P-119

Adipose Tissue-derived Mesenchymal Stem cells Ameliorate Severe Acute Pancreatitis via Downregulating ER stress and NF-κB Activity in Pancreatic Acinar Cells

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Endoplasmic Reticulum (ER) stress damaged the acinar cells function and even led to the apoptosis and inflammation response, respectively via ER stress and NF-κB signaling pathway. Aim of present study investigated whether TSG-6 secreted by human adipose tissue mesenchymal stem cells (hAT-MSCs) have potential therapeutic effects on pancreatic acinar cells (PAC). To evaluate effects of hAT-MSCs on PAC, the experiments were conducted in 6-well cell culture plate containing transwell inserts. hAT-MSCs or siRNA (control or TSG-6) transduced hAT-MSCs were plated into the bottom of the 6-well plate. Once hAT-MSCs adherent to the plate, isolated PAC were seeded onto transwell insert and stimulated by 100nM caerulein and 10mg/ml LPS for 12 hours. Subsequently, the level of ER stress markers were evaluated in primary PAC. In addition, NF-κB activity and ER stress-associated apoptosis were measured by western blot analysis and tunnel assay. Data were compared by one-way analysis of variance (ANOVA). The results showed both hAT-MSCs and hAT-MSCs transduced with control siRNA were significant alleviate ER stress makers in PAC. Interestingly, we found that treated TSG-6 siRNA hAT-MSCs were not significantly suppress ER stress makers measured by qRT-PCR and western blot analysis. Although treatment of naïve hAT-MSCs or hAT-MSCs transduced with control siRNA can significantly reduce the apoptotic ratio compare with positive group, but the similar effect was not observed in hAT-MSCs transduced with TSG-6 siRNA. These findings indicate that hAT-MSCs have a therapeutic effect on PAC through ameliorate ER stress and NF-κB signaling pathway.

***keywords*:** mesenchymal stem cells, pancreatic acinar cells, ER stress, NF-κB

P-120

Melatonin treatment during *in vitro* culture enhances *in vitro* fertilized porcine embryo development

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It has been reported that melatonin promotes metabolisms in porcine oocytes and acts as an antioxidant. Furthermore, when gametes are exposed to *in vitro* environment, the level of reactive oxygen species is much higher than those are *in vivo*. Thus, the aim of this study is to investigate the effects of melatonin on *in vitro* fertilized porcine embryos, and their subsequent development. Immature cumulus-oocyte complexes were collected and cultured for 44 hrs. After denuding, They were fertilized in modified Tris-Buffer Medium co-cultured with porcine sperm at the final concentration of 5×10^5 cells/mL. Then, zygotes were cultured in porcine zygote medium 5 supplemented with melatonin at increasing concentrations (0, 10^{-9}M, 10^{-7}M, and 10^{-5}M). The experiment was repeated 4 times. Statistical analyses were performed using one-way ANOVA with Tukey's Multiple Comparison Test, PRISM 5. Results are expressed as the mean ±SEM, significant at $P<0.05$. As the results, the concentration of 10^{-5}M significantly increased blastocyst formation rate compared with the control group (27.20 ± 2.49 vs. 16.15 ± 2.19, $P<0.05$), but not with other groups (10^{-7}M, 19.73 ± 0.53; 10^{-9}M, 18.05 ± 3.51). There was no conspicuous effect on cleavage rate and blastocyst cell number among the groups. In conclusion, we suggested that treatment with 10^{-5}M melatonin positively promoted the blastocyst formation rate of porcine IVF embryos with no beneficial effects on their blastocyst cell numbers and cleavage rate. This study was supported by the National Research Foundation (#2015R1C1A2A01054373; 2016M3A9B6903410), Research Institute for Veterinary Science and the BK21 PLUS Program.

P-121

Chitosan nanoparticles(CNP) improve development competence of *in vitro*- matured porcineoocytes

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This study was carried out to investigate theprotective effect of chitosan nanoparticles (CNP) against hydrogen peroxide (H_2O_2)-inducedoxidative damage in porcine oocytes. Cumulus-oocyte complexes (COCs) derivedfrom the ovaries of slaughterhouse porcine underwent IVM with CNP (0, 10, 25,50 μg/mL). GSH was significantly higher in CNP25treated group than other groups and ROS reduction significantly in CNP25treated group than others groups. In parthenogenetic embryos, rates ofmaturation, cleaved and developed to blastocysts were significantly greater inCNP25 group (91.0, 90.0, and 36.5%, respectively) than groups. Higherconcentration of nanoparticles reduced the total cell numbers and percentagesof ICM:TE cells in parthenogenetic embryos. In cloned embryos, CNP25 group was significantly higher on maturation,cleavage and blastocysts rates (91.0, 90.2, and 30.1%) than other groups.Percentages of total cells and ICM higher in CNP25 group than other groups. In cloned embryos treated with chitosan with conc.25 (μg/mL) showed greater expression levels of POU5F1, DPPA2 andNDP52Il mRNA compared with control group. Our results demonstrate that chitosantreatment prior to IVM improves the development competence of porcine oocyte byreducing oxidative stress.

P-122

Successful Treatment of Severe Hypoglycemia Induced by Non-Islet Cell Tumors in Two Dogs

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Two dogs were referred for further examinations of hepatic and mammary tumors, respectively. At presentation, they showed lethargy, quadriplegia and abnormal mentation. Blood analyses showed severe hypoglycemia. Although prompt treatments were initiated, blood glucose concentrations did not restore within normal limit. Because onset of non-islet cell tumor hypoglycemia (NICTH) as a paraneoplastic syndrome was highly suspected, both cases received hepatic lobectomy and total mastectomy with ovariohysterectomy, respectively. Within 12 hours after surgery, the blood glucose concentrations of both cases were normalized even without the administration with dextrose solution. Histopathological examinations indicated hepatocellular adenoma and mammary carcinoma, respectively. Endocrine analyses on the serum at admission showed low serum insulin concentration and high serum concentration of insulin-like growth factor 2 in both cases. Based these findings, two dogs were confirmed to NICTH. Both cases remain alive without recurrence of hypoglycemia over 18 months. Previously, the diagnosis of NICTH has been described sporadically as case reports in veterinary literature, but there is no report describing successful treatment of NITCH in dogs. Two cases described herein show that rapid surgical intervention can have good prognosis in dogs with NICTH.