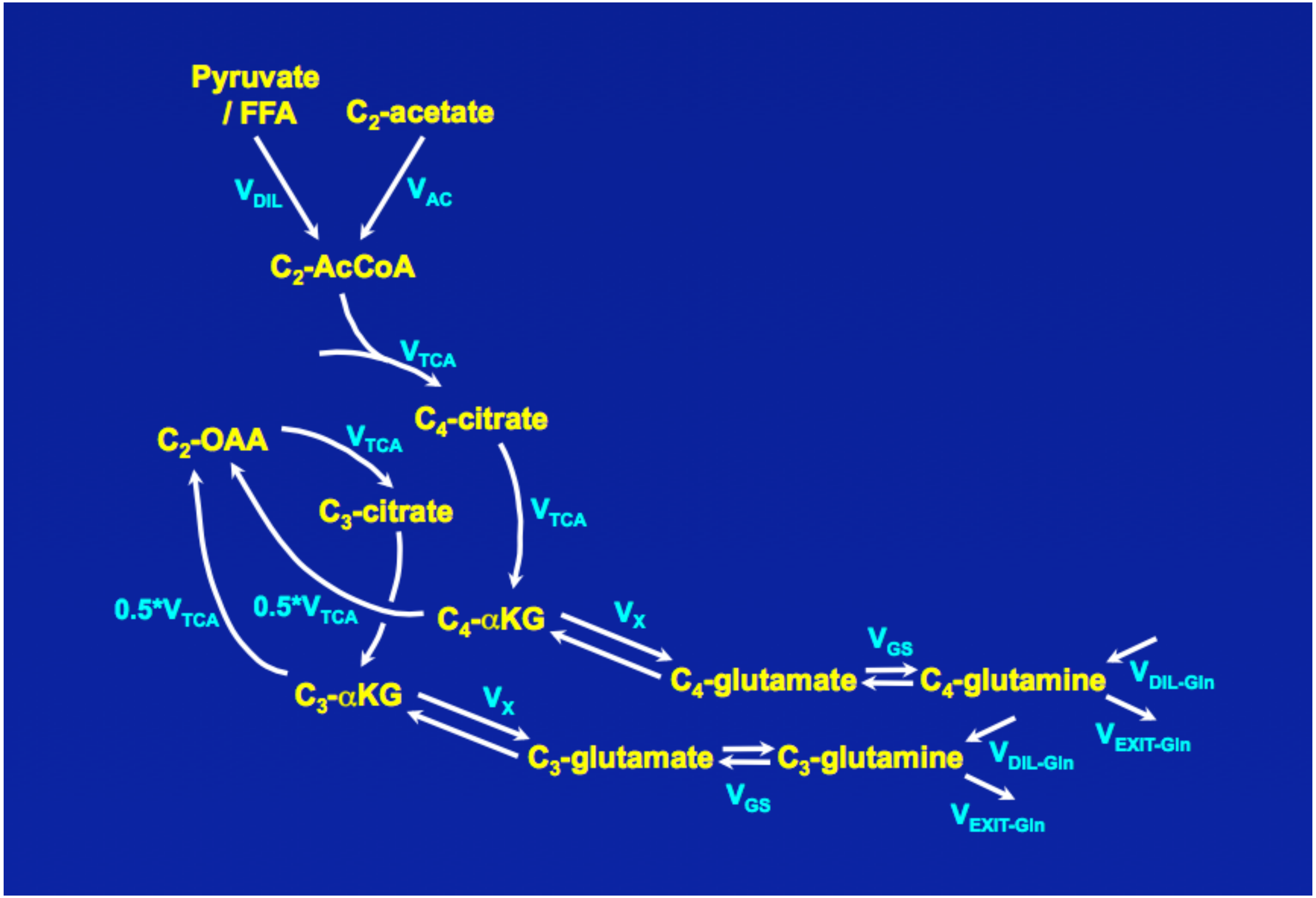


Fig. 5. Metabolic modelling

	WT (n = 6)	UCP3-TG (n = 6)
V_{ATP} (μmol/g/min)	5.65 ± 0.27	4.55 ± 0.29 *
k_f (sec^{-1})	0.069 ± 0.01	0.060 ± 0.01
M'/M_0	0.768 ± 0.02	0.771 ± 0.01
$T_1'(P_i)$ (sec)	3.34 ± 0.14	3.94 ± 0.26
$[P_i]$ (μmol/g)	1.37 ± 0.07	1.30 ± 0.07
[ATP] (μmol/g)	3.36 ± 0.34	3.41 ± 0.53
[PCr] (μmol/g)	9.25 ± 0.87	9.98 ± 0.49

* $p < 0.03$

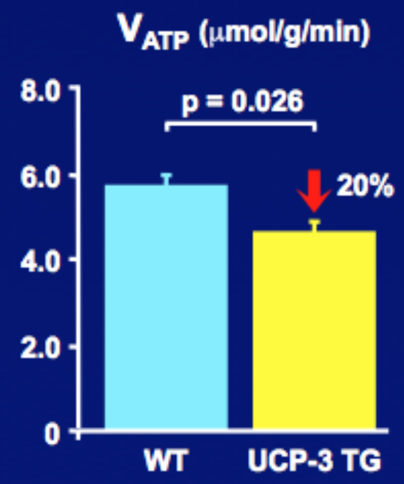


Fig. 6. Results: energy production via in vivo ATP synthesis (V_{ATP})

