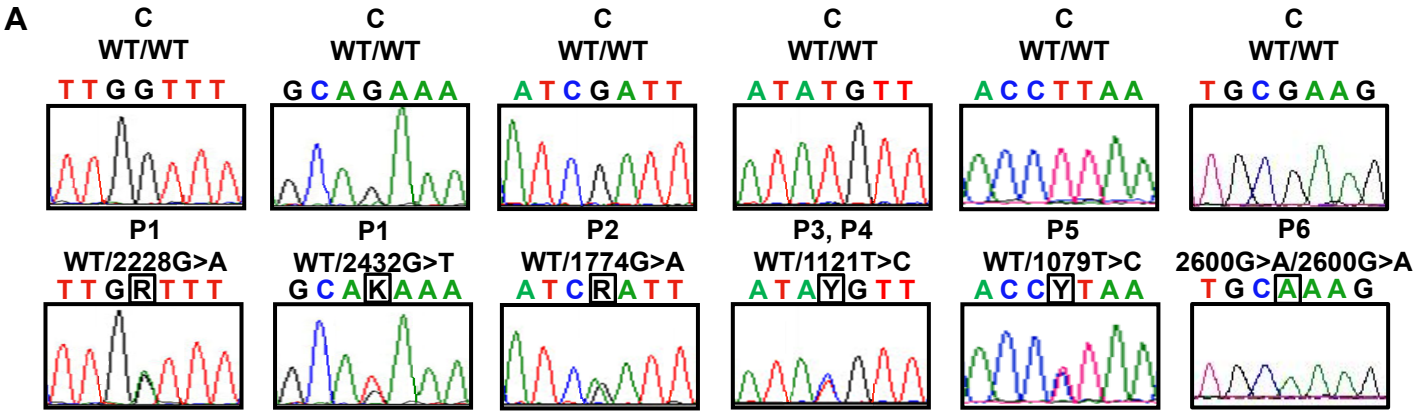
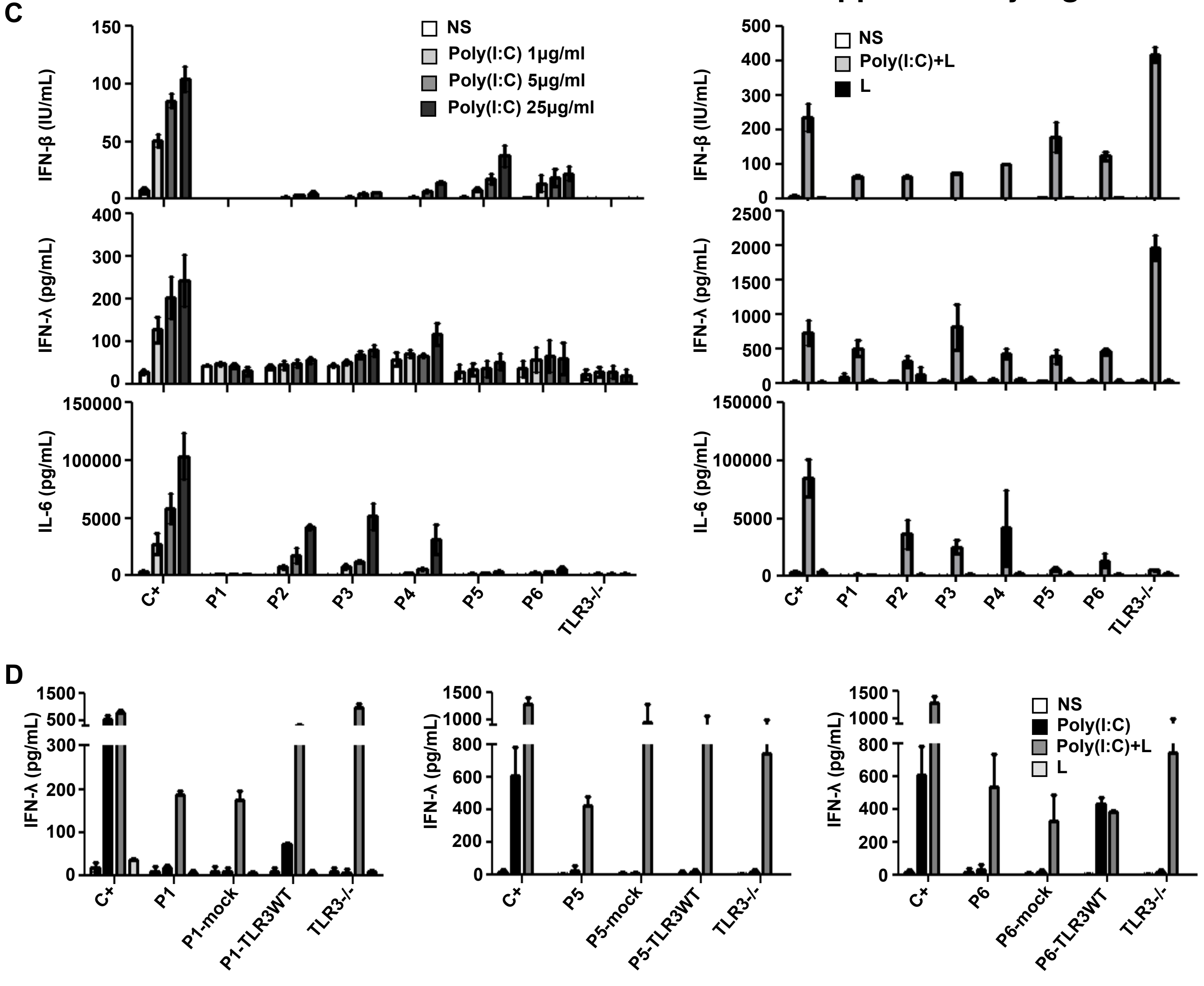
Supplementary Figure e-1



