MB-83. OMEGA-3 FATTY ACIDS DHA AND EPA SUPPRESS ONCOGENIC PGE2 IN MEDULLOBLASTOMA
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BACKGROUND: Inflammation plays an important role in the tumor microenvironment where the pro-inflammatory prostaglandin E2 (PGE2) is an important player. Previous work from us show that medulloblastomas express high levels of COX-2 and mPGES-1, key enzymes for PGE2 production. The ω-3 fatty acids docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) show anti-inflammatory characteristics and exert anti-tumoral properties. Here we investigate the potential role of DHA and EPA in treatment of medulloblastoma and their effect on prostaglandins in vitro and in vivo.

METHODS: Cell viability and PGE2 levels were analyzed in medulloblastoma cell lines after DHA and EPA treatment. Also, prostaglandins and incorporation of fatty acids were evaluated in medulloblastoma xenografts treated with DHA or DHA/EPA. Prostaglandins were analyzed with LC-MS/MS and incorporation of fatty acids with GC-MS/MS. RESULTS: DHA and EPA exerted cell toxicity in a dose dependent manner in vitro. DHA reduced the PGE2 production in all cell lines investigated. In vivo, the treatment with DHA and the combination of DHA and EPA significantly increased the omega-3 index in tumors, erythrocytes and normal brain. The PGE2, and prostacyclin were significantly reduced in both treatment groups while thromboxane levels remained unchanged. The in vivo treatment was non-toxic.

CONCLUSIONS: Lowering PGE2 levels could mitigate the ongoing inflammation in the tumor microenvironment. We show that the ω-3 fatty acids exert toxic effects on medulloblastoma cells in vitro and reduce PGE2 both in vitro and in vivo. We propose that DHA and EPA are interesting candidates to improve current medulloblastoma therapy.