1. No.
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2. Title
   The effect of nicotine on the chronic inflammation mediated by autophagy dysfunction in cerebral endotherial cells

3. Period
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4. Summary
   cAMP has been reported to activate autophagy in vascular endothelial cells and suppresses chronic inflammation of blood vessels. However, it is unclear whether autophagy in the vascular endothelium is involved in the pathology of cerebral infarction and arteriosclerosis. Ischemia *in vitro* activated autophagy-related factors in vascular endothelial cells. High-fat dietary increased cerebral infarction size and increased inflammatory cytokines, along with decreased cerebral blood flow. Both CRTC1 and 2 were expressed in vascular endothelial cells. In the vascular endothelial-specific CRTC2KO mice, the neurological function after stroke was significantly poor, and angiogenesis was also reduced. In NVU, the permeability of BBB was enhanced by the decrease of p190RhoGAP-A in the endothelium. Since CRTC2 in the cerebrovascular endothelium contributes to autophagy, it was suggested that autophagy dysfunction is also associated. CRTC1 regulated miR-132, and miRNA-132 from neurons acted on TJ Claudin-1, TJAP-1 in cerebrovascular endothelial cells via the paracrine mechanism. We considered the importance of crosstalk between the cAMP-CRTC system and autophagy.

   Netosis is also a theme shared by this research group. Therefore, in order to investigate the association of NETosis in patients with cancer-bearing cerebral infarction, we examined the neutrophil / lymphocyte ratio (NLR) using the registry at Osaka University Hospital. Multivariate Cox proportional hazard models, adjusted for cancer type and stage, revealed that patients with high NLR (>15) had higher stroke risk than patients with low NLR (<5). NLR can be a predictor of ischemic stroke in cancer patients.

   For the treatment of cerebral infarction and cerebral arteriosclerosis, it is important to develop new therapies that activate autophagy in vascular endothelial cells.