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Influence of THP-1 cells on endothelial cells tube formation in the presence of soluble factors derived from the placentas on early and late stage of pregnancy

Lvova T Yu, Stepanova O I, Okorokova L S, Beljakova K L, Selkov S A and **Sokolov D I**
D.O.Ott Research Institute of Obstetrics and Gynecology, Russia

Macrophages play an essential role in angiogenesis regulation. The aim of the research was investigation of THP-1 cells influence on capillary-like tube formation of endothelial cells EA.Hy926 (EC) at presence of soluble placental products obtained from healthy pregnant women on 9-11 weeks of gestation (n=20, group 1) and from healthy pregnant women on 38-39 weeks of gestation (n=20, group 2). EC were seeded on Matrigel-coated 24-well plates (BD, USA) at a density of 150000 cells/well, also were added placental tissue supernatants and 2,5% fetal bovine serum. To part of wells THP-1 cells were added (250000 cells/well), to part of wells - the cultural medium without THP-1 cells. Tube formation was assessed 24 hours later using microscope AxioObserver Z1. Addition of THP-1 cells to the EC cultivated in the presence of soluble placental products of group 1 resulted in increasing of tube length and reducing of tube number, while in the presence of soluble placental products of group 2 addition of THP-1 cells did not lead to changes in length and number of tubes. In monoculture system and in co-culture system were established increasing of tube length in the presence of soluble placental products of group 2 compared to group 1. Our data suggest that THP-1 cells can modulate tube formation of EC in the presence of soluble placental products. Obtained data may reflect the influence of monocytes/macrophages on EC tube formation in placenta at different stages of physiological pregnancy.

lvov_spb@mail.ru

Fine-tuning of host immune responses: A tale of adeno-vector expressing hepatitis C virus antigen NS4

Shakti Singh, Satish Vedi, Wen Li, Subodh Kumar Samrat, Rakesh Kumar and **Babita Agrawal**
University of Alberta, Canada

Non-replicative adenoviral vectors expressing antigens induce strong cellular and humoral immune responses, and are the basis of several vaccines being developed. The critical role of both route and doses of immunization is still unknown. Hepatitis C virus (HCV) leads to chronic infection in the majority of infected patients due to failure or inefficiency of the immune responses generated, but can be resolved in those who mount strong immune responses directed against various structural and non-structural antigens of HCV. In this study, we sought to analyze the influence of both route and dose of immunization by non-replicative recombinant adenovirus expressing HCV NS4 protein (rAd-NS4) on antigen specific cellular and humoral immune responses, and their role in viral clearance. Female C57BL/6 mice were immunized with various doses of rAd-NS4 via intramuscular (i.m.) or intraperitoneal (i.p.) route. The induction of antigen specific antibodies, T cell proliferation and pro-inflammatory cytokine responses in both spleen and lymph nodes and their role in the clearance of Vaccinia-HCV chimeric virus in a mouse challenge model were evaluated. Our results show that an optimum dose of adenovirus vector (2x107 PFU/Mouse) administered by i.m. route induces high T cell proliferation, granzyme B-expressing CD8+ T cells, pro-inflammatory cytokines such as IFN-γ, TNF-α, IL-2 and IL-6, and antibody responses that can significantly reduce the Vaccinia-HCV viral load in the ovaries of female C57BL/6 mice. Interestingly, immunization by i.m. route induces lower adeno vector antigens specific neutralizing antibodies compared to i.p. route. Our results clearly demonstrate that recombinant adenovirus vector can induce strong humoral and cellular protective immunity against HCV-NS4 antigen, and that immunity is intricately controlled by route and dose of immunizing vector.

shakti.singh@ualberta.ca