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Research Letter

Mutational analysis of 29 patients with autosomal recessive woolly hair and hypotrichosis: *LIPH* mutations are extremely predominant in autosomal recessive woolly hair and hypotrichosis in Japan

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Supplementary files

Supplementary results

Figure S1.

Table S1.

Supplementary results

Case 1 with the previously unreported *LIPH* mutation was a 6-year-old girl. She was the youngest of 3 siblings, born to non-related parents, with no family history of any similar disorder. She was born at full term after an uneventful pregnancy, and there were no perinatal abnormalities. After one year, however, she was noticed to have woolly hair with mild hypotrichosis. Examination found entire her hair to be thin and chestnut in color (versus black in her other family members) (Fig. S1a). No nail or dental abnormalities, mucosal changes, or visual or hearing difficulties were seen. Her *LIPH* genotype was compound heterozygous for c.558_559insT (p.Lys187Ter) (Fig. S1b) and c.736T>A (p.Cys246Ser). The missense mutation c.736T>A was present in the father, and the insertion mutation c.558_559insT was demonstrated as maternal.

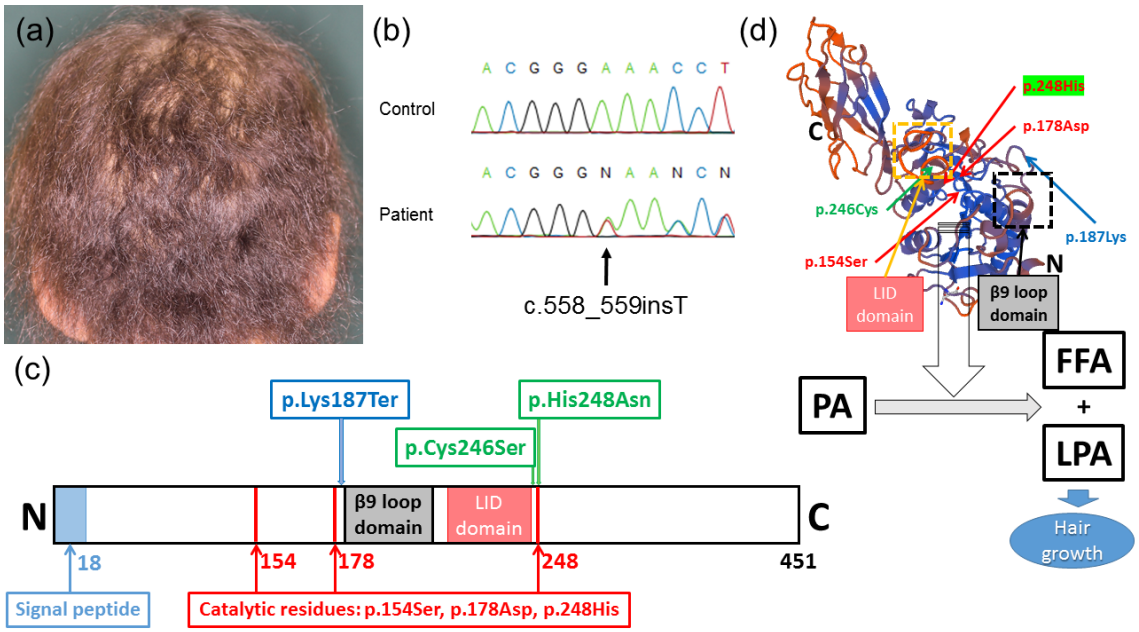

Figure S1. Clinical and molecular features of Case 1. (a) She has woolly hair and mild hypotrichosis on the scalp. (b) Sanger sequencing in Case 1 reveals the novel frameshift mutation c.558_559insT in *LIPH*. (c) A schematic of the LIPH domain structure. The blue

area indicates the signal peptide (amino acids 1-18). The three reported catalytic residues are marked by red arrows (amino acids: p.154Ser, p.178Asp, p.248His). The present mutations in the ARWH patients are marked by green arrows (the founder mutations) or by a blue arrow (the novel mutation). (d) The three-dimensional-structure model[1] and the speculated signalling pathway via lysophosphatidic acid production by LIPH. The three catalytic residues are marked by red arrows. The present mutations in the ARWH patients are marked by green arrows (the founder mutations) or by a blue arrow (the previously unreported mutation). Lid domain is in orange and β9 loop is in grey. Abbreviations: PA, phosphatidic acid; FFA, free fatty acid; LPA, 2-acyl lysophosphatidic acid.

Reference for Supplementary results

[1] Biasini M, Bienert S, Waterhouse A *et al.* SWISS-MODEL: modelling protein tertiary and quaternary structure using evolutionary information. *Nucleic Acids Res* 2014; **42**(Web Server issue): W252-8.

Table S1. Number of each mutant allele of our reported ARWH pedigrees having *LIPH* mutations

Types of mutant allele	Number of identified mutant alleles in ARWH pedigrees /Total number of alleles on which mutational analysis in *LIPH* was performed
c.736T>A	67/88 (76%)
c.742C>A	16/88 (18%)
c.558_559insT	1/88 (1%)
Abbreviations: ARWH, autosomal recessive woolly hair; LIPH, Lipase, member H	