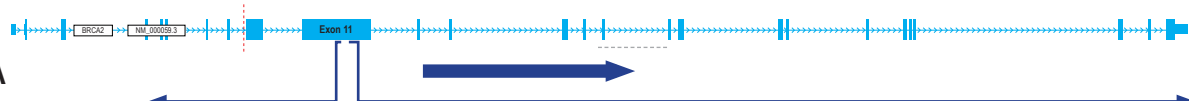


Figure S4



A

<b>Patient 3 (Reversion 2)</b>	Reference genome (Chr13: 32,914,415 - 32,914,520) C1975 - Q2009	t g t g g g a t t t t a g c a c a g c a a g t g g a a a t c t g t c c a g g t a t c a g a t g c t t c a t t a c a a a c g c a a g a c a a g t g t t t c t g a a a t a g a a g a t a g t a c c a a g c a a g C G I F S T A S G K S V Q V S D A S L Q N A R Q V F S E I E D S T K Q	WT
Pre-treatment cDNA (Primary mutation)	t g t g g g a t t t t a g c a c a g c a a g t g g a a a t c t g t c c a g g t a t c a g a t g c t t c a t t a c a a a c g c a a g a c a a g t g t t t c t g a a a t a g a a g a t a g t a c c a a g c a a g C G I F S T A R E N L S R Y Q M L H Y K T Q D K C F L K STOP - - - - -	LOF	
Cycle 3 cDNA	t g t g g g a t t t t a g c a c a g c a a g t g g a a a t c t g t c c a g g t a t c a g a t g c t t c a t t a c a a a c g c a a g a c a a g t g t t t c t g a a a t a g a a g a t a g t a c c a a g c a a g C G I F S T A R E N L S R Y Q M L H Y K T Q D K C F L K STOP - - - - -	LOF	
Progression cDNA (Reversion mutation #1)	t g t g g g a t t t t a g c a c a g c a a g t g g a a a t c t g t c c a g g t a t c a g a t g c t t c a t t a c a a a c g c - - - - - a a g a t a g t a c c a a g c a a g C G I F S T A R E N L S R Y Q M L H Y K T - - - - - Q D N T K Q	Restored ORF	
Progression cDNA (Reversion mutation #2)	t g t g g g a t t t t a g c a c a g c a a g t g g a a a t c t g t c c a g g t a t c a g a t g c t t c a t t a c a a a c g c a a g A T G C A T a c a a g t g t t t c t g a a a t a g a a g a t a g t a c c C G I F S T A R E N L S R Y Q M L H Y K T Q D A L Q V F S E I E D S T	Restored ORF	
Progression cDNA (Reversion mutation #3)	t g t g g g a t t t t a g c a c a g c a a g t g g a a a t c t g t c c a g g t a t c a g a t g c t t c a t t a c a a a c g c a a g A T G C c a a g t g t t t c t g a a a t a g a a g a t a g t a c c a a g C G I F S T A R E N L S R Y Q M L H Y K T Q D A Q V F S E I E D S T K	Restored ORF	



B

<b>Patient 4</b>	Reference genome (Chr17: 41,256,174 - 41,256,226) K119 - K135	a a a a g a t g a a g t t t c t a t c a t c c a a a g t a t g g g c t a c a g a a a c c g t g c c a a a a K D E V S I I Q S M G Y R N R A K	WT function
Pre-treatment cDNA (Primary mutation)	a a a a g a t g a a g t t t c t a t c a t c c a a a g t a t g g g c t a A a g a a a c c g t g c c a a a a K D E V S I I Q S M G STOP	LOF	
Cycle 3 cDNA	a a a a g a t g a a g t t t c t a t c a t c c a a a g t a t g g g c t a A a g a a a c c g t g c c a a a a K D E V S I I Q S M G STOP	LOF	
Progression cDNA (Reversion mutation)	a a a a g a t g a a g t t t c t a - - - - - a c c g t g c c a a a a K D E V S - - - - - N R A K	Restored function	

**A** Insertion    - DNA bp deletion    **A** Single base change    - Amino acid deletion    **STOP** Stop codon