Network pharmacology and drug repurposing paves the way for precision medicine in DIPG patients

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(350 words)

Children diagnosed with diffuse intrinsic pontine glioma (DIPG) die within 12-16 months of their diagnosis with a median life expectancy of less than a year [1,2]. The anatomic location and infiltrative nature of DIPG, makes it not amenable to surgical resection leading to paucity of primary tissues. At the current moment, no effective therapy exists for DIPG, despite the fact that more than 200 clinical trials were performed over the last four decades, making radiation therapy the only standard treatment that temporarily decreases symptoms [3].

Given the genomic heterogeneity of DIPGs and lack of effective therapies, it is important to incorporate novel emerging platforms for treating children diagnosed with DIPG.

The current practice of targeting a single protein per disease or even combination therapy with drugs targeting single, mechanistically unrelated, and noncausal proteins has been proven to be ineffective and or insufficient especially in complex diseases that harbour robust biological networks such as cancer [4,5]. Instead, concerted network modulation with multiple mechanistically related drugs will be much more effective [6]. Here, we construct a de-novo DIPG-relevant disease network to identify suitable disease modules, drug targets and drug repurposing candidates and apply diagnostic assays to detect the patient specific perturbed modules. [7] and decide on the therapeutic strategy to correct such a module by network pharmacology.

This allows an approach that is not only personalized to the individual but also defines the fundamental biological process that should be targeted by a combinational therapy in this specific disease. Our goal is to improve patient survival by implementing biology-informed clinical interventions.

Keywords: DIPG, Network pharmacology, Precision oncology

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