

The **CHRNA7** and its duplicate isoform, **CHRFAM7A**, gene regulation and expression in neuronal and immune cell model

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The $\alpha 7$ neuronal nicotinic receptor, CHRNA7 (Chr. 15, 15q13-q14 region), is a homopentameric ligand gated ion channel with high permeability to Ca^{2+} . It is widely expressed in both the brain, where presynaptically it modulates the release of neurotransmitters and postsynaptically, its activation leads to changes in gene expression, and in periphery, with multiple important role in cognition and in the immune system. In the periphery, CHRNA7 is expressed in neuroendocrine cells of the lung, in keratinocytes, bone marrow, sperm and macrophages. Here, it has a role of modulator of the inflammatory response through the 'cholinergic anti-inflammatory pathway', whose activation prevents the release of cytokines such as $\text{TNF}\alpha$, IL-6, IL-8 and HMGB1. Decreased expression and function of CHRNA7 have been associated with many diseases including schizophrenia, bipolar disorder, ADHD, Alzheimer's disease, autism, epilepsy, RETT syndrome and learning disorders. Recently, CHRFAM7A gene was discovered. It is the product of a recombination event that occurred in human where exon 5 to 10 of CHRNA7 gene fused to four novel exons A, B and C (FAM7A gene) from the serine/threonine kinase ULK4 gene, and exon D of unknown provenance, located 1.6 Mb apart from CHRNA7 gene, in the direction of the centromere, and in the opposite orientation with respect to CHRNA7. In vitro experiments have shown that CHRFAM7A protein assembles with $\alpha 7$ resulting in a dominant negative regulation of its function. Thus, the number of copies of CHRFAM7A can regulate CHRNA7 function. The promoter for the CHRFAM7A gene has not been characterized so far. Here we show that the gene encoding CHRFAM7A is expressed both in cells of innate immunity and in neuronal cells; experiments in two cell models, a human monocytic cell line (THP-1), and a neuroblastoma cell line (SH-SY5Y) revealed the presence of different regulatory regions important for proper CHRFAM7A gene expression in different tissues.