



Fig. S3. Mutations in the NIPAL4 gene and their deduced amino acid changes in the NIPAL4/Ichthyin protein. The NIPAL4 gene consists of 6 exons encoding the transmembrane protein NIPAL4/ichthyin. Approximately half of the mutations reported previously are in the helical transmembrane domains, while the others are in the loop domains of the protein. The mutation in the present case, c.458G>A in exon 2, leads to p.Arg153Gln in the first cytoplasmic loop of the protein. The precise effects of the mutation Arg153Gln from a positive-charged to a non-charged amino acid could not be assessed because the crystal structure of NIPAL4 has not been delineated. However, when the effect of that mutation was predicted by PROVEAN Protein (<http://provean.jcvi.org/index.php>) *in silico*, the score of the amino acid change was -3.568 (< or = -2.5), which is suggestive of a deleterious effect of the mutation. In addition, the alignment of the amino acid residues of the first cytoplasmic loop showed that the Arg residue is highly conserved among species. This suggests a functional importance of the Arg residue that is mutated in the present case.