S58-3 Ion channels as potential targets of drugs development

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Ion channel, as well as GPCR, enzyme and transporter, is one of the members of functional proteins, which are the major drug targets in pharmacotherapy. Even though, drugs acting on ion channels are rather limited alongside of drugs acting on GPCR. Recently, researches for new developments of drugs acting on ion channels are gaining momentum because of the rapidly accumulating information about non-selective cation channels (TRP channels) and also the progress in high throughput screening system. It is particularly noteworthy that, in addition to ion channels in excitable cells, those in non-excitable cell membranes such as epithelium, endothelium, immune cells, osteoclastic/osteoblastic cells and chondrocytes or those in organelle are now considered to be potential targets of new drug developments. In non-excitable cells, where the expression of voltage-dependent Ca^{2+} channels is low and TRP channels are main pathways for Ca^{2+} influx, membrane hyperpolarization enhances Ca^{2+} influx and, thus, cell activities including proliferation and differentiation. Moreover, excess Ca^{2+} influx results in cell death. Ca^{2+}-activated K^+ (K_{Ca}) channels are subclassified into B(ig)K, I(ntermediate)K and S(mall)K channels. K_{Ca} channels are unique, since they are responsible for negative and positive feed-back mechanisms in excitable and non-excitable cells, respectively. The cutting edge of researches on ion channels, particularly on K_{Ca} channels as potential targets of new drug development, will be discussed with respect to their cellular functions, functional coupling with other proteins and related diseases, based on recent knowledge including results from our group.