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**A <sup>1</sup>H MRS study of tumour overexpression of dimethylarginine dimethylaminohydrolase (DDAH) and response to taxotere**

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Dimethylarginine dimethylaminohydrolase (DDAH) is a cytoplasmic enzyme that metabolises endogenous inhibitors of nitric oxide synthase (NOS). Overexpression of DDAH indirectly increases nitric oxide (NO) production, and enhances C6 glioma growth and angiogenesis. NO has been shown to be both pro- and anti-apoptotic, with the nature and degree of response varying with both cell type and NO concentration.

The aim of this study was to investigate the utility of *in vivo* <sup>1</sup>H magnetic resonance spectroscopy to assess choline concentrations and water diffusion of tumours overexpressing DDAH, and their response to mitotic catastrophe/apoptosis following treatment with taxotere. Despite the increased growth rates of the DDAH overexpressed glioma clone (D26 and D27) tumours compared to mock transfected (M8) C6 gliomas, there was no significant difference in baseline choline concentration, implying no apparent link between choline metabolism and DDAH-enhanced vascularisation. The significantly longer baseline water T<sub>2</sub> and faster DDC in the M8 tumours is consistent with a greater extravascular space and lower degree of vascularisation, compared to the D26 and D27 tumours overexpressing DDAH which results in an enhanced angiogenic phenotype. The choline concentration of the M8, but not D26 or D27 tumours, increased following treatment with 15mg/kg taxotere. This suggests that overexpression of DDAH enhances apoptotic tumour response to taxotere, and was supported by subsequent detection of elevated caspase-3 activity by western blot. The data also suggest that increased NO production through overexpression of DDAH confers pro-apoptotic activity *in vivo*.