We have previously reported the association of the R563Q mutation in the beta subunit of the ENaC in black and mixed ancestry patients with hypertension, and Liddle’s syndrome in the minority. The purpose of the study was to investigate the association of hypertension and Liddle’s syndrome, and the mutation within affected families.

The study was approved by the Research Ethics Committee of the University of Cape Town. After informed consent family members of affected persons with the R563Q mutation 29 (78.3%) had their blood pressure (BP) measured according to University of Cape Town. After informed consent family members of the ENaC was sequenced for the R563Q mutation. Only first degree relatives of the ENaC were sequenced for the R563Q mutation. Only first degree relatives of the ENaC were sequenced for the R563Q mutation. Only first degree relatives of the ENaC were sequenced for the R563Q mutation. Only first degree relatives of the ENaC were sequenced for the R563Q mutation.

Of the 37 affected persons with the R563Q mutation 29 (78.3%) had hypertension and 11 (34.3%) of the negatives (p=0.0002). Both the mean systolic and diastolic BP was higher in the R563Q positive individuals than negatives (table 1). Only 1 positive individual had unprovoked hypokalaemia.

In conclusion the R563Q mutation strongly associates with hypertension and 11 (34.3%) of the negatives (p=0.0002). Both the mean systolic and diastolic BP was higher in the R563Q positive individuals than negatives (table 1). Only 1 positive individual had unprovoked hypokalaemia.

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In conclusion the R563Q mutation strongly associates with hypertension in family members, but not Liddle’s syndrome. Further research is needed to define the prevalence of this mutation in our hypertensive population.

Key Words: Epithelial Sodium Channel, Hypertension, R563Q Mutation

P-217
THE R563Q MUTATION OF THE B-SUBUNIT OF THE EPITHELIAL SODIUM CHANNEL (ENAC) STRONGLY ASSOCIATES WITH HYPERTENSION
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We have previously reported the association of the R563Q mutation in the beta subunit of the ENaC in black and mixed ancestry patients with hypertension, and Liddle’s syndrome in the minority. The purpose of the study was to investigate the association of hypertension and Liddle’s syndrome, and the mutation within affected families.

The study was approved by the Research Ethics Committee of the University of Cape Town. After informed consent family members of index patients had their the blood pressure (BP) measured according to standard guidelines, and bloods drawn for K⁺, renin, aldosterone and DNA analysis. DNA was extracted from whole blood and the beta subunit of the ENaC was sequenced for the R563Q mutation. Only first degree relatives ≥ 20 years were included. Hypertension was defined by a BP > 140 systolic or 90 mmHg diastolic, or the use of antihypertensive medication.

Fourteen families were studied totalling 69 individuals, of whom 37 were heterozygous for the R563Q mutation and 32 negative. The mean age of the R563Q positive individuals was significantly greater than the negatives, but there was no difference in renin, aldosterone and K⁺ levels (table 1).

Demographics of R563Q positive and negative family members

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Negative (s.d.)</th>
<th>Positive (s.d.)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>39 (12.2)</td>
<td>46.7 (24.2)</td>
<td>0.01</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>130.9 (18.7)</td>
<td>158.4 (37.4)</td>
<td>0.00004</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>84.4 (13.81)</td>
<td>98.3 (24.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.2 (0.39)</td>
<td>4.1 (0.52)</td>
<td>0.67</td>
</tr>
<tr>
<td>Renin</td>
<td>29.03 (55.9)</td>
<td>19.42 (11.6)</td>
<td>0.32</td>
</tr>
<tr>
<td>Aldosterone</td>
<td>214 (108.7)</td>
<td>257 (145.6)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Of the 37 affected persons with the R563Q mutation 29 (78.3%) had hypertension and 11 (34.3%) of the negatives (p=0.0002). Both the mean systolic and diastolic BP was higher in the R563Q positive individuals than negatives (table 1). Only 1 positive individual had unprovoked hypokalaemia.

