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SNO abstract

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Characterisation of cell migration in low and high grade paediatric gliomas for assessment of the fibroblast growth factor receptor 1 (FGFR1) as a therapeutic target

INTRODUCTION: Our previous research in anti-migratory intervention in paediatric gliomas has highlighted the need for novel treatments to target tumour invasion based on individual tumour biology. Recurrent fibroblast growth factor receptor 1 (FGFR1) mutations in paediatric gliomas have been recently reported. Here we characterised cell migration in rare paediatric low-grade gliomas (pLGG) and high-grade gliomas (pHGG) and investigated FGFR1 as a suitable target for chemotherapeutic intervention. METHODS: Five patient derived pLGG cell lines (IN1520, IN1591, IN2017, IN2566, IN2866) and two established pHGG cell lines (SF188 and KNS42) were examined for their migratory ability in 2D and 3D migration models as well as for their responses to treatment with three different FGFR1 inhibitors. FGFR1 levels (both inactive and active) were assessed by immunofluorescence. We also carried out mutational analysis of exons containing codons 546 and 655,656 & 658. RESULTS: We established distinct migratory abilities in all cell lines. In 2D, random migration velocity values ranged from 0.06 to 0.12 μM/min (pLGG cell lines) and 0.1 and 0.2 μM/min (KNS42 and SF188). In 3D invasion assays the migration indices (MI) ranged from 0.28 to 0.54 (pLGG) and were 0.07 and 0.53 for KNS42 and SF188. All pLGG cell lines had higher levels of FGFR1 and activated FGFR1 compared to the pHGG cell lines. Three pLGG cell lines migrated faster after FGFR1 stimulation with FGF2. Significant anti-migratory effects were observed in pHGG with two inhibitors; however, inhibition elicited pro- or anti-migratory responses among the different pLGG cell lines. No mutations in the investigated exons were detected. DISCUSSION: We describe for the first time the migratory ability of patient-derived pLGG cell lines and their response to FGFR1 inhibition. Different responses in these cell lines highlights the importance of personalised treatment and a possible role of FGFR1 in paediatric glioma cell migration.