A Novel Homozygous MYO7A Mutation: Case Report

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Abstract- *MYO7A* is an unconventional myosin that is essential for ordinary hearing and vision; mutations in the *MYO7A* gene result in Usher syndrome type 1B and other disorders. In this manuscript, we reported a mutation (c.4705delA) in exon 35, causing the alteration of a Ser amino acid to Ala at codon 1569 (p.H2027del) located within the first FERMdomain of the human protein myosin VIIA. This mutation involved in the pathogenesis of hearing loss, congenital night blindness, muscular weakness, skin problem, and difficulty in keeping balance in the 13-year-old female. After checkup the patient's DNA was extracted from peripheral blood and amplification was performed by PCR. Sequencing method was performed for identification of the mutation. The c.4705delA mutation in exon 35 was found in the patient in heterozygosis form; this means that her mother and father were carriers. This mutation is located on the tail of the myosinVIIA protein and is associated with several disorders.

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Introduction

MYO7A (encoding myosin VIIa) is an unconventional myosin that is essential for the normal activity of eyes and ears, which Usher syndrome type 1B is because of mutations in the *MYO7A* gene (1) and recognized by progressive degeneration of the retina and congenital deafness (2). The *MYO7A* gene is located at 11q13.5 region (3). Actin-based motor activity was first demonstrated with *MYO7A* by using protein purified from mouse testes and retinas (4). Recent studies in *MYO7A* motor activity showed monomer structure for MYO7A gene primarily (5,6). As a monomer, *MYO7A* seems less likely to function in organelle or protein transport and a function better appropriated for the dimeric motor. However, some studies showed that *MYO7A* gene likely is dimerized following interaction with cargo molecules (7). In this report, we describe a female with disorders related to mutations in the *MYO7A* gene.

Case Report

In autumn 2016, a thirteen-year-old female was reported for hearing loss, congenital night blindness, muscular weakness, skin problem, and difficulty in keeping balance. A complete examination was performed on the patient. After ophthalmologic and audiologic examination, and its record, it was known as *MYO7A* gene dysfunction. Also family history demonstrated parental consanguineous marriage. 5 mL of peripheral blood were referred to Gholhak Genetic Laboratory and genomic DNA was extracted by proteinase K method. Amplification by PCR of the MYO7A gene exons was carried out using the primers. Finally, Sanger sequencing method was performed for mutation identification. Test information is showed in table 1.

Table 1. Test Information

Gene	Chromosomal location	Ref-Seq	Mutation location	Nucleotide alteration	Amino acid alteration	Homozygous/ Heterozygous
MYO7A	chr11:76910716	NM_000260.3	EX35	c.4705delA	p.Ser1569Alafs*30	Hom

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Discussion

Here, we report a novel mutation in the MYO7A gene which is located on the tail (first FERM domain) of the myosinVIIA protein. (Figure 1) and was associated with several disorders in a thirteen-year-old female Iranian families. The c.4705delA mutation in exon 35 was found in the patient in heterozygosis form; her mother and father were carrier for mentioned mutation. This mutation is located in the first FERM domain of the myosin VIIa protein.

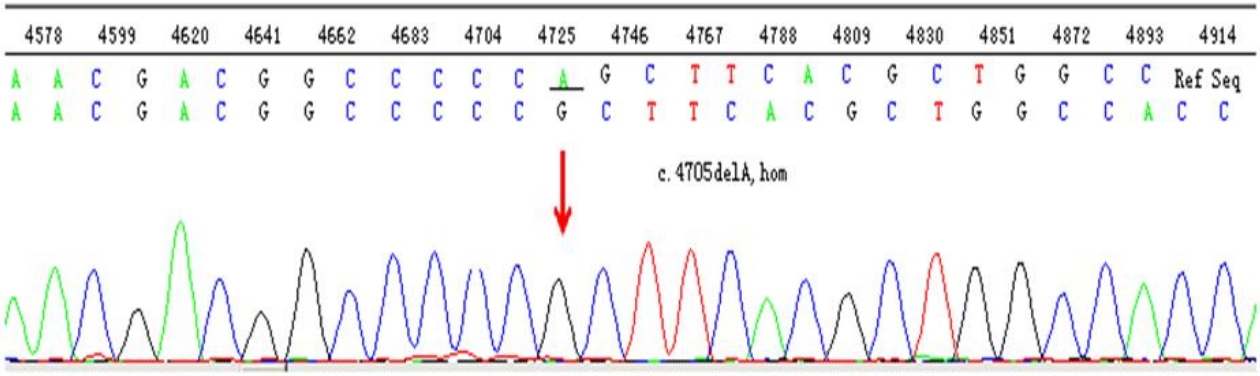

Figure 1. The sequencing results which performed by Sanger sequencing method

In humans, the myosin VIIA protein contains two FERM domains located on the tail region, separated by two domains, SH3, and MyTH4 (8). Several studies have suggested that mutations located at the tail of the myosin VIIA protein (5,9). Furthermore, mutations in the C-terminal FERM1 domain of the myosin VIIA protein have been associated with the development of the pathogenesis of hearing loss, congenital night blindness, muscular weakness, skin problem, and difficulty in keeping balance. All these evidence suggest that such mutations in FERM1domain damage the membrane-binding function of the protein, affecting the normal functions both in the inner ear, retina, muscular and skin.

Several functions of myosin VIIa has been suggested, such as the trafficking of ribbon synaptic vesicle complexes and the renewal operations of the outer photoreceptor disk (10). Another proposed function is the conservation of the stability of the stereocilia during the dynamic movements of the bundle (11).

In any case, anyway, the relationship among the various mutations along this gene and their pathological implications remains unknown. Additional studies are essential to understanding the biochemical picture of the myosin VIIa role in cellular function.

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