Results: STB-HO blocked the anti-apoptotic gene BIRC5 and activated p53, p21 and the pro-apoptotic proteins Bim, Puma and p-Bad during early spontaneous differentiation. Moreover, STB-HO-pretreated differentiating hES cells did not give rise to teratomas following *in vivo*stem cell transplantation.

Conclusions: Our *in vitro* and *in vivo* results suggest a method for teratoma prevention in the context of PSC-derived cell transplantation. This novel MFP could break through the limitations of PSC therapy.

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DNA methyltransferase inhibition accelerates the immunomodulation and migration of human mesenchymal stem cells

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Introduction: DNA methyltransferase (DNMT) inhibitors regulate target gene expression through epigenetic modifications, and these compounds have primarily been studied for cancer therapy or reprogramming. However, the effect of DNMT inhibitors on the immunomodulatory capacity of human mesenchymal stem cells (hMSCs) has not been investigated.

Materials and Methods: Mixed leukocyte reaction was performed to determine the alteration in the immunomodulatory function of MSCs by the treatment of 5-azacytidine (5-aza), a DNMT inhibitor. Migration of MSCs toward inflammatory environment was detected by migration assay using transwell. Methylation array was cunducted to explore the immunomodulatory factors stimulated by 5-aza treatment. Physiological function of MSCs was finally determined using dextran sulfate sodium (DSS)-induce colitis model.

Results: In the present study, we treated hMSCs with 5-aza and confirmed that the inhibitory effects on mononuclear cell proliferation and cell migration toward activated T cells were increased. In methylation array, we observed that the promoters of immunomodulatory factors, *COX2* and *PTGES*, and migration-related factors, *CXCR2* and *CXCR4*, were hypomethylated after 5-aza treatment. In addition, we observed that the COX2-PGE_2 pathway is one of the main pathways for the enhanced immunosuppressive activity of hMSCs through 5-aza treatment. We also determined that the migration of hMSCs toward ligands for CXCR2/CXCR4 was increased after 5-aza treatment. Moreover, using an experimental colitis model, we showed that 5-aza pre-treatment could enhance the therapeutic effect of MSCs against immune-related diseases.

Conclusions: The treatment with a demethylating agent (5-aza) increased the immunomodulation and migration of hMSCs through the demethylation of target gene promoters.

References

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PR-domain containing protein 12 (*Prdm12*) is a downstream target of transcription factor *Zic1* during brain cell differentiation

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Introduction: Transcription factor *zic1* is an important regulator of neural plate patterning, formation of neural crest and cerebellar development where its main function is neuronal cell differentiation. Studies reported that *prdm* family is expressed in the nervous system of developing mice and zebrafish. However, the function of *prdm* in neurogenesis is still unclear. Here, we identified *prdm12* in *Xenopus* as a downstream of *zic1* transcription factor. We propose that *prdm12* is a novel and essential component of the *Xenopus* brain regulatory network downstream of *zic1*.

Materials and Methods: RT-PCR was performed by using Maxim RT-PCR Premix Kit (iNtRON). The mRNA sequence of the *Xenopus laevis prdm12* were amplified using PCR from stage 30 cDNA using a set of primers. RNA encoding *zic1*GR were synthesized in vitro with the Message Machine kit. One blastomere of 2-cell stage embryos were injected in the animal pole, with *zic1*-GR mRNA (0.5 ng), dominant negative TCF-GR, *zic1*MO (AAGTCTTCCAACAATGGGC AGCGAA), or *prdm12*MO (GCAGCACCGAGCCCATCATTAATTC). The embryos were cultured in 0.1X NAM. Embryos analyzed by *in situ* hybridization To identify the injected side, β-galactosidase mRNA was co-injected as a lineage tracer.

Results: The *prdm12* expression started from the gastrulation stage (stage 9) and continues to be present until stage 40, the last stage examined in this study. In the earlier stage, *prdm12* was detected at at the animal hemisphere and in the neuro-ectoderm. *prdm12* specifically expressed in the pre-placodal ectoderm, trigeminal ganglion, along with the dorsal spinal cord. *prdm12* expression was more prominent in the midbrain, ventral part of the forebrain and hindbrain domain, neural crest, trigeminal ganglion. In the posterior region, the *prdm12* expression was restricted to the motor neuron of the spinal cord. In a large proportion of embryos injected with *zic1*-MO