The 1st International Neuroinflammation Congress and 1st Student Festival of Neurosience

Shefa Neuroscience Research Center, Tehran, Iran, 11-13 April, 2017

The Neuroscience Journal of Shefaye Khatam

Volume 5, No. 2, Suppl 2

Oral Presentation

Functional Role of The K2p Potassium Channel Task-3 in A Syngeneic Murine Glioma Model

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***Published:* 11 April, 2017**

Abstract

To investigate the effects of the two-pore-domain potassium (K2P) channel TASK-3 in a syngeneic murine model for malignant glioma. Malignant or high-grade glioma (WHO grade III and IV) are the most common and most aggressive primary brain tumors in adults. Despite aggressive multimodal therapy, the outcome of patients with malignant glioma remains poor. However, recent phase I and II trials have shown promising results for immunotherapies. The potassium-selective K2P ion channel TASK-3 plays a key role in modulating T cell effector functions. TASK-3 has been shown to functionally impact survival in human glioma cells in vivo and in vitro. We used a syngeneic murine glioma model based on the GL261 glioma cell line. Intracranial injection of GL261 cells leads to development of brain tumors in C57BL/6 wildtype and TASK-3-/- mice. On day 29 after tumor cell implantation eight asymptomatic animals (n = 4 C57BL/6 and n = 4 TASK-3-/- mice) were taken for MRI investigation. Symptom-free survival of GL261 tumor-bearing TASK-3-/- mice was significantly longer as compared to C57BL/6 mice (31 days (29-33 days, 95% confidence interval) versus 23 days (20-26 days, 95% confidence interval); Log-rank test $P < 0.001$). On MRI, tumors of TASK-3-/- mice showed a clear tendency to have smaller volumes as compared to C57BL/6 wildtype mice (5,25 μm^3 vs. 15,48 μm^3, n.s.). The K2P ion channel TASK-3 plays an important role in local tumor control, as knockout mice exhibit a delayed onset of symptoms and a longer survival after tumor cell implantation. The mechanisms of these effects and the role of other K2P channels are currently under investigation.

Keywords: Glioma, Brain Tumors, Patient

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