MUTATION IN THE CALCIUM-SENSING RECEPTOR IN AN ITALIAN FAMILY WITH AUTOSOMAL DOMINANT HYPOCALCEMIA

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The calcium sensing receptor (CaR) was first identified in the parathyroid cells and was later found to be expressed in the kidney and other tissues. The human CaR gene encodes a polypeptide of 1078 amino acids. Inactivating mutations in the CaR gene are responsible of an elevation in extracellular calcium, leading to mild moderate hypercalcemia and relative hypocalciuria called Familial Hypocalciuric Hypocalcemia (FHH). Conversely, activating mutations in the CaR gene are associated with reverse phenotype: autosomal dominant hypocalcemia (ADH) and a sporadic hypoparathyroidism. Recently a $Ser^{820}Phe$ mutation in the CaR has been described in Japanese family. In the present study we described an Italian family affected by ADH in whom a CaR mutation was identified. The proband was a girl 13 year old affected by a mild hypocalcemia and hypercalciuria with normal range value of PTH. TC exam showed the presence of calcificatin of the basal gangilia. In addition a juvanile hypertension was present in the patient. Baseline biochemical data of the family members showed a mild hypocalcemia and hypertension in the mather and two of four uncles.

Genomic DNA of all subjects was extracted from white blood cells with standard procedure. In the proband, all protein-coding exons (exons 2-7) of the CaR gene were amplified by PCR with standard procedures using primer pairs as described in the literature. Nucleotide sequences of both strands of the PCR products were determined by direct sequencing with a DNA kit and an automated DNA sequencer (ABI PRISM 3100, Perkiln-Elmer Corp). A $Ser^{820}Phe$ activating mutation of the CaR was found. In summary, we have idenfied the $Ser^{820}Phe$ activating mutation in a Italian familiy affected by hypertension and ADH.