NOX4 affects the stage of neural differentiation in the hippocampus through independent with an inflammatory contribution

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NOX4 affects the stage of neural differentiation in the hippocampus through independent with an inflammatory contribution

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It has been known that reactive oxygen species (ROS) regulate diverse complex cellular processes including angiogenesis, inflammation, differentiation, and proliferation. The family of NADPH oxidases (Nox) consists of 7 iso-forms with tissue- and cell type-specific expression profiles and Nox4 is constitutively active and predominantly produces H2O2 among these. It is known that the difference in the amount of hippocampal neurogenesis in the brain is compassionate, especially the continuous supply of high-fat diet (HF) has a very negative effect on hippocampal neurogenesis. Therefore, if NOX4 is specifically removed, it is expected that the expression of ROS to the brain would be limited, which could result in an increase of neurogenesis in NOX4 KO mice. To this end, Normal chow (NC) and HF were supplied to WT and NOX4 KO mice for seven weeks from 7 weeks, and their body weight and food intake were tracked. The volume of white adipose tissue (WAT) in animals, cell proliferation (Ki67) in walruses, hippocampal neurogenesis (DCX) and distribution of microglia (microglia) were observed by immunohistochemistry (IHC) after sacrificing animals. The results showed that NOX4 KO animals had a significant difference in weight gain over seven weeks in comparison to WT animals in the HF supply group, but there was no difference in NC. Interestingly, while the number of Ki67 positive cells in the hippocampus in NOX4 KO has been confirmed to increase compared to WT animals in the NC and HF, DCX has been confirmed to be very low in NOX4 KO. Although NOX4 is a critical gene for inflammatory control mechanisms, it is believed that it affects the stage of neural differentiation in the hippocampus through independent channels in the neurogenesis of the hippocampus.

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Keywords : NOX4, Inflammation, Cell proliferation, Neurogenesis, Hippocampus

PS-D-10

A novel gene expression signature for gastric cancer stemness

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Gastric cancer (GC) is the leading cause of cancer-associated death in Korea. In our previous study, we established GC stem cell-like murine cell line, namely S1M, lacking Smad4, p53, and E-cadherin. We identified 295 differentially upregulated genes in S1M cells from muti-omics analyses. Here, we tried to explore a novel gene expression signature associated with GC stemness by in-vivo transplantations of S1M cells in immunocompetent mice. From the 295 gene expression profile, we selected 30 candidate genes based on their clinical relevance for GC patients. S1M cells were transduced with cas9 and lentiviral gRNAs for these 30 genes and transplanted into subcutaneous tissues and spleens of immunocompetent mice. Genomic DNA was collected from the subcutaneous tumors or metastatic lesions in livers and the integrated gRNA were retrieved by PCR. The proportional changes of each gRNA in the retrieved gRNAs were evaluated by quantitative real-time PCR analysis. As a result, gRNAs for several genes including Spp1, Il1rl1 and Tmsb4x showed statistically significant reductions of proportions in both subcutaneous tumors and liver metastases, implying that these genes might contribute to GC tumorigenesis and metastasis. Especially, knockout of Tmsb4x in S1M cells showed a greater suppressive effect on the drug resistance and stem cell sphere forming ability in-vitro. Collectively, we discover the novel gene expression signature for GC stemness.

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Keywords : Immunocompetent, Gastric cancer, Metastasis

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Effects of e2f3 gene deletion in mice

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E2F transcription factors (E2Fs) are found in most cell types of the body and contribute to cell cycle progression, cell proliferation, differentiation, and apoptosis processes. These E2F transcription factors are potent regulators of a variety of genes, including cell-cycle checkpoints controlling genes in mammalian cells. Until now, eight members have been characterized, E2F1 to 8, and they are generally classified into transcriptional activators (E2F1-3) and repressors (E2F4-8). Some of these E2F family members have also a key role, in myeloid development and cardiac neovascularization. For transcriptional regulation, dimerization partner (DP) family and retinoblastoma (RB) family collaborate with E2Fs, by binding to E2F proteins. DP proteins identified DP1-3 form a heterodimer with an E2F, and allow it to bind to target promoters. A member of the E2F family, E2f3 plays a critical role in cell cycle and proliferation by targeting downstream, retinoblastoma (RB) a tumor suppressor family protein. The aim of this study, was to investigate the effects of E2F3 deficiency in vivo. We examined phenotypic abnormalities, by mutation of the E2f3 gene in mice. Complete deletion of the E2F3 was fully penetrant, in the pure C57BL/6N background. The E2f3 heterozygous mouse embryo developed normally without fatal abnormality. However, they exhibited altered phenotypes in body weight, growth rate, skeletal perfection, and grip strength ability. Findings suggest that E2F3 has a critical role in muscle and bone development, and affect normal mouse growth.

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Keywords : E2f3, Gene deletion, Phenotype

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The effect of Importin-11 is in the normal embryonic development

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Importin-11 (Ipo11) is a newl member of the human importin family of transport receptors which are well-known to mediate the nucleocytoplasmic transport of protein and RNA cargos. Despite its role in the transport of some proteins, we found that deletion of importin-11 affects normal embryonic development and govern embryo-lethality in mice. In this study, we for the first time produced a mouse line containing complete null mutation in Ipo11 gene utilized by gene trapping method. The Ipo11 deficient mouse embryos showed an embryonic lethal phenotype. The Ipo11 deficient embryos showed a reduced size at embryonic day 10.5 (E10.5) when compared with Ipo11 wild type or Ipo11 heterozygous embryos and died by E11.5. Whereas Ipo11 heterozygous mice were healthy and fertile, and there was no detectable abnormality in their appearance when reviewed. In the X-gal staining with the Ipo11 homozygous or Ipo11 heterozygous embryos, strong X-gal staining positivity was detected systematically in the whole mount embryos at E10.5, although almost no X-gal positive signal was detected at E9.5, indicating that the embryos die soon after the stage of Ipo11 expression in the embryos. These results indicate that Ipo11 is critical for the normal embryonic development in mice indicating its novel role.

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Keywords : Ipo11, Gene deletion, Mouse