Warren Haynes Research Fellowship

Doctor Jordan Jones | Final Report

Research project

Plasma circulating tumour DNA and early phase clinical trials in glioma

Publications

Jones J et al. Plasma ctDNA enables early detection of temozolomide resistance mutations in glioma. Neurooncol Adv. 2024. Mar 19;6(1);vdae041

Jones J et al. Plasma ctDNA liquid biopsy of IDH1, TERTp and EGFRvIII mutations in glioma. Neurooncol Adv, 2024. Mar 4;6(1);vdae027

Drummond KJ, Spiteri M, Cain S, Jones J et al. Perioperative clinical trial reveals decreased synaptic signalling and altered metabolism as consequences of mutant IDH inhibition. Second round review Nature Medicine 2025 (in review)

Jones J et al. Pre and Post-operative serum miRNA can identify gliomas at risk of early progression. Submitted Journal of Neuro-oncology. 2025 (in review)

Presentations

2024 Royal Melbourne Hospital Research Conference

Project aims

Aim 1: Create a biobank of longitudinally collected plasma samples for circulating tumour DNA analysis

To date we have collected 326 blood samples from 138 patients diagnosed with glioma in one of the largest cohorts of longitudinal sampled blood reported in the literature. This addition brings the total number of blood samples to over 1000 in 250 patients since 2019. Collection and storage have been aided by members of the Royal Melbourne Hospital Biobank and Department of Surgery, University of Melbourne (Nguyen, Stylli and Fahkri). Cell free DNA has been made from the above samples for use in aim 2.

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Aim 2: Test samples from aim 1 for individual ctDNA mutations in a cohort of glioma

Samples from aim 1 have been used in multi-modal analysis including digital droplet PCR and next-generation sequencing. Consistent detection of the isocitrate dehydrogenase-1 (IDH1) mutation has been found in the plasma of patients who are known to have the mutation in the tumour tissue. Importantly, we noted reductions in plasma IDH1 concentration in response to surgery and IDH inhibition (IDHi), as well as elevations in the setting of tumour recurrence suggesting a role in tumour monitoring (Fig 1).

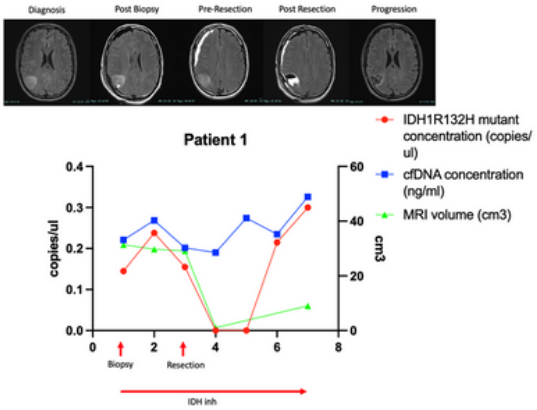

Fig 1. Linear graph showing IDH1 mutant copies (red dot) and cfDNA concentration (blue square) on left y-axis, right y-axis shows tumour volume (green triangle). Blood dates are on x-axis, time of biopsy and tumour resection shown and time on IDH inhibitor shown in long red arrow. Representative MRI images shown above graph.

The IDH1 ddPCR and comparison to tumour volume as seen in figure 1 has been completed for the 15 patients enrolled into the perioperative IDHi trial. We plan to combine these results with circulating methylation status to create a predictive model for LGGs treated with IDHi. We aim to publish this model as the first paper assessing circulating biomarkers and treatment response with IDHi.

Numerous samples from aim 1 have been used to validate a targeted next generation sequencing platform with collaborators at the VCCC (Wong). Validation of genes of interest (MSH2/6, TERTp, MGMT, EGFRv3) with ddPCR has been commenced and we expect the results from over 400 plasma samples in the next few months. We aim to compare tumour volumes, outcome data and development of tumour hypermutation following the results of ddPCR.

Aim 3: Provide key contribution to perioperative clinical trial performed at Royal Melbourne Hospital in collaboration with WEHI

The perioperative trial with the IDHi safusedinib was a major clinical and research project over the last 12 months. This was led by PI (Drummond) with recruitment now finished. We were responsible for the clinical care of these patients including in surgery and the pre and post-operative care as well as key research aims including consent, sample collection, data analysis/interpretation and manuscript writing. The manuscript is currently under revision.

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