B

	L360	M374	D592	G743	R811	R867
Homo sapiens	KCLEHLNMEDNDIPGIKSNMFTGLI	ELKIIDLGLNN	VHRVLGFKEID	SIKRSRKIIFV	HALCLRRGMFK	
Gorilla gorilla	KCLEHLNMEDNDIPGIKSNMFTGLI	ELKIIDLGLNN	VHRVLGFKEID	SIKRSRKIIFV	HALCLRRGMFK	
Pan troglodytes	KCLEHLNMEDNDIPGIKSNMFTGLI	ELKIIDLGLNN	VHRVLGFKEID	SIKRSRKIIFV	HALCLRRGMFK	
Macaca mulatta	TCLEHLNMEDNDISGIKSNMFTGLI	ELKIIDLGLNN	VHRVLGFKEID	SIKRSRKIIFI	HALCLRRGMFK	
Felis catus	KCLEYLNMGDNNFPGIRSNMFTGLI	ELKSIDLGLNN	VHRVLGFKEID	SIKRSRKTIFV	HALCLRRGMFK	
Canis lupus familiaris	KCLQYLNMEDNYFAGIKSNMFTGLI	ELKSIDLGLNN	VHRILGFKEID	SIKKSRKTIFV	HALCLRRGMFK	
Loxodonta Africana	KYLEHLNMEDNNFPGIKNNMFTGLI	ELKSIDLGLNN	VHRILGFKEID	SIKRSRKTIFV	HALCLRRGMFK	
Equus caballus	KCLEYLNMEDNNFPGIKSNMFTGLV	ELKSINLGLNN	VHRVLGFKEID	SIKRSRKIIFI	HALCLRRGMFK	
Bos Taurus	KCLEYLNMDDNNFPGIKRNTFTGLV	ELKSIDLGMNN	VHRVLGFKEID	SIRRSRKIIFV	HALCLRRGMFK	
Rattus norvegicus	KCLEHLNMDDNTIPGIKSNTFTGLV	ELKSINLGLNN	VHRILGFKEID	SIKRSRKIIFV	HALCLRRGMFK	
Mus musculus	KYLEYLNMDDNNIPSTKSNTFTGLV	ELKSINLGLNN	VHRILGFKEID	SIKRSRKIIFV	HALCLRRGMFK	
Gallus gallus	HHLEYLIMDNNNFPRITTNMFTGLK	QLKDIDLGSNN	INRILGFKELD	CIRRSRKIIFI	HALCLRRGMFR	
Pan Paniscus	KCLEHLNMEDNDIPGIKSNMFTGLI	ELKIIDLGLNN	VHRVLGFKEID	SIKRSRKIIFV	HALCLRRGMFK	
Pongo abelii	KSLEHLNMEDNDIPGIKSNMFTGLI	ELKIIDLGLNN	VHRVLGFKEID	SIKRSRKIIFV	HALCLRRGMFK	
Pongo pygmaeus	KSLEHLNMEDNDIPGIKSNMFTGLI	ELKIIDLGLNN	VHRVLGFKEID	SIKRSRKIIFV	HALCLRRGMFK	
Nomascus leucogenys	KCLEHLNMEDNDIPGIKSNMFTGLI	ELKIIDLGLNN	VHRVLGFKEID	SIKRSRKIIFI	HALCLRRGMFK	
Hylobates lar	KCLEHLNMEDNDIPGIKSNMFTGLI	ELKIIDLGLNN	VHRVLGFKEID	SIKRSRKIIFV	HALCLRRGMFK	
Papio anubis	TCLEHLNMEDNDISGIKSNMFTGLI	ELKIIDLGLNN	VHRVLGFREID	SIKRSRKIIFI	HALCLRRGMFK	
Macaca fascicularis	TCLEHLNMEDNDISGIKSNMFTGLI	ELKIIDLGLNN	VHRVLGFKEID	SIKRSRKIIFI	HALCLRRGMFK	
Cercocebus atys	TCLEHLNMEDNDISGIKSNMFTGLI	ELKIIDLGLNN	VHRVLGFKEID	SIKRSRKIIFI	HALCLRRGMFK	
Saimiri boliviensis	KCLEHLNMDDNDIPGIKSNMFTGLI	ELKIIDLGLNN	VHRVLGFKEID	SIKRSRKIIFV	HALCLRRGMFK	
Callithrix jacchus	KCLEHLSMDDNDIPGIKSNMFTGLI	ELKVIDLGLNN	VHRVLGFKEID	SIKRSRKIIFV	HALCLRRGMFK	
Ceratotherium simum	KCLEYLNMEDNNFPGIKNNMFTGLV	ELKSIILGLNN	VHRVLGFKEID	SIQRSRKIIFV	HALCLRRGMFK	
Otolemur garnettii	KRLEYLNMEDNDIPGIKSHMFTGLI	ELKSIDLGLNN	VHRVLGFKEID	SIRRSKKIIFV	HALCLRRGMFK	
Cavia porcellus	KCLEYLNMDDNNIPGIKSGMFTGLI	ELKSINLGLNN	VHRVLGFKEVD	SIKRSRKIVFI	HALCLRRGMFR	
Pteropus alecto	KCLEYLNMEDNNFQGIKSDMFTGLI	ELKSISLGLSN	VHRILGFKEID	SIKKSRKIIFV	HALCLRRGMFK	
Orcinus orca	KVLEYLNMEDNTFPGIKSNTFTGLT	ELKSIDLGLNN	VHRVLGFKEID	SIRRSRKIIFV	HALCLRRGMFK	
Tursiops truncates	KFLEYLNMEDNTFPGIKSNTFTGLT	ELKSIDLGWNN	VHRVLGFKEID	SIRRSRKIIFV	HALCLRRGMFK	
Rousettus leschenaultii	KCLEYLNMEDNNFQGIKSNMFTGLI	ELKSINLGLNN	VHRILGFKEID	SIKKSRKIIFV	HALCLRRGMFK	
Sus scrofa	KSLEYLNMEDNNFPGIKRNTFTGLI	ELKSIDLGLNN	VHRVLGFKEID	SIKRSRKIIFV	HALCLRRGMFK	
Bubalus bubalis	KCLEYLNMEDNNFPGIKRNTFTGLV	ELKSIDLGMNN	VHRVLGFKEID	SIRRSRKIIFV	HALCLRRGMFK	
Capra hircus	KRLEYLNMEDNNFPGIKRNTFTGLV	ELKSIDLGMNN	VHRVLGFKEID	SIRRSRKIIFV	HALCLRRGMFK	

