1. No.
   2019Y004

2. Title
   Identification of active ingredients in the cigarette smoke extract that decrease the expression level of the tumor suppressor Pdcd4

3. Period
   2019-2021

4. Summary
   In this study, I tried to identify the ingredients in nicotine- and tar- removed cigarette smoke extract (CSE) that reduce the expression levels of Pdcd4. ACR, CA and MVK significantly decreased the expression levels of Pdcd4. In addition, to elucidate the mechanism how ACR, CA and MVK decreased the expression levels of Pdcd4, we investigated the effect of NAC, an antioxidant in cells. As a result, pretreatment with NAC did not significantly antagonize the effect of α, β-unsaturated carbonyl compounds. Moreover, ACR, CA and MVK significantly increased the intracellular glutathione level under the condition that the expression level of Pdcd4 protein was decreased. Furthermore, ACR, CA and MVK significantly reduced the migration ability of cells, and their effects were antagonized by NAC pretreatment. It has been reported that inhibition of NADPH oxidase reduced the amount of intracellular GSH, and the cytotoxic effects of ACR and MVK were mediated by NADPH oxidase. Although we pretreated with Apocynin, a NADPH oxidase inhibitor, it did not significantly antagonize the effect of ACR, CA and MVK to decrease the expression levels of Pdcd4. ACR, CA and MVK significantly reduced the Pdcd4 protein expression and their actions were not inhibited by treatment with NAC and Apocynin. Therefore, these α, β-unsaturated carbonyl compounds may not be through oxidation as a mechanism of decrease the expression levels of Pdcd4 protein, while these results suggest also not be affected by the intracellular glutathione level.