

Monoterpenes are Powerful Modulators of K_{2P} Channels

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Abstract

K_{2P} potassium channels display constant conductance in the physiological membrane potential range and their activity is highly regulated by both chemical and physical modulators. K_{2P} channels' activity affects numerous physiological processes such as cardiac function, pain perception, depression, neuroprotection and cancer development. Terpenes are a large family of compounds, mostly produced in plants. Several monoterpenes were found to affect the activity of a variety of ion channels. To date, the effect of terpenes on K_{2P} channels has not been studied. Human K_{2P} channels were expressed in *Xenopus* oocytes and currents were measured using the two-electrode voltage clamp technique. Channels' activity was found to be highly affected by monoterpenes. The currents of $K_{2P2.1}$, and other mechanosensitive K_{2P} channels, were enhanced several fold by carvacrol, thymol and menthol. $K_{2P2.1}$ currents were decreased twofold by eugenol. The effect of monoterpenes was not limited to the known stretch-activated K_{2P} channels, as $K_{2P5.1}$ and $K_{2P18.1}$ currents were also elevated by up to 15- fold by carvacrol. Currents of $K_{2P3.1}$ and $K_{2P9.1}$ were twofold decreased by the same substance. Cinnamaldehyde elevated $K_{2P5.1}$ currents, but decreased $K_{2P18.1}$ currents. The influence on $K_{2P2.1}$ currents was indifferent to the phosphorylation state of the channel, and was mediated by a novel domain at the C-terminus, which contains a three arginines sequence. Our results demonstrate, for the first time, that terpenes might serve as powerful modulators of K_{2P} channels, and that the mechanism of action involves the C-terminus regulatory domain.

Speaker Publications:

1. "A regulatory domain in the $K_{2.1}$ (TREK-1) carboxyl-terminal allows for channel activation by monoterpenes"; *Mol Cell Neurosci*, 2020, 06 19;105:103496

[12th World Congress on Neuropharmacology](#); Webinar; June 29-30, 2020.

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Biography:

Eden Arazi had completed her master degree in Immunology at the Hebrew University, Israel, and worked for many years at several Israeli Biotech companies. Eden is currently in the last year of her PhD studies in Electrophysiology at the Ben-Gurion University, Israel.