

**Figure S5.** Alignments of 12 *USP9* Genes to Human *USP9Y* near the D65E Mutation.

Usp9x-isof2-Rattus-norvegicus	EQQQGDAPPQIEDEE	PAFPHTDLAKLDDMINRPRWVVPVLPKGELEVLL
Usp9x-Mus-musculus	EQQQGDAPPQIEDEE	PAFPHTDLAKLDDMINRPRWVVPVLPKGELEVLL
USP9X-isof4-Homo-sapiens	EQQQGDAPPQLEDEE	PAFPHTDLAKLDDMINRPRWVVPVLPKGELEVLL
USP9X-isof2-Macaca-mulatta	EQQQGDAPPQLEDEE	PAFPHTDLAKLDDMINRPRWVVPVLPKGELEVLL
USP9X-isof3-Equus-caballus	EQQQGDAPPQLEDEE	PAFPHTDLAKLDDMINRPRWVVPVLPKGELEVLL
USP9-isof3-Monodelphis-domesti	EQQQGDAPPQLEDEE	PAFPHTDLAKLDDMINRPRWVVPVLPKGELEVLL
USP9-isof1-Ornithorhynchus-ana	EQQQGDAPPQLEDEE	PAFPHTDLAKLDDMINRPRWVVPVLPKGELEVLL
USP9-isof1-Gallus-gallus	EQQQGDAPPQLEDEE	PAFPHTDLAKLDDMINRPRWVVPVLPKGELEVLL
USP9-Taeniopygia-guttata	EQQQADAPPQLEDEE	PAFPHTDLAKLDDMINRPRWVVPVLPKGELEVLL
USP9-Danio-rerio	DQQQGDSPPLEEEE	PAFPHTDLAKLDDMINRPRWVVPVLPKGELEVLL
USP9Y-Bos-taurus	EQQQGDAPPQHEDEE	PAFPHADLAKLDDMINRPRWVVPVLPKGELEVLL
<b>USP9Y-Homo-sapiens</b>	<b>EQQQGDAPPQHEDED</b>	<b>PAFPHTELANLDDMINRPRWVVPVLPKGELEVLL</b>
Usp9y-Mus-musculus	EQQQGDAPPQHEEED	PSFPHTDLAKLEDMINRSRWVVPVLPKGELEVLL

These alignments show the preponderance of glutamic acid at sites corresponding to the human D65E mutation. Region shown corresponds to residues 51 through 100 in the human *USP9Y* sequence. Vertical rectangle indicates residue 65 in human *USP9Y*.

We selected sequences for this multiple alignment by first querying the NCBI refseq\_protein database for best matches to human *USP9Y*. We did this using the blast server (BLASTP 2.2.21+ at <http://blast.ncbi.nlm.nih.gov/Blast.cgi>) using default parameters. In instances where multiple isoforms for a given species provided good matches to human *USP9Y*, we retained only the best match. We then selected the 12 best matches to human *USP9Y* and computed a multiple alignment with clustalw2 2.0.10 (<ftp://ftp.ebi.ac.uk/pub/software/clustalw2/>) with default parameters.