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Targeting ep2-mediated inflammation for neuroblastoma

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Prostaglandin E2 (PGE2), via acting on four G protein-coupled receptors (EP1-EP4), facilitates tumour cell growth, invasion and migration, and nurtures inflammation-enriched microenvironments to favour tumour angiogenesis and immune evasion. However, which EP receptor subtype is directly involved in the development and progression of neuroblastoma, a common pediatric cancer, remains largely unknown. We show the expression of EP2 receptor is highly correlated with neuroblastoma aggressiveness and acts as a dominant Gαs-coupled receptor mediating PGE2-initiated cAMP signalling in human neuroblastoma cells featured with high-risk factors. Genetic deletion of EP2 by CRISPR/Cas9 blocks the development of neuroblastoma. Pharmacological inhibition of EP2 by our recently developed small-molecule antagonists suppresses the progression of neuroblastoma, accompanied by broad anti-inflammatory, antiangiogenic, and apoptotic effects. Our proof-of-concept study suggests that the PGE2 signalling via EP2 receptor contributes to neuroblastoma malignancy and that EP2 inhibition by our drug-like compounds represents a feasible strategy to treat this deadly pediatric cancer.

Recent Publication

1. Sluter MN, Bhuniya R, Yuan X, Ramaraju A, Chen Y, Yu Y, Parmar KR, Temrikar ZH, Srivastava A, Meibohm B, Jiang J, Yang C-Y (2023) A Novel, Brain-Permeable, Cross-Species Benzothiazole Inhibitor of Microsomal Prostaglandin E Synthase-1 (mPGES-1) Dampens Neuroinflammation In Vitro and In Vivo. ACS Pharmacology & Translational Science (In Press)
2. Hou R, Yu Y, and Jiang J (2022) Prostaglandin E2 in neuroblastoma: Targeting synthesis or signaling? Biomedicine & Pharmacotherapy 156:113966.
3. Hou R, Yu Y, Sluter MN, Li L, Hao J, Fang J, Yang J, and Jiang J (2022) Targeting EP2 receptor with multifaceted mechanisms for high-risk neuroblastoma. Cell Reports 39:111000.

Biography

Jianxiong Jiang completed his Ph.D. in 2008 from Auburn University, USA. He is currently a tenured Associate Professor at the University of Tennessee Health Science Center, Memphis, Tennessee, USA. He has over 60 peer-reviewed publications that have been cited nearly 3000 times, and his current publication H-index is 27. He has been serving as an editorial board member of several reputed Journals, such as British Journal of Pharmacology, Inflammation Research, Neurochemical Research, and Experimental Biology and Medicine.

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