Supplementary Figure e-1



Supplemental Figure e-1.

(A) Confirmation of the single nucleotide substitution for each patients. The PCR products were amplified from genomic DNA from the granulocytes and fibroblasts of a control and patients. **(B)** Multiple alignments of relevant amino-acid sequences of human TLR3, with its homologs from 32 species, with the residues mutated in P1-P6 highlighted. **(C)** Production of IFN-β, IFN-λ and IL-6 by SV40-fibroblasts after stimulation with 1, 5, 25 µg/mL poly(I:C) for 24 h **(C)**, or after 24 h of stimulation with 25 µg/mL poly(I:C) in the presence of Lipofectamine (poly(I:C)+L) or Lipofectamine alone (L), as assessed by ELISA, with cells from four healthy controls (C+), patients (P1-P6), and a TLR3-/- patient. **(D)** Production of IFN-λ, in the absence of stimulation (NS), after 24h of stimulation with 25 µg/mL poly(I:C) in the presence of Lipofectamine (poly(I:C)+L) or without Lipofectamine (poly(I:C)), or Lipofectamine alone (L), as assessed by ELISA, in SV40-fibroblasts from patients (P1, P5, and P6) transfected with the mock construct or with HA-tagged WT *TLR3*, a healthy control (C+) and a TLR3-/- patient. Mean values ± SD were calculated from four **(C)** or three **(D)** independent experiments.