1. No.
   2017G031

2. Title
   The Role of Nicotine acetylcholine receptors on human ES/iPS cells

3. Period
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4. Summary
   The effects of smoking on the fetus and stem cell differentiation are not fully understood. At first, we found that nicotinic acetylcholine receptor subunits of α3, α4, α7 and β4 were strongly detected in undifferentiated human ES/iPS cells. Next, we investigated the influence of nicotine on undifferentiated human iPS cells by using Clariom S Array and revealed that nicotine could change gene expression levels of metallothionein (MT) which are known as decreasing reactive oxygen species (ROS). The ROS production was significantly decreased at 72 h after nicotine administration even though the expression levels of MT genes were suppressed. On the other, a significant increase of ROS was found in human iPS cells with nicotine and α4 antagonist or mecamylamine compared to those with only nicotine. The number of undifferentiated human iPS cells was increased by nicotine administration, which was canceled by α4 antagonist. Under the condition of 0.003% H_2O_2, not 0.03% H_2O_2, the number of hiPSCs added nicotine was significantly higher than that in control groups without nicotine. At last, to clarify the relationship between ROS and cell proliferation, we cultured iPS cells with N-acethylcysteine (NAC). As observed with nicotine treatment, the cell number of iPS cells were significantly increased and the gene expressions of MT were significantly decreased in the cells cultured with NAC.

   In conclusion, nicotine could decrease ROS and enhance cell proliferation via α4 nAChR subunit in hiPSCs, which might provide new insights into the effects of nicotine on human stem cells and fertilized human eggs.