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Synthetic Lead Compounds Modulate Activity of Large-conductance Ca^{2+}-activated Potassium Channels Expressed in *Xenopus Oocytes*

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Large-conductance Ca^{2+}-activated potassium channels (BK_{Ca}) are a widely distributed and play key roles in various cell functions. In nerve cells, BK_{Ca} channels shorten the duration of action potentials and block Ca^{2+} entry thereby repolarizing excitable cells after excitation. BK_{Ca} channel opening has been postulated to confer neuroprotection during stroke, and has attracted attention as a means for therapeutic intervention in asthma, hypertension, convulsions, and traumatic brain injury. Several natural and synthetic compounds including a steroid hormone, β-estradiol, have been identified as the activators of BK_{Ca} channels. Based on the structural features of the previously reported activators of BK_{Ca} channels, we designed several lead compounds, synthesized chemically, and tested their functional activity on cloned BK_{Ca} channels. The α subunit of rat BK_{Ca} channel was expressed alone or with different β subunits in *Xenopus* oocytes and the effects of the compounds were tested electrophysiological means. One of the lead compounds affected the activity of the α subunit of BK_{Ca} channel in a β subunit-specific manner. While the activity of BK_{Ca} channel α subunit was potentiated, the channel composed of α and β1 subunits were inhibited by this compound. We are currently investigating the mechanism of the β subunit-dependent effects and planning to localize the receptor site of the lead compound.