Single Nucleotide Polymorphisms (SNPs) Expressed in the P2Y₁₁ Coding Region of Hypertensive Patients

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P2Y₁₁ is one of a family of eight (P2Y₁, P2Y₂, P2Y₄, P2Y₆, P2Y₁₁, P2Y₁₂, P2Y₁₃, P2Y₁₄) P2Y G-protein coupled receptors that are activated by either purines, pyrimidines, or both. Once the P2Y receptors are activated, they perform a variety of functions depending on the G-protein they are coupled to. P2Y₁₁ is the only P2Y receptor that is ATP-sensitive and is coupled to both the Gs and Gq proteins, of which, both play a role in hypertension. The P2Y₁₁ receptor, when activated, results in the activation of phospholipase C (PLC) and adenylyl cyclase (AC), which in turn leads to the accumulation of cyclic AMP (cAMP) and inositol triphosphate (IP₃). However, it is not known whether P2Y₁₁ is significant in the expression of hypertension. We believe and thus hypothesize that the specific DNA region coded for the P2Y₁₁ receptor would express genetic variations, which would contribute to human hypertension. To test this hypothesis, the P2Y₁₁ coding region of both hypertensive and normotensive subjects, was analyzed for the presence of single nucleotide polymorphisms (SNPs). The genomic DNA of 53 subjects was amplified via polymerase chain reaction (PCR), and the PCR products were purified and sequenced. The sequences were then aligned by a multiple-sequence alignment software to detect the genetic variations. Corresponding changes resulting from SNPs on the polypeptide sequence of P2Y₁₁ were then determined. Regions including the SNPs were compared to the P2Y₁₁ protein sequence using Swiss Prot database. In summary, we discovered the presence of ten SNPs, including three synonymous and seven non-synonymous SNPs. Three out of ten SNPs had minor allelic frequency >5%: Leu⁵⁰→Met (5.7%), Ala⁷⁹→Ala (33%), and Ala⁸⁷→Thr (7.5%). Leu⁵⁰→Met was located in the first extracellular loop of the protein, whereas, Ala⁷⁹→Ala and Ala⁸⁷→Thr were located in the transmembrane region. These data suggest the presence of multiple SNPs within the P2Y₁₁ gene, may play a role in the expression of hypertension.