1. No.
   2021G012

2. Title
   Influence of smoking related factors on signaling pathways for cardiovascular development

3. Period
   2021-2023

4. Summary
   Maternal smoking during pregnancy is likely to compromise cardiovascular development *in utero*; however, it is unclear whether smoking-related factors directly influence the cellular signaling pathways that regulate cardiovascular development. To examine the effects of smoking-related factors on cardiovascular development, we developed two experimental systems using new fluorescent reporter zebrafish lines and mouse embryo rotation culture. The new endothelial reporter zebrafish lines were useful to visualize vascular network formation in various organs at different developmental stages. Inhibitors and activators of cellular signaling pathways caused abnormalities of vascular development in developing organs. We also examined the effects of smoking-related substances, such as hydrogen peroxide that caused severe developmental defects in zebrafish embryos. In addition, the rotation culture of wild-type and genetically-modified mouse embryos was performed. Inhibition of Notch signaling in the embryo culture resulted in vascular abnormalities similar to those in Notch receptor deficient mice, while the treatment with cigarette smoke extract did not have apparent effects on embryonic growth and organ development in our experimental condition. The experimental systems that we used in this project will help clarify direct effects of smoking-related factors upon embryonic cardiovascular development and relationship between maternal smoking and cardiovascular diseases.