IL-18 levels were significantly ($p < 0.05$) increased in 1.0×10^5 eAD-MSCs when compared to those in monolayer eAD-MSCs. CCL2 levels were also significantly ($p < 0.05$) increased in 2.0×10^5 eAD-MSCs when compared to those in monolayer eAD-MSCs.

Conclusions: Angiogenesisis the physiological process through which new blood vessels will be formed from pre-existing vessels. Angiogenesis is a normal and vital process in growth and development. It is also important for wound healing and the formation of granulation tissue. VEGF has been demonstrated to be a major contributor to angiogenesis. It can increase the number of capillaries in a given network. Second, IL-6 plays multiple roles in angiogenesis and vascular remodeling. IL-8 can also enhance endothelial cell proliferation, survival, and MMP expression in CXCR1- and CXCR2-expressing endothelial cells and regulated angiogenesis. IL-18-mediated angiogenesis depends on Src and Jnk. Inhibitors of Src and Jnk can block IL-18-induced HMVEC chemotaxis, tube formation, and angiogenesis in Matrigel plugs. Lastly, CCL2 regulates angiogenesis via activating Ets-1 transcription factor. In this study, we observed that angiogenic factors such as IL-6, IL-8, IL-18, VEGF, and CCL2 were expressed under spheroid formation of eAD-MSCs. Our results suggest that angiogenesis function of eAD-MSCs is increased under spheroid formation.

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Regulatory Mechanisms of Glucocorticoid on BACE1 Expression and Amyloidogenesis in SK-N-MC: Involvement of Lipid Raft Dependent cAMP-CREB Pathway

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Introduction: Non-genomication of glucocorticoid has diverse signaling pathways which can suggest novel mechanism of glucocorticoid on Amyloid β (Aβ) production in AD patients leading to finding the new therapeutic target. Here, we investigated the non-genomic effect of glucocorticoid on Aβ processing enzymes as well as Aβ production and demonstrated detailed mechanism how glucocorticoid controls amyloidogenesis.

Materials and Methods: Neuroblastoma SK-N-MC cells were used. Western blot analysis, immunocytochemistry, immunoprecipitation, cAMP parameter assay, chromatin immunoprecipitation, and polymerase chain reaction were done in this study.

Results: Cortisol-BSA treated in SK-N-MC augmented expression of BACE1 (Beta-site Amyloid precursor protein Cleaving Enzyme 1) and the level of CTF-β (C-Terminal Fragment β ofAPP) in a time-dependent manner. RU486, nuclear glucocorticoid receptor blocker, treated with cortisol-BSA did not down regulate BACE1 expression and CTF-β level indicating that non-genomic signaling does not overlap with classical pathway. The interaction of membrane glucocorticoid receptor (mGR)and Gαs was enhanced when bound to cortisol-BSA in SK-N-MC showing that cortisol-BSA is highly associated with plasma membrane signaling. Our data showed binding of mGRα and Gαs co-localized in lipid raft, blocked by the lipid raft disruptor MβCD. Cortisol-BSA augmented cAMP level and PKA nuclear translocation which was blocked by adenylyl cyclase inhibitor, SQ22536. Furthermore, PKI 14/22amide, specific PKA inhibitor, down regulated phosphorylation of CREB induced by cortisol-BSA. Sustained phosphorylation of CREB up-regulated the BACE1 expression binding to CRE site of BACE1 promoter and inhibiting phosphorylation of CREB significantly downregulated amyloidogenesis.

Conclusions: Cortisol-BSA bound mGR stimulated BACE1 upregulation via interaction with Gαs and induced c AMP-PKA-CREB pathway depending on lipid raft, followed by amyloidogenesis.

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Ephrin B2-induced Sirt3 expression suppresses hMSCs senescence via MnSOD-mediated scavenging mitochondrial ROS

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Introduction: Though expansion of human mesenchymal stem cells (hMSCs) *in vitro* is inevitable for clinical use, their limitation of replicative capacity is an obstacle in challenging hMSCs for regenerative medicine. Disruption of mitochondrial reactive oxygen species (mtROS) homeostasis is a key factor of inducing hMSCs senescence, and consequently to develop the approach of preventing mtROS accumulation will help to prolong the conversion into senescent state of hMSCs.

