to less than 0.5 for aldosterone/MN below the PV was seen in unilateral disease. With regards to the six co-secretors, all had elevated cortisol/MN ratios of more than 2 on the affected side. Three had concordant results but the other three had discrepant results, with MN analysis suggesting unilateral disease and cortisol measurements suggesting bilateral disease. Two had undergone surgery with biopsy confirming unilateral disease that correlated with MN analysis. The third is under medical management. **Conclusion:** This is the first study evaluating the use of MN to determine lateralisation of aldosterone production in PA. Further studies are needed, but using MN may be a more reliable alternative to cortisol in the analysis of AVS before definitive surgery in particular in patients with cortisol co-secretion.

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Visualization of Ca Channel Blocker on Human Adrenal Tissue by Mass Spectrometry Imaging ~Its Predominant Distribution at Aldosterone-Producing Cells ~

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Primary aldosteronism (PA) is the main cause of secondary hypertension, accounting for approximately 5–10% of all hypertension. Amlodipine, a third-generation calcium channel blocker, is one of the most frequently administered pharmaceuticals medications of hypertension, binds specifically to Cav1.2, a calcium channel primarily localized in the cardiovascular system, and exerts antihypertensive effects through inhibiting calcium influx into the vascular smooth muscle cells. In addition, calcium influx also plays important roles in aldosterone production and amlodipine was also reported to influence *in vitro* functions of Cav1.3, a calcium channel involved in aldosterone secretion. Ca channel blockers were also reported to reduce plasma aldosterone concentration by some clinical studies although with mild degrees. However, *in vivo* effects of amlodipine to aldosterone secretion has remained virtually unknown. A novel technique "Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry Imaging (MALDI-MSI)" has been recently developed, which did make it possible to visualize non-labeled small molecules on tissue sections. Therefore, in this study, we firstly applied MALDI-MSI to visualize amlodipine on human adrenal glands including aldosterone producing adenoma (APA). We performed selective imaging of amlodipine using MALDI-MSI on the resected adrenal tissues from APA patients. Frozen sections containing whole representative tumor area were coated with a matrix called CHCA (α-Cyano-4-hydroxycinnamic acid) by deposition as a pretreatment. We subsequently analyzed and detected a precursor ion with MS at m/z 407.1 and then an amlodipine-specific ion with MS/MS at m/z 318.1. We also examined the concordance of amlodipine distribution obtained by this method with immunohistochemistry. Human resected adrenal tissues obtained from the patients APAs treated with and without amlodipine before adrenalectomy were examined. Periadrenal adipose tissues were also analyzed as a control tissue of non-aldosterone-producing tissues. Amlodipine was specifically detected and visualized only in the administered cases. Amlodipine was more abundantly detected in adrenal tissues than periadrenal adipose tissues. On the other hand, significant different was not detected between tumors and adjacent adrenal glands by semi-quantification using MALDI-MSI. In this study, we firstly visualized amlodipine directly in human tissue sections using MALDI-MSI. Increased accumulation of amlodipine in APAs treated with amlodipine did indicate direct effects of amlodipine on aldosterone production but further investigations are required for clarification between neoplastic and non-neoplastic aldosterone producing cells.

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Vitamin D Deficiency Induces Macrophage Pro-Inflammatory Phenotype via ER Stress-Mediated Activation of Renin-Angiotensin System

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Chronic inflammation and local activation of the renin-angiotensin-aldosterone system (RAAS) play a pivotal role in the pathogenesis and progression of diabetic complications. In patients with type 2 diabetes (T2DM), the prevalence of vitamin D deficiency is almost twice that of non-diabetics, and vitamin d deficiency nearly doubles the risk of developing hypertension and cardiovascular complications compared to diabetics with normal vitamin D levels. Interestingly, mice lacking the vitamin D receptor (VDR) in macrophages (KODMAC) develop renin-dependent hypertension, insulin resistance, and inflammation via up-regulation of macrophage ER stress. Macrophages also express all major components of the RAAS system. However, little is known about the regulation of macrophage-generated renin and its role in modulating the sequelae of VDR signaling in macrophage function and cytokine production. This study found that KODMAC macrophages and vitamin D-deficient macrophages have increased expression and secretion of renin, angiotensin II, ACE, and AT1 receptor and that adhesion, migration, and cytokine release were also increased. Inhibition of ER stress in KODMAC macrophages and vitamin D-deficient macrophages with 4-Phenylbutyric acid (PBA) reduced RAS gene expression and macrophage pro-inflammatory phenotype. Renin 1c gene deletion decreased macrophage