



Deposited via The University of Leeds.

White Rose Research Online URL for this paper:

<https://eprints.whiterose.ac.uk/id/eprint/162285/>

Version: Accepted Version

Conference or Workshop Item:

Bruns, A-F, Rippaus, N, Droop, A et al. (2019) Chromatin remodelling to facilitate treatment resistance in glioblastoma. In: British Neuro-Oncology Society Annual Meeting 2019 (BNOS 2019), 03-05 Jul 2019, London, UK.

<https://doi.org/10.1093/neuonc/noz167.027>

© The Author(s) 2019. Published by Oxford University Press on behalf of the Society for Neuro-Oncology. All rights reserved. This is an author produced version of a conference abstract published in Neuro-Oncology. Uploaded in accordance with the publisher's self-archiving policy.

Reuse

Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

Chromatin remodelling of adult glioblastoma through standard treatment

Recent findings from our group, and the wider community, show that standard treatment does not impose an apparent bottleneck on the clonal evolution of adult glioblastoma (GBM), implying a lack of direct therapeutic opportunity. This does not negate the possibility that multiple treatment-resistance mechanisms co-exist in tumours, repeated across patients, making a combination of targeted therapies a potentially effective approach. We investigated whether treatment resistance may be driven by selection of cellular properties conferred above the level of the genome. Differential expression analysis was performed on 23 pairs of primary and recurrent tumours from patients who received standard treatment and had a local recurrence treated by surgery and second line chemotherapy. This revealed a treatment-induced shift in cell states linked to normal neurodevelopment. The latter is orchestrated by cascades of transcription factors. We, therefore, applied a bespoke gene set enrichment analysis to our paired expression data to investigate whether any factors were implicated in co-regulation of the genes that were altered through therapy. This identified a specific chromatin remodelling machinery, instrumental in normal neurogenesis. We validated our results in an independent cohort of 22 paired GBM samples. Our results suggest that the chromatin remodelling machinery is responsible for determining transcriptional hierarchies in GBM, shown elsewhere to have different treatment sensitivities such that their relative abundances are altered through treatment.