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2. **Title**

   The Effect of Smoking on the Mechanism of the Preeclamptic Pathogenesis: The Possibility of Intervention of Smoking on the Poor Placentation Using Model Mice and Cell Cultivation

3. **Period**

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4. **Summary**

Although the effect of smoking on hypertensive disorders of pregnancy is favorable, it is known to cause vascular disorders in the uteroplacental circulation, resulting in fetal growth restriction and abruptio placentae, and smoking cannot be recommended for pregnant women. Therefore, this study aims to investigate the effects of nicotine, a major component of smoking, on the pathogenesis of hypertensive disorders of pregnancy and to detect some substances related to nicotine that can be used in pregnant women. We have investigated the effects of HMGA1 on EVTs since HMGA1 has a significant effect on the pathogenesis of hypertensive disorders of pregnancy. In the present study, we found that nicotine reduced HMGA1 mRNA expression in EVTs, which acts to promote proliferation and invasion of EVTs into maternal myometrium. These results suggest that nicotine might promote the pathogenesis of hypertensive disorders of pregnancy by suppressing normal placentation by inhibiting the proliferation and invasion of EVTs into the decidua and myometrium. However, this effect did not lead to an increase in intracellular proteins, and an increased expression of HMGA1 and HGMN1 proteins was observed in the nicotine-induced exosome from EVTs. HMGA1 is essential for normal placentation in the nuclei; however, the effects disappear and is involved in the pathogenesis of hypertensive disorders of pregnancy in translocating to the cytoplasm, and may also have adverse effects on EVTs in the pericellular region. HMGA1 and HMGN1 in the exosome released by nicotine may have an inhibitory effect on the pathogenesis of gestational hypertension. In future, we will investigate the effects of HMGA1 and HMGN1 conjugated exosomes on the hypertensive disorders of pregnancy model mice. In addition, four proteins were found to be involved in the effects of nicotine on EVTs by proteosome assay. The effects of these proteins will be also investigated in the future.