1. No.
   2017T006

2. Title
   The molecular mechanisms of vascular inflammtion and atherosclerosis mediated by aryl hydrocarbon receptor

3. Period
   2017-2021

4. Summary
   Ischemic heart disease and stroke based on vascular inflammation and atherosclerosis keeps increasing in the world including Japan. Some reports revealed that smoking increases morbidity and mortality rates of ischemic heart disease and stroke. Arteriosclerosis is enhanced by chronic inflammation of endothelial cells. The aim of this study is to clarify the molecular mechanisms of a novel inflammation signals that exacerbate the vascular pathogenesis associated with atherosclerosis and pulmonary arterial hypertension (PAH).
   AHR agonistic activity in serum was significantly higher in PAH patients than in healthy volunteers and was associated with poor prognosis of PAH. AHR makes a causal contribution to the pathogenesis of PAH, and activating a focal inflammatory response in the lung endothelial cells and promoting infiltration of immune cells in rats. In the paigen-diet fed ApoE KO mice, the accumulation of multinucleated giant cell were shown in the severe PAH model. We also revealed that IL-6 is basically essential for the pathogenesis of PAH using several rat models. We also suggest that CSC harboring AHR agonistic activity do not necessarily exacerbate the pathogenesis of PAH.
   In conclusion, AHR signals are essential for the vascular pathogenesis associated with PAH.