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A functional variant in the catestatin peptide modulates the endothelial nitric oxide pathway and increases the risk for hypertension

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Chromogranin A (CHGA), A 48--kDa protein ubiquitously expressed in the secretory cells of the endocrine, neuro--endocrine and neuronal tissues is a candidate gene for metabolic syndrome. It is involved in the sorting and packaging of catecholamines, neuropeptides and biogenic amines into the secretory granules of these cells. It also functions as a pro--hormone and gives rise to numerous bioactive peptides, one of which is Catestatin (Human CHGA352--372), a catecholamine release--inhibitory peptide with antihypertensive properties. We probed for the occurrence of a functional variant, Gly364Ser In the Catestatin peptide in two independent Indian populations. In both the populations, not only was the Ser364 allele found to be occurring at a higher frequency in the hypertensive population as compared to controls, it also showed associations with elevated blood pressure levels. Computational studies suggested that the drastic differences between the secondary structures of the wild--type and variant peptides may account for their differential interactions with the ADRB2 receptor. Building upon that, we investigated whether the differential modulation of the ADRB2--mediated NO pathway by the Catestatin peptides might be the underlying cause for the differences in the physiological blood pressure levels observed in the human population studies. This study provides new insights into the role of the Catestatin peptide in the pathophysiology of hypertension.

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