Magnetic delivered human CD133+ cells promote functional recovery in the rat spinal cord injury

INTRODUCTION:
Various cell-based therapies for Spinal cord injury (SCI) are reported; however their effect for regeneration after SCI are still limited and optimal cell source has not been determined. Recently, many commonalities between angiogenesis and neurogenesis have been identified. We focused the angiogenesis enhanced with cell transplantation as a factor for the spinal cord regeneration. Therefore, we examined CD133+ cell, a rare fraction of endothelial progenitor cell from human peripheral blood, as the therapeutic agent which can provide both neurogenesis and angiogenesis in the damaged spinal cord.

CD133+ cells were isolated from peripheral blood by magnetic separation, with the cell-specific antibody coupled to the magnetic beads. Accordingly, CD133+ cells with magnetic beads must be controlled by magnetic force. We established delivery system of CD133+ cells using extra-magnetic device.

The purpose of this study was to clarify the therapeutic effects of CD133+ cells on spinal cord contusion by intrathecal administration via lumbar puncture, and to clarify the efficacy of delivery of magnetic labeled CD133+ cells.

METHODS:
Contusion SCI was induced by IH impactor (200 kdyn) at T10 level in athymic nude rats. Human peripheral blood derived CD133+ cells(CD133 group; 1×10^5 in 50 µl/rat, n=5) or phosphate-buffered saline (PBS group; 50µl/rat, n=5) was administered into the subarachnoid space at L4/5 level immediately after SCI. Animals lies under the magnetic field, maximum 0.6T, generated from variable direct-current electromagnet.(CD133+M group; 1×10^5 in 50 µl/rat, n=5).

The hind-limb motor function of rats after spinal cord contusion injury was scored with the the BBB locomotor rating scale on days 1 to 7, and then, every week up to the sixth week.

Motor evoked potentials (MEPs) were recorded in the hamstring muscles following transcranial stimulation of the cortex at sixth week after injury. The responses to 20 stimulations, bandpass filtered at 0.5–2000 Hz, were collected using a commercially available system (Viking Quest). An epoch of 10 msec after stimulation was digitized at a sampling rate of 5 kHz. Base-to-peak amplitudes were measured at each recording.

Immunohistochemistry for descending nerve fiber in each groups were evaluated. Tyrosine hydroxylase(TH) positive fibers were presented at the rostral, epicenter and caudal levels.

BBB locomators rating scale scores were analyzed with repeated-measures analysis of variance at all time points and with the Mann-Whitney U test at each time point. Base-to-peak amplitudes of MEPs and the number of TH positive fibers were analyzed with the Mann-Whitney U test.

RESULTS:
The BBB locomators rating scale of rats after spinal cord contusion injury was gradually improved in each groups. After 3 week, the score of the experimental group demonstrates significant improvement compared with that of the other groups at every week up to the sixth week.

Base-to-peak amplitudes of MEPs in the experimental groups reveal significantly large than other groups. Immunohistochemistry for TH shows significantly large number of positive fiber at the caudal level.

DISCUSSION:
We demonstrated that the administration of human peripheral blood-derived CD133+ cells via lumbar puncture accelerated functional recovery of injured spinal cord in rat SCI model. Administration of CD133+ cells with magnetic delivery system has a therapeutic potential to a spinal cord injury model. That could be an optional less invasive treatment for spinal cord injury in the clinical settings.