In conclusion the R563Q mutation strongly associates with hypertension in family members, but not Liddle’s syndrome. Further research is needed to define the prevalence of this mutation in our hypertensive population.

Key Words: Baroreflex Sensitivity, Bradykinin B2 Receptor, Genetic Polymorphisms

P-218
ROLE OF ANP GENE ON CARDIAC HYPERTROPHY IN ESSENTIAL HYPERTENSION
Speranza Rubatti, Giada Bigatti, Anna Evangelista, Rosita Stanzone, Chiara Lanzani, Paolo Manunta, Silvia Tedoldi, Teresa Aracidacono, Giuseppe Bianchi, Massimo Volf, Paola Stella. Cardiology, 2nd School of Medicine, University La Sapienza, Ospedale S. Andrea, Rome, Italy; Cardiology, IRCCS Neumomed, Pozzilli, Italy; Nephrology, University Vita e salute, San Raffaele Hospital, Milan, Italy.

The atrial natriuretic peptide (ANP) exerts an important role in cardiovascular functions and remodeling. In particular, experimental evidence support a critical role for ANP in the regulation of cardiac hypertrophy. In fact, lack of ANP favours the hypertrophic process, whereas higher ANP levels reduce it in animal models. No evidence of an involvement of ANP in the hypertrophic response in the human disease was yet available.

In the present study we investigated the influence of the ANP gene on dimensions of cardiac chambers in never treated mild to moderate essential hypertensives. Two-hundreds and thirteen individuals were studied by mono-bidimensional echocardiography and three markers of the ANP gene were characterized (a promoter variant, an exon 1 and exon 3 mutations). We found that subjects carrying the ANP gene promoter variant had an increased cardiac mass (117±11.8 g/m2 vs 95±1.6 g/m2; P<0.001), left posterior wall thickness (11.4±0.7 mm vs 9.7±0.1 mm, P<0.0002), septal wall thickness (12.0±1.0 mm vs 10.5±0.1 mm, P<0.02), independently from the blood pressure levels. In order to assess the effect of the promoter gene variant on circulating proANP levels, we characterized the peptide levels in a subgroup of wild type and heterozygous hypertensives, as well as in a cohort of healthy wild type and heterozygous individuals. Plasma proANP levels were 3110±547 and 1395±228 fmol/L in wild type and heterozygous hypertensives, respectively (P<0.01); 2319±223 and 1165±150 fmol/L in wild type and heterozygous healthy subjects, respectively (P<0.001).

In summary, a promoter ANP gene variant, responsible of a significant reduction of plasma proANP levels, is strongly associated with cardiac hypertrophy development in untreated essential hypertensives. Therefore, lower levels of atrial natriuretic peptide favours the hypertrophic process in human hypertension, as well as in animal models. Moreover, our results, that demonstrate a direct contribution of ANP to left ventricular hypertrophy (as an intermediate phenotype) further support the role of ANP as an independent predictor of cardiovascular events.

Key Words: Atrial Natriuretic Peptide, Cardiac Hypertrophy, Hypertension

P-219
β2-ADRENERGIC RECEPTOR GENE AND ELEVATED BLOOD PRESSURE
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Background: We tested the hypothesis that Gly16Arg, Gln27Glu and Thr164Ile in the β2-adrenergic receptor gene associate with elevated blood pressure.

Methods and Results: We genotyped 9185 individuals from the Danish general population. Allele frequencies of 16Arg, 27Glu and 164Ile were 0.38, 0.44, and 0.01, respectively. Female Thr164Ile heterozygotes versus non-carriers had increased systolic and diastolic blood pressure (P=0.02 and P=0.01). Women double heterozygous for Thr164Ile and Gln27Glu had the highest systolic and diastolic blood pressure, which differed from levels in women non-carrier at all three loci (P= 0.001 and P= 0.01). Female Thr164Ile heterozygotes versus non-