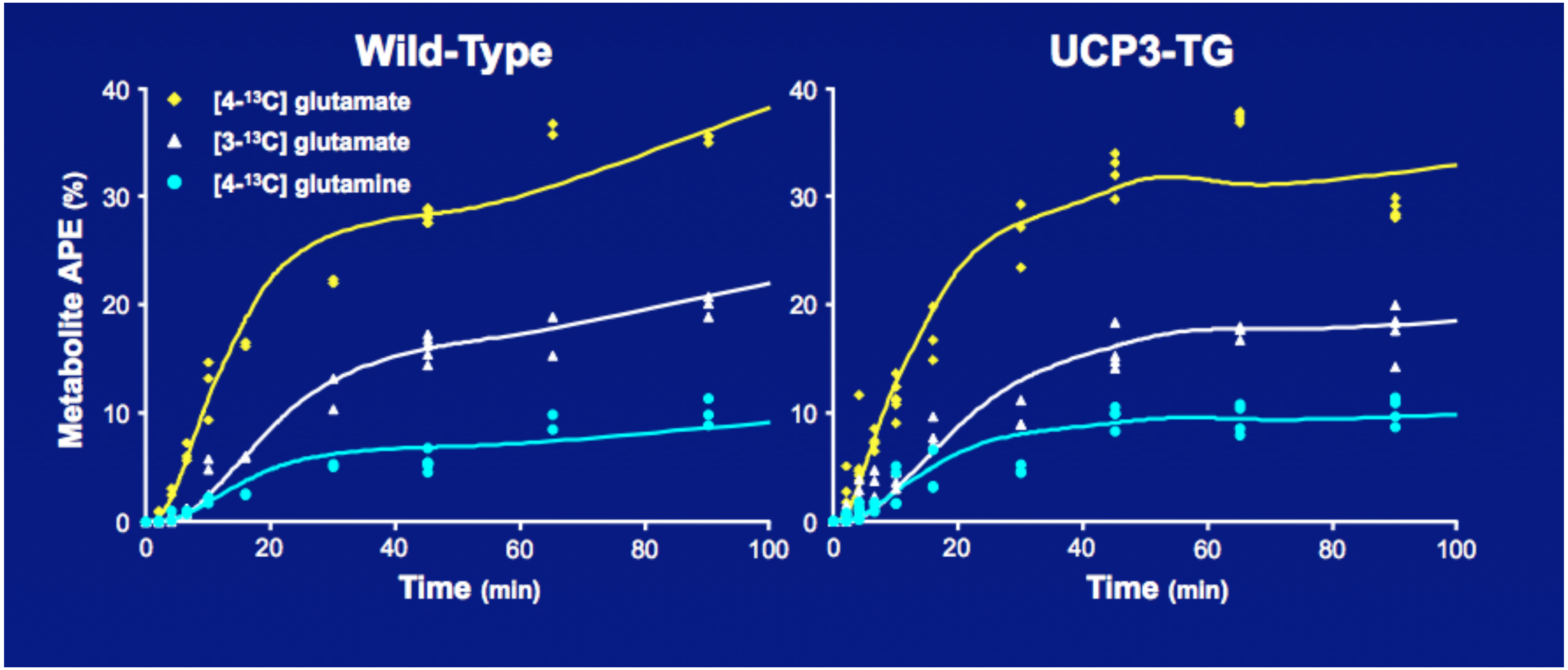


Fig. 7. Results: timecourses of muscle metabolite 13C-enrichment during the [2-13C]-acetate infusion.

	WT	UCP3-TG
V_{TCA} (nmol/g/min)	94.3 ± 5.8	120.3 ± 9.9 *
V_{AC} (nmol/g/min)	88.5 ± 6.8	100.8 ± 11.2
V_{DIL} (nmol/g/min)	5.8 ± 7.8	19.5 ± 15.8
V_{X} (nmol/g/min)	86.1 ± 23.1	211.1 ± 138.7
V_{GS} (nmol/g/min)	63.0 ± 6.2	88.6 ± 11.6 *
$V_{DIL\text{-}Gln}$ (nmol/g/min)	295.0 ± 20.1	305.3 ± 29.7

* $p < 0.03$

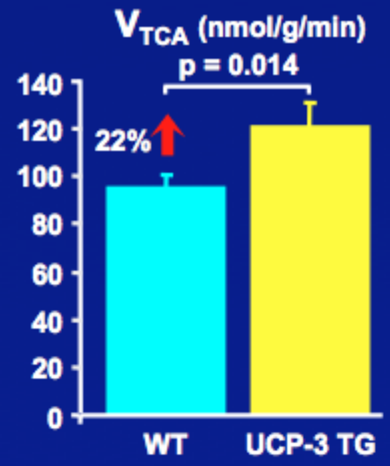


Fig. 8. Results: substrate oxidation via TCA (V_{TCA}) metabolic flux (Montecarlo analysis).