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RESEARCH AREA

In Parkinson's disease, the progressive neuronal cell death is mainly mediated by the pathological activation of microglial cells. The voltage-gated potassium channel KV1.3 was shown to play a crucial role in this process due to a selective increase in its expression and its disease-specific phosphorylation. We found that these channels are located and phosphorylated in specific membrane microdomains. Since KV1.3 also has numerous physiological functions, such as in lymphocyte activation, fewer side effects are expected by targeting its inhibitor to these disease-specific membrane microdomains. By hampering the KV1.3-dependent pathological microglia activation with the targeted inhibitor, the amount of inflammatory cytokines produced and the rate of consequent neuronal death can be decreased. Functional consequences of KV1.3 in Parkinson's disease are investigated by molecular biological and immunological methods, confocal microscopy and flow cytometry in mouse microglial cells. To examine the effects of membrane lipids on KV1.3 gating we use two-electrode voltage-clamp fluorometry, with which the voltage-sensor and pore domains of the channel can be tracked simultaneously.

TECHNIQUES AVAILABLE IN THE LAB

Basic cell biological, molecular biological and immunological techniques (cell culturing, transfection, immunofluorescence labeling, Western blot, design of point mutations, cloning, DNA and RNA synthesis, ELISA), electrophysiological methods (patch-clamp, two-electrode voltage-clamp fluorometry, RNA microinjection into frog oocytes), quantitative fluorescence methods (spectro-fluorometry, flow cytometry and confocal laser scanning microscopy), and animal models are applied in this research.

SELECTED PUBLICATIONS

Kovacs, T., Kurtan, K., Varga, Z., Nagy, P., Panyi, G., **Zakany, F.** (2023) Veklury® (remdesivir) formulations inhibit initial membrane-coupled events of SARS-CoV-2 infection due to their sulfobutylether-β-cyclodextrin content. **Br J Pharmacol 180(16):** 2064–2084.

Zakany, F., Mandity, I., Varga, Z., Panyi, G., Nagy, P., Kovacs, T. (2023) Effect of the lipid landscape on the efficacy of cell-penetrating peptides. **Cells 12:** 1700.

Kovacs,T., Nagy, P., Panyi, G., Szente, L., Varga, Z., **Zakany, F.** (2022) Cyclodextrins: Only Pharmaceutical Excipients or Full-Fledged Drug Candidates? **Pharmaceutics 14:** 2559.

Kovacs, T., Sohajda, T., Szente, L., Nagy, P., Panyi, G., Varga, Z.,* **Zakany, F.*** (2021) Cyclodextrins exert a ligand-like current inhibitory effect on the KV1.3 ion channel independent of membrane cholesterol extraction. **Front Mol Biosci 8:** 735357. *Contributed equally

Zakany, F.,* Kovacs, T.,* Panyi, G., Varga, Z. (2020) Direct and indirect cholesterol effects on membrane proteins with special focus on potassium channels. **Biochim Biophys Acta Mol Cell Biol Lipids 1865:** 158706. *Contributed equally