Glucocorticoids promote DNA repair to reduce efficacy of radiotherapy in Glioblastoma

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Steroid use in GBM correlates with poor outcome

Glucocorticoids (Gc) are steroid hormones and potent anti-inflammatory drugs. Gc, including Dexamethasone, are given to reduce cerebral oedema caused by brain tumours, such as glioblastoma, which is a highly aggressive form of brain cancer.

Aims and Experimental Design

To characterize the cellular response of GBM cells to Gc treatment at the transcriptional level using RNA-seq.
1) To measure genome wide transcriptional responses of GBM cells to steroids
2) To identify pathways regulated by steroids in GBM cells relevant to cancer
3) To investigate the effect of Gc on therapeutic efficacy

The study aims to investigate the GBM cell response to both the endogenous Gc, cortisol, and the synthetic Gc, Dexamethasone, which forms part of therapy.

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Genome wide transcriptional response to steroids in GBM

GBM (M059K) cells were treated for 4 hours with vehicle, low HC, high HC or Dex and analysed by RNA-seq.

In total, we identify 266 genes that are regulated by Gc in GBM cells.
- 37 genes were regulated by all 3 treatments
- 72 genes were only regulated in response to peak HC and Dex
- 140 genes were regulated in response to Dex alone

Gene ontology analysis of the Gc regulated genes using Enrichr identifies key pathways under Gc control in GBM, relevant to inflammation (green) and cancer (red).

Effect of steroids on cancer cell survival

M059K cells were irradiated (IR) or treated with chemotherapy, temozolomide (TMZ) following Gc or vehicle treatment. Cell survival was analysed by MTT assay (n=3).

References