1. **No.**

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2. **Title**

   Analysis of SNPs of Zinc Finger Protein CASZ1 in Risk Control of Smoking Related Diseases

3. **Period**

   2016-2018

4. **Summary**

Previous studies have demonstrated that smoking induces aldosterone production, which activates MR and causes hypertension, CKD and cardiovascular disease. However, the underlying molecular mechanism of MR activation remains unknown. We recently identified CASZ1 as a novel mineralocorticoid receptor (MR) co-regulator through a biochemical approach with LC-MS/MS analysis. The purpose of this study was to clarify molecular mechanisms of MR activation through functional analysis of CASZ1. *In vitro* experiments showed that in renal tubule cells, CASZ1 associated with both MR and Mi-2/NuRD complex in aldosterone dependent manner and functioned as a corepressor of MR through histone H3 deacetylation activity of Mi-2/NuRD complex. Renal tubule specific Casz1 knockout mouse (KspCasz1-KO) have elevated blood pressure and increased urinary excretion of K compared with controls under DOCA/salt loading condition. We also demonstrated that the hypertension associated SNP in CASZ1 gene was related to enhancer activity. These data suggested that CASZ1 plays a pivotal role in MR activation.