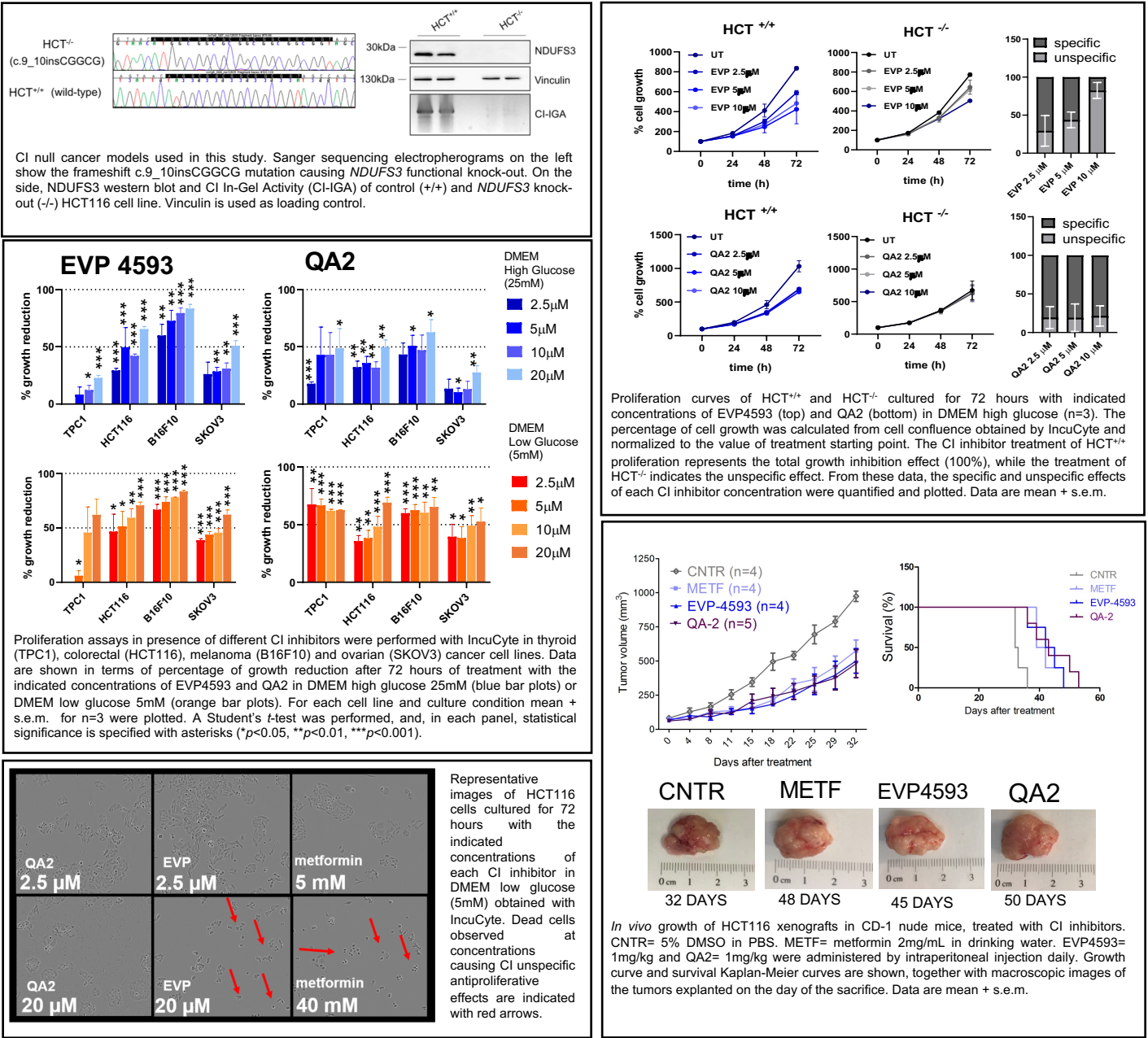


Mitochondrial complex I null cancer models reveal unspecific antiproliferative effects of complex I inhibitors

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INTRODUCTION: Respiratory complex I (CI) inhibitors are gaining momentum as anticancer strategy, mainly due to the epidemiological data linking the use of biguanidine metformin with lower incidence of neoplastic disease. Nonetheless, clinical trials specifically designed to test metformin efficacy in improving patient survival are revealing conflicting results. Currently, several novel CI inhibitors are available and show encouraging preclinical data, here we evaluate and compare their efficiency as anticancer agents, with the aim of optimizing the strategy of targeting CI.



CONCLUSIONS: Our data demonstrate antitumorigenic effect of two novel CI inhibitors, and prompt for caution when testing CI inhibitors in preclinical and clinical trials. In particular, optimal concentrations and the specificity of inhibitor action should be determined by taking advantage of CI null cancer models.