ABSTRACT

Charles University
Faculty of Pharmacy in Hradec Králové
Department of Pharmacology & Toxicology
Student: Aigul Sagandykova
Supervisor: PharmDr. Martina Čečková, Ph.D.
Consultant: Dr. Mikko Gynther Ph.D.
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Nowadays cancer remains one of the most challenging health issues worldwide. Chemotherapy represents one of the essential approaches in the treatment of malignant diseases. However, multidrug resistance (MDR), a multifactorial phenomenon described as a loss of sensitivity of cancer cells to several diverse chemotherapeutic agents at the same time, often compromises the therapy outcomes. A well-known cause of MDR is an increased expression or/and an enhanced activity of efflux drug transporters of ATP binding cassette (ABC) superfamily, which has been found in many types of cancer.
In the last decade, an expanding body of literature suggested a new hallmark of cancer cells – inflammation. An inflammatory microenvironment potentiates tumorigenesis and upregulation of transporters. Moreover, several observations show that ABC transporters mediate the transport of some signalling lipids. This new insight provided possibilities for novel anti-inflammation approach of cancer treatment. Compounds that target the upregulated release of arachidonic acid and its proinflammatory products leukotrienes and prostaglandins, could represent an alternative treatment. In this study we aimed to find out whether the new "theoretical" strategy of general downregulation of ABC transporters overexpression can be achieved using two experimental compounds, LBG-10119 and JJKK-048, an *N*-methyl-*D*-aspartic acid (NMDA) receptor competitive antagonist and monoacylglycerol lipase (MAGL) inhibitor respectively, each in their own way interfere in lipid signalling pathway. We hypothesised that these compounds by restraining inflammation could increase the intracellular accumulation of efflux probes and elevate the antiproliferative efficacy of sorafenib. In this work, the hypothesis was evaluated using two mouse hepatocellular carcinoma cell lines.