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Enhancing neurogenesis and angiogenesis with targeted delivery of stromal cell-derived factor-1 α by using a pH-sensitive polymer in a rat stroke model

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We hypothesized that delivery of molecules which regulate the microenvironment after cerebral infarction can influence regeneration potential after stroke. Stromal cell-derived factor-1 α (SDF-1 α) is a chemoattractant molecule that increases in the infarct region after stroke and induces neurogenesis, angiogenesis, neuroprotection, and stem cell homing. Thus, we evaluated the effects of targeted delivery of SDF-1 α by using a pH-sensitive polymer, a synthetic macromolecule with potential for targeted drug delivery in acidic conditions, to enhance therapeutic neurogenesis and angiogenesis in a rat model of permanent middle cerebral artery occlusion. First, the neurogenic and angiogenic potential of SDF-1 α was measured in in vitro and in vivo. We observed that SDF-1 α intracerebrally infused into the striatum increased BrdU/doublecortin-positive cells in the subventricular zone and vWF-positive microvessels and apoptotic cells in the ischemic border zone 7 days after cerebral ischemia. We then investigated the effect of a SDF-1 α -Cy5.5-loaded pH-sensitive polymer systemically administered 3 hours after onset. ELISA showed increased tissue levels of SDF-1 α in the ischemic region, indicating that the pH-sensitive polymer effectively delivered SDF-1 α into the ischemic region. In addition, optical imaging showed that Cy5.5 signal increased in the infarct region 24 hours after administration. Immunohistochemistry data showed that delivered SDF-1 α enhanced neurogenesis and angiogenesis, but did not influence cell survival or inflammation. The results of the present study show a novel approach to control the microenvironment by using targeted delivery of a polymer. SDF-1 α -loaded pH-sensitive polymers can be used as pH-triggered targeting agents and effectively modify the microenvironment to increase innate neurorestorative processes.

Biography

Dong Hee Kim is a PhD student at Samsung Advanced Institute for Health Sciences and Technology, Sungkyunkwan University. He is a Senior Researcher at Samsung Medical Center.

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