Unsuccessful drug against anxiety opens a novel gateway for the treatment of cancer

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Unsatisfying drug for anxiety reveals scientists a promising novel anti-cancer drug target. Cancer cells have multiple ways to avoid apoptosis, programmed cell death the means by which organisms deal with defective cells. One defense is to produce quantities of phosphatic acid, a phospholipid constituent of cellular membranes.

Unlike other phospholipids, phosphatidic acid also acts as a signaling molecule for cells promoting cellular growth and preventing apoptosis. Finnish and Danish researchers have now shown that phosphatidic acid may well be a target molecule for novel anti-cancer drugs.

Siramesine is a drug molecule developed and synthesized by Lundbeck A/S for the treatment of anxiety. Its development was discontinued due to unsatisfying efficacy in clinical trials in 2002. Later professor Marja Jäättelä and co-workers at the Danish cancer institute discovered that siramesine effectively inhibits the growth of both cultured cancer cells as well as solid tumors in mice. Siramesine is known to bind sigma-receptors, which physiological role remains unknown, on the cellular surface and this interaction was also believed to underlie its anti-tumor actions.

Researchers at the University of Helsinki, Finland, lead by Professor Paavo Kinnunen, studied the interaction of this drug with different phospholipids using biophysical methods and different model cellular membranes. In addition a computer simulation was performed as collaboration with MEMPHYS, Odense, Denmark, to further their

understanding of this interaction.

"The key finding of our study was that siramesine avidly and specifically binds to phosphatidic acid", says MD Mikko Parry from Helsinki Biophysics & Biomembrane group at the Institute of Biomedicine, University of Helsinki.

"Importantly, this is the first time it's shown that a lipid second messenger can act as a drug target: it is a totally new mechanism of action and constitutes a novel paradigm for developing new, more effective anti-cancer drugs."

Source: University of Helsinki

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