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Relationship between Homeostasis of Intracellular Magnesium Ion and Cell Senescence

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Summary

Magnesium ion (Mg^{2+}) plays broad range of roles in human body, and the disruption of regulatory systems for Mg^{2+} homeostasis is observed in various age-related diseases such as cancer, diabetes, nervous diseases etc. The tight link between Mg^{2+} homeostasis and age-related diseases is caused by the multiple roles of intracellular Mg^{2+} such as DNA/RNA stability, metabolic regulation, signal transduction etc. Previously, using fluorescence probes for intracellular Mg^{2+} imaging methods developed by our group, we revealed that physiological stimuli and biological contexts induce the changes in intracellular [Mg^{2+}], and they regulate intracellular metabolism and signal transduction, and consequently impact cellular fates and phenotypes. In present study, mesenchymal stem cells derived from human bone marrow were cultured *in vitro* for about 100 days. Cells continuously cultured for more than about 90 days halted their proliferation and exhibited the morphological changes which is characteristic of senescent cells. Next, the convolutional neural network (CNN) model that predict culture day of human mesenchymal stem cells (hMSCs) *in vitro* based on the phase-contrast imaging was constructed for quantitatively estimating the degree of cellular senescence non-invasively. The learned CNN model accurately quantified the degree of cellular senescence, and it also can detect the chemically-induced cellular senescence. Next, the progression of cellular senescence in hMSCs at several concentrations of extracellular Mg^{2+} were observed for the investigation of Mg^{2+} effects on the progression of cellular senescence. The high concentration of extracellular Mg^{2+} suppressed the progression of naturally-occurring cellular senescence, and Mg^{2+} deficiency promoted the chemically-induced cellular senescence. Taken together, Mg^{2+} exhibits the anti-cellular senescence effects.