GENE	GENE NAME	OMIM	MOI	OMIM DISEASE NAME	REASON FOR IN/EXCLUDING THE VARIANT AS PATHOGENIC	ENSEMBL TRANSCRIPT	CHR	POS [HG19]	VARIANT [RefSeq Number]	AAE	COVERAGE [fold]	VARIANT FREQUENCY [%]	dbSNP	MAJOR ALLELE HOMO *	HET *	MINOR ALLELE HOMO *	ExAC SERVER: VARIANTS PER ALLELES (TOTAL)
Patient III:04																	
HGSNAT	Heparan-α-glucosaminide N-acetyltransferase	#252930	AR	Mucopolysaccharidosis type IIIC, Sanfilippo syndrome type C	**confirmed:** missense mutation of a conserved amino acid, biochemical proof of an Acetyl-CoA:α-glucosaminide N-acetyltransferase deficiency	ENST00000458501	8	43,016,605	c.518G>A [NM_152419]	p.(G173D)	68	100	rs370717845	2494	0	0	119,776 / 0
					excluded: NO splice defect found on the cDNA level.	ENST00000458501	8	43,046,607	c.1770-10C>A [NM_152419]		123	100					120,638 / 0
CYP7A1	cytochrome P450, family 7, subfamily A, polypeptide 1				**excluded:** 393 heterozygous and 1 homozygous variants in ExAC	ENST00000301645	8	59,404,935	c.1192G>C [NM_000780]	p.(P398A)	73	100	rs142708991	2497	7	0	121,410 / 394
MYBL1	V-myb myeloblastosis viral oncogene homolog (avian)-like 1				**excluded:** predicted splice site change at position +3 of splice acceptor, but **NO** splicing defect on cDNA detected, **NO** abnomality of the hematopoietic system	ENST00000522677	8	67,479,108	c.2543+3T>C [NM_001080416]		133	100					120,080 / 6
JPH1	Junctophilin 1	#607706	AR	Charcot-Marie-Tooth disease, axonal, with vocal cord paresis	**excluded:** phenotype does not fit to predescibed disease in OMIM, exon only present in rare transcript. **NO** vocal cord paresis, amyotrophy, neuropathy, vocal cord paresis, hand abnormalities	ENST00000342232	8	75,233,509	c.14T>C [NM_020647]	p.(R5K)	12	100					47,352 / 0
COL14A1	Collagen, type XIV, alpha 1	614936%	AR	Punctate palmoplantar keratoderma type 1	**excluded:** 625 heterozygous and 4 homozygous varaints in ExAC, phenotpye does not fit to predescribed disease in OMIM: **no** skin abnormalities (elasticicity, punctate palmoplantar keratorderma), does not correspond to mouse phenotype (decreased body weight, impaired glucose tolerance)	ENST00000309791	8	121,267,490	c.2764G>A [NM_021110]	p.(V922I)	117	100	rs11774228	2491	12	1	121,378 / 629

Supplementary Table 2: Homozygous variants in the autozygous region that cause an amino acid exchange and were predicted to be disease causing by the MutationTaster or MERAP software. MOI, mode of inheritance; **AR,** autosomal recessive; **AD,** autosomal dominant; **AAE,** amino acid exchange, ***** Frequencies refer to the genotypes of the 1000 Genome Project; **ExAC,** Exome Aggregation Consortium (http://exac.broadinstitute.org/); Mouse phenotype data were obtained from the mouse phenotype database: http://www.mousephenotype.org/data/search/gene