Reviewer's report

Title: Genetic Variation of NEDD4L Is Associated with Essential Hypertension in Female Kazakh General Population

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Reviewer: Tomohiro Katsuya

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Li NF et al examined the association of genetic variants of NEDD4L gene and predisposition to essential hypertension in Kazakh population, resulted that two variants of NEDD4L were significantly associated with hypertension only in females. The advantage of this study is to use Kazakh population which has unique custom culture background and hood habit, especially high salt intake. The number of subjects examined seems to be enough to discuss the statistical significance between genotype and disease susceptibility. The statistical analysis was carried out appropriately, and the results presentation and discussions were feasible. The following comments are minor but should be responded correctly.

The characteristics of the participants should be described precisely. Especially, the amount of salt should be described or discussed in the comparison with other races, such as Han Chinese. This is a critical point to consider the function of NEDD4L in the pathogenesis of hypertension.

The mean age of the participants in this study is quite young to discuss the predisposition to hypertension in general population. Thus, the morbidity of hypertension and the mortality of cardiovascular disease in Kazakh population should be shown in forties to seventies.

The excess salt intake associates with not only hypertension but also obesity and diabetes. In the basic characteristics of cases, the frequency of obese, dyslipidemia and hyperglycemia were significantly higher than that in controls, suggesting that NEDD4# increased risk for volume retention or visceral obesity. These possibilities are also examined in the data analysis and discussion.