Blocking aquaporins inhibits brain cancer cell migration

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High-grade glioblastoma (HGG) is the most common brain cancer and is among the most lethal and difficult to treat of all cancers. Treatment involves surgical resection of the glial-cell-based tumour, followed by radiation and chemotherapy, but is almost never curative because of the highly invasive nature of HGG within the brain. Patients with HGG also experience brain oedema, leading to serious clinical problems. This oedema is associated with aquaporin1 (AQP1) and AQP4, which belong to a family of integral-membrane-protein water channels. These channels have a range of additional cellular functions, including cell migration. Significantly, recent studies have shown that AQP1 and AQP4 are expressed on the surface of HGG cells and therefore might also have a direct role in HGG migration and invasion. As a potential treatment strategy for HGG, we assessed the effects of blocking aquaporins on HGG cells. We tested AqB013, a selective inhibitor of AQP1 and AQP4 (which blocks their cytoplasmic side) developed by us, against several HGG cell lines. We found that AqB013 markedly inhibited the migration of HGG cells in vitro at low micromolar concentrations. We then further analysed cellular responses to AqB013 by measuring real-time electrical impedance (using the xCELLigence platform), which reflects cell attachment and spreading. HGG cells displayed a dose-dependent reduction in impedance, indicating significant cellular responses as the inhibitor concentration increased. *In vitro* growth assays showed that this response was not due to inhibition of cell growth but rather to substantial alterations in cell morphology. Specifically, HGG cells treated with AqB013 were more rounded and more loosely attached to the culture dish plastic, consistent with the reduction in cell migration. Thus, we confirmed that AQP are expressed on the surface of HGG cells and showed that targeting these channels could be a novel approach to inhibiting HGG migration and invasion while simultaneously reducing HGG-associated brain oedema.