Anti-inflammatory strategy stops aggressive childhood cancer

May 29 2018, by Felicia Lindberg

Researchers at Karolinska Institutet and Karolinska University Hospital have discovered that an anti-inflammatory drug candidate inhibiting the prostaglandin E2 producing enzyme mPGES-1 in the tumour stroma reduces tumour growth in experimental neuroblastoma models. The findings are published in *EBioMedicine* and open for new treatment strategies for this aggressive childhood cancer.

"High-risk neuroblastoma is the most common and deadly cancer in infants. Novel therapies are highly warranted, in particular if they improve survival without adding adverse side effects," says Professor Per Kogner at Karolinska Institutet's Department of Women's and Children's Health, who led the study together with Professor Per-Johan Jakobsson at Karolinska Institutet's Department of Medicine, Solna.

Neuroblastoma is an aggressive nerve cell tumour which is diagnosed early, often before two years of age, and is stratified into different risk categories: low-risk, intermediate-risk and high-risk. Children with high-risk neuroblastoma receive intensive multi-modal treatment that has increased survival over the years but survivors both have high risk of life-threatening relapse and severe life-long side effects. Targeting of the stromal compartment has been suggested as a new strategy to increase survival further and to increase the quality of life of children who survive the disease.

Targeting benign cells

"We found that the dominant cell type in the tumour stroma, benign cancer-associated fibroblasts, were the main producers of prostaglandin E2 in neuroblastoma," says Anna Kock, Ph.D. at the Department of Women's and Children's Health and first author of the study. "These normal cells support the growth of cancer cells and should be targeted since they are more genetically stable than the malignant cells, and therefore less prone to develop resistance."

Assistant professor Karin Larsson at the Department of Medicine, Solna, who has worked on the project for several years, explains:

"Prostaglandin E2 not only mediates fever and pain, but also drives inflammation in the tumours, promoting tumour growth. Inhibition of the enzyme mPGES-1, that catalyses the production of prostaglandin E2, resulted in reduced tumour growth in experimental neuroblastoma models."

The researchers believe that the finding could lead to improved survival with fewer side effects for children with neuroblastoma.

Begin to understand the mechanisms

"mPGES-1 is an emerging target for treatment of inflammation and pain with cardioprotective properties. NSAIDs, which result in reduced prostaglandin levels, have long been implicated as prophylaxis against certain cancers. Our present study pinpoints mPGES-1 in neuroblastoma and we now begin to understand the mechanisms behind its involvement in cancer growth," says Professor Per-Johan Jakobsson, who discovered mPGES-1.

More information: Anna Kock et al. Inhibition of Microsomal Prostaglandin E Synthase-1 in Cancer-Associated Fibroblasts Suppresses Neuroblastoma Tumor Growth, *EBioMedicine* (2018). DOI:

10.1016/j.ebiom.2018.05.008