Targeting the tumor microenvironment in gliomas

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Abstract

The prognosis for patients with GBM remains poor and novel therapeutic approaches to address this unmet clinical need are urgently required. Recently we discovered that angiotensin II (AngII), a peptide involved in salt & water balance, is produced endogenously by GBM cells and drives proliferation via the type 2 receptor of AngII (AT_2R). Along these lines, we will illustrate an approach we followed to repurpose a peripherally restricted AT_2R antagonist, originally developed for the treatment of neuropathic pain, through the generation of a novel compound, A3E, that has greater efficacy in vitro and optimized CNS penetration with minimal toxicity [1]. Furthermore, we will illustrate other approaches that we are following to develop novel compounds that will be able to target the tumor microenvironment.

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[1] Perryman, R., et al., *Inhibition of the angiotensin II type 2 receptor AT2R is a novel therapeutic strategy for glioblastoma.* Proceedings of the National Academy of Sciences, 2022. **119**(32): p. e2116289119.