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Regulation of Ca^{2+} Influx by Membrane Potential in Microglia

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Microglia are known to have an important function as brain macrophage during immunological processes, oncogenesis, and regeneration in the central nervous system (CNS). A wide variety of ion channels have been identified and characterized in microglia including inward rectifier K^+ channel (Kir), voltage dependent K^+ channel (Kv), Ca^{2+}-release activated Ca^{2+} channel (CRAC). Kv current was shown to play a direct role in maintaining the resting membrane potential of this non-excitable cell to near –45 mV. Recently, we observed that cytosolic Ca^{2+} was reduced by applying high concentration of KCl into the extracellular side of microglia. We hypothesis that the voltage dependent fluctuation of Ca^{2+} concentration reflect the Ca^{2+} entry through CRAC channels.

We added Ca^{2+}-sensitive fluorescent dye Fura-2 into the pipette solution of whole-cell patches to measure the membrane potential or current and free Ca^{2+} concentrations, simultaneously. Increasing the extracellular KCl concentration stepwise from 5 mM to 75 mM induced stepwise membrane depolarization and at the same time reduced the cytosolic Ca^{2+} in KCl concentration dependent manner. When the membrane potential was clamped at depolarizing voltages, Ca^{2+} concentration decreased. In contrast, Ca^{2+} concentration increased by clamping the membrane potential at hyperpolarizing voltages. There existed a linear relationship between clamped membrane voltages and Ca^{2+} levels. These results suggest that the voltage dependent fluctuation of Ca^{2+} concentration reflect the changes in the driving force for Ca^{2+} entry. The addition of CRAC channel blocker, 50 μM La^{3+}, reduced Ca^{2+} concentration implying that CRAC channel is the Ca^{2+} entry pathway in microglia. (Supported by Brain Science and Engineering Research Program from Korean Ministry of Science and Technology to S.C.)