1-LBS-19 Late-Breaking Session

BK_{Ca} channel inhibition decreases the proliferation of human hepatic stellate cells

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Hepatic stellate cells are liver-specific pericytes that play central roles in the development of liver fibrosis. During liver injury, hepatic stellate cells transdifferentiate from the quiescent phenotype into the myofibroblast-like phenotype, resulting in high proliferation and extracellular matrix production. Large-conductance Ca^{2+}-activated K^+ (BK_{Ca}) channels are expressed in many types of tissues and involved in the regulation of membrane potential, intracellular Ca^{2+} concentration, and cell proliferation. However, the involvement of BK_{Ca} channels on liver fibrosis remains unclear. In this study, we investigated the pathophysiological roles of BK_{Ca} channels in a human hepatic stellate cell line, LX-2. The mRNA expression analysis revealed that LX-2 cells highly expressed the α subunit of BK_{Ca} channels. In LX-2 cells, extracellular Ca^{2+} restoration in the presence of thapsigargin induced store-operated Ca^{2+} (SOC) entry, which potentially mediated by Orai/STIM channels. The SOC entry was significantly reduced by a specific inhibitor of BK_{Ca} channels, paxilline. In addition, the proliferation of LX-2 cells was clearly attenuated by paxilline. These results suggest that BK_{Ca} channels are functionally expressed in LX-2 cells and contribute to cell proliferation by regulating intracellular Ca^{2+} signaling.