The role of the KCNJ5 potassium channel in aldosterone release

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Introduction: Primary aldosteronism (PA) is the most prevalent form of endocrine hypertension, due to autonomous aldosterone production. The two main causes of PA are aldosterone-producing adenome (APA) and bilateral adrenal hyperplasia (BAH), also called idiopathic hyperaldosteronism. Aldosterone, synthesized and secreted by the zona glomerulosa (ZG) of the adrenal gland, is physiologically regulated by Angiotensin II (AngII), potassium concentration [K^+], ACTH. The mechanisms that lead to the aldosterone hyperproduction are not completely understood. Recent studies revealed the presence of a few recurrent somatic mutations of the inwardly-rectifying potassium channel (KCNJ5) gene, coding for the K^+ channel KCNJ5. These mutations lie near or within the selectivity filter of the Kir3.4 channel, changing the normal Na^+/K^+ flow. Genotyping studies conducted on an Australian pedigree revealed the presence of functional single nucleotide polymorphisms (*SNP*) for KCNJ5 gene, such as Q282E, E246K and G247R

Patients (or Materials) and Methods: The functional aspects of these mutants were studied by applying the two-electrode voltage clamp technique on *Xenopus oocytes* expressing them. A Human H295R adrenocortical cell line was used as the experimental model to study the effects of the mutations on aldosterone release. These cells were transiently transfected with the *WT* KCNJ5 and the Mutant forms respectively, and the aldosterone release was evaluated using a radioimmunoassay, both in normal conditions and following depolarization with high extracellular K^+ and Ang II

Results: The Q282E and E246K KCNJ5 showed change in the selectivity of the channel, with Na^+ currents being observed in both of them. However, the G247R KCNJ5 behaved like the WT KCNJ5 channel. Differences were also observed in the levels of aldosterone release from H295R cells expressing the different mutations, the details of which will be presented in the poster

Conclusion: The findings from this work could help to clarify the normal role of wt KCNJ5 channels in the adrenal glomerulosa cells. The molecular mechanisms of mutant KCNJ5 channels would shed light on the underlying mechanisms involved in the aldosterone release in adrenal glands and thus the regulation of blood pressure

Disclosure of Interest: None Declared