Materials and Methods: Umbilical cord blood derived mesenchymal stem cells (UCB-MSCs) were provided by Medipost. UCB-MSCs were grown in α-MEM with 10% FBS and 1% antibiotics. Protein expression was analyzed by western blot analysis with specific antibody. EphrinB

receptors and Sirtuin family gene expression were determined by Real-Time PCR using a Rotor-Gene 6000. Senescence-associated beta-galactosidase (SA-b-gal) activity was assessed with Senescence Cells Histochemical Staining Kit (Sigma-Aldrich). MitoTempo was used as a mitochondria-targeted superoxide dismutase (SOD) mimetic. mtROS level of UCB-MSCs was stained with MitoSOX and analyzed by flow cytometry.

Results: In this study, we observed that the expression of ephrinB2 and its receptor, EphB2, was regulated reversely during serial culture expansion of hMSCs. Activation of EphB2 by treatment with ephrinB2-Fc dose-dependently decreased the SA-β-galactivity and expression of p21 and p27, cellular senescence markers. EphrinB2-Fc increased the expression and mitochondrial translocation of Sirt3, a major mitochondria NAD^+-dependent deacetylase. Knock down of *Sirt3* by siRNA transfection inhibited the effect of ephrinB2-reduced senescence of hMSCs. EphrinB2-Fc lead to nuclear translocation of Nrf2, and Sirt3 expression was regulated by Nrf2 transcripional activity dependent manner. Among the Sirt3 target genes, ephrinB2-Fc increased the expression of MnSOD, an mtROS scavenger, and reduced mtROS level of hMSCs. Furthermore, ephrinB2-induced Sirt3 increased MnSOD activity by deacetylation at lysine 68 residue.

Conclusions: EphB2-mediated signaling has a crucial role in maintaining replicative ability of hMSCs and EphB2 receptor can be a novel hMSCs marker for optimization of therapeutic use of hMSCs in regenerative medicine. In conclusion, these results indicate that ephrinB2-induced prevention of senescence progression is facilitated by MnSOD-mediated mtROS scavenging through EphB2-Nrf2-Sirt3 signaling pathway.

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Transcriptomics of neurogenesis in chronic RF-exposed hippocampus

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Introduction: The issue of possible neurobiological effects of the radiofrequency (RF) electromagnetic fields (EMF) emitted from mobile phone is highly controversial and yet the molecular consequences of RF exposure are poorly understood. Since previously we have reported the beneficial effect of chronic RF-EMFs on brain with Aβ pathology[1,2]. We investigate the chronic effect of radiofrequency electromagnetic fields on some of gene transcription in hippocampus in this study.

Materials and Methods: Young and aged female C57BL/6 mice at 2 months and 12 months of age were exposed to a 1.95 GHz EMF at a specific absorption rate (SAR) of 5 W/kg or sham condition for 8 months. We investigated age-dependent gene expression profile changes occurring in the hippocampus using whole gene microarray approach. Global gene expression profiles of hippocampus from RF-exposed and sham-exposed mice were analyzed by hierarchical clustering.

Results: We selected presence of aging-related genes from sham-RF exposed mice at 10 months and 20 months of age comparing gene expression profiles of hippocampus obtained from normal mice at 3 months age. Cluster analysis reveals chronic RF exposure showed similarities between young mice and aged mice against aging-related genes that occur in sham-RF exposed mice. We identified 9 upregulated and 183 downregulated genes of total probes in both young and aged brain. And we identified 3 upregulated and 12 down-regulated genes in neurogenesis.

Conclusions: The study showed overlapping changes in hippocampus of young and aged mice following chronic RF-EMF exposure, suggesting altered expression of neurogenesis-related genes. Our study could provide a basis for further studies to clarify the neurobiological effects of RF-EMF exposure on brain

Acknowledgement: This work was supported by the IT R&D program of MSIP/IITP. [B0138-15-1002, Study on the EMF exposure control in smart society]

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Modulation of radiation response in endothelial cells by GGA

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Introduction: Geranylgeranylacetone (GGA),an acyclic polyisoprenoid, has been widely used as an anti-ulcer drug. It hasbeen reported that GGA has protective effect on the