ПАМ
Альянс компетенций
Парк активных молекул

PAM
Alliance of Competences
Park of Active Molecules

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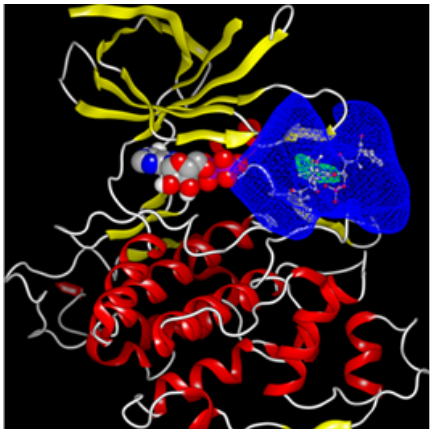
Dear colleagues,

Today cancer is becoming the priority problem. According to the World Health Organization research, the number of cancer cases is increasing rapidly and in 2020 it is expected to reach about 20 million per year.

The Alliance of Competence "PAM" is actively developing PAM-14 - "An Anticancer Compound". The project is currently at the stage of preclinical studies. This compound is supposed to interact with tyrosine kinases, by blocking their activity and inducing apoptosis, and with GSK3b serine-threonine protein kinase. Its hyperactivity is associated with tumorogenesis. Due to such multi-target mechanism, the compound is of interest as a promising anticancer drug.



The target and the space area used for docking. The molecule is presented as a ball-and-stick model, the outer edge is marked with blue bars, the internal outline with green.

The majority of chemotherapeutic agents are highly toxic with severe side effects. They are intended for intravenous administration and can provoke hypersensitivity and infusion reactions. In addition, patients often develop multidrug resistance to various anticancer drugs, which significantly complicates the treatment.

The report results show that unlike other anticancer drugs PAM-14 has a significantly lower toxicity. The intragastric administration of PAM-14 to mice at a dose of 7000 mg/kg of body weight did not cause death of the animals. This dose is more than 280 times higher than the daily effective dose of 25 mg/kg. The studies have shown that the drug is not mutagenic.

The compound might be effective even in cases of resistance to other antitumor drugs. Moreover, PAM-14 could be used in both: monotherapy and in combination with other anti-cancer chemotherapeutics, thus contributing to the treatment efficiency.

Antitumor, antiproliferative and antimetastatic properties of the drug were studied in vivo and in vitro. The results show that PAM-14 inhibits the growth of B16 melanoma cell culture and MCF-7 mammary gland adenocarcinoma. According to MTT-test data cell viability was radically lower after incubation with the drug than in the control. The distribution in cell cycle was notably changed: under the influence of PAM-14 there was a rapid accumulation of cells in G2+M phases. This effect was continuously maintained and finally led to cell death. The migration activity of cells after incubation with PAM-14 was reduced compared to the control. Statistically significant reduction of migration activity was observed after 48 hours of incubation with the drug ($p<0.05$).

In vivo research was carried out in mice with B16 melanoma and Lewis lung carcinoma. The administration of PAM-14 in dose 25 mg/kg led to decrease of tumor growth index, as well as to reduction of the number of lung metastatic lesions by 2-3 times.

Preclinical studies of the project PAM-14 "An Anticancer Compound" are continued in accordance with the Guidelines for conducting preclinical research of pharmaceutics products.

Best regards,
Rakhim Roziev.