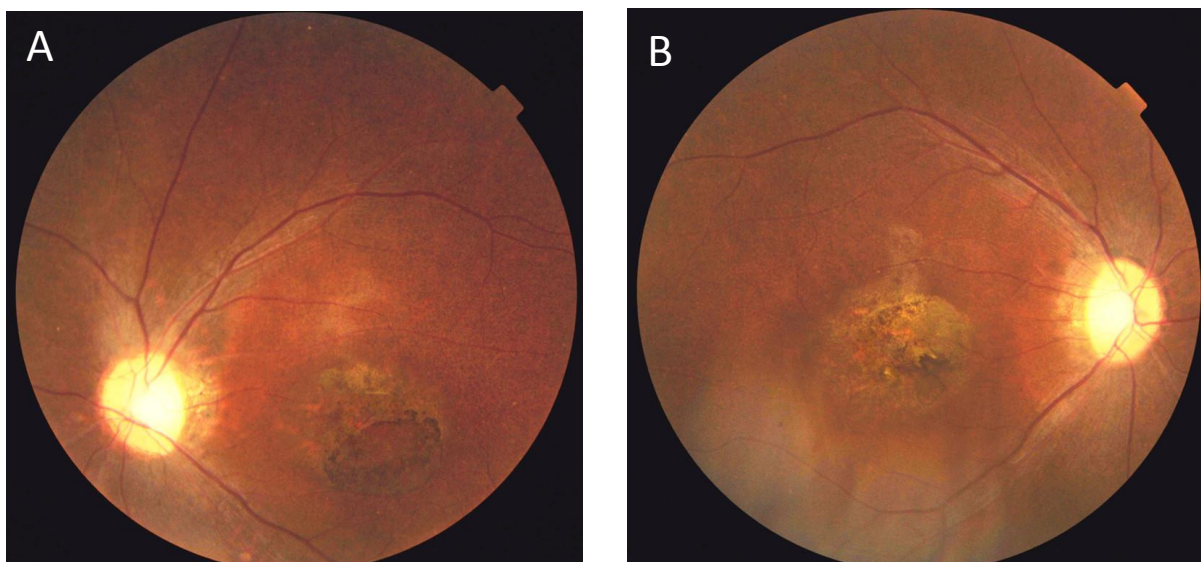
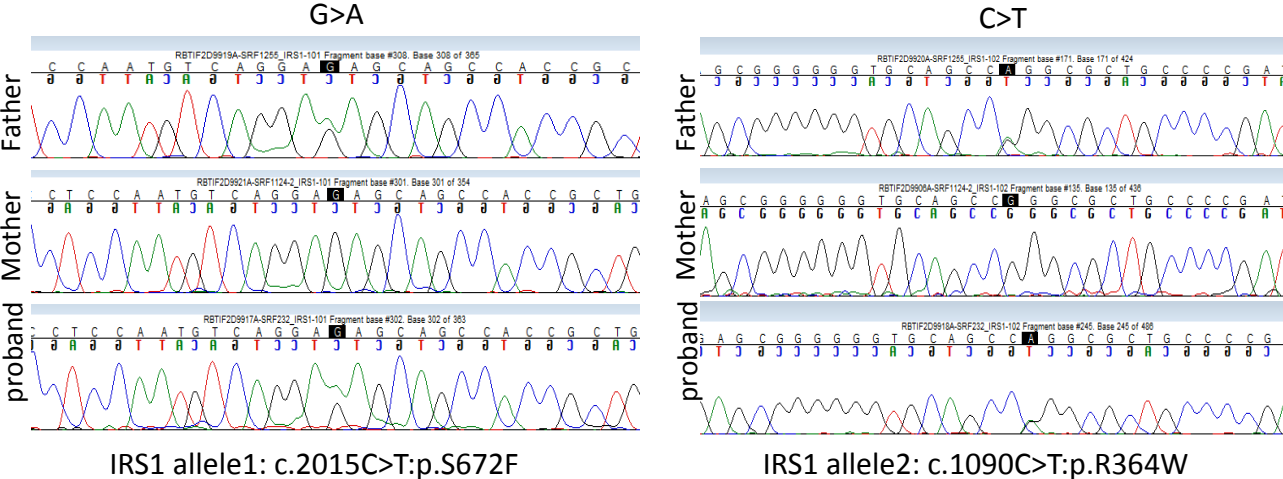


## Supplementary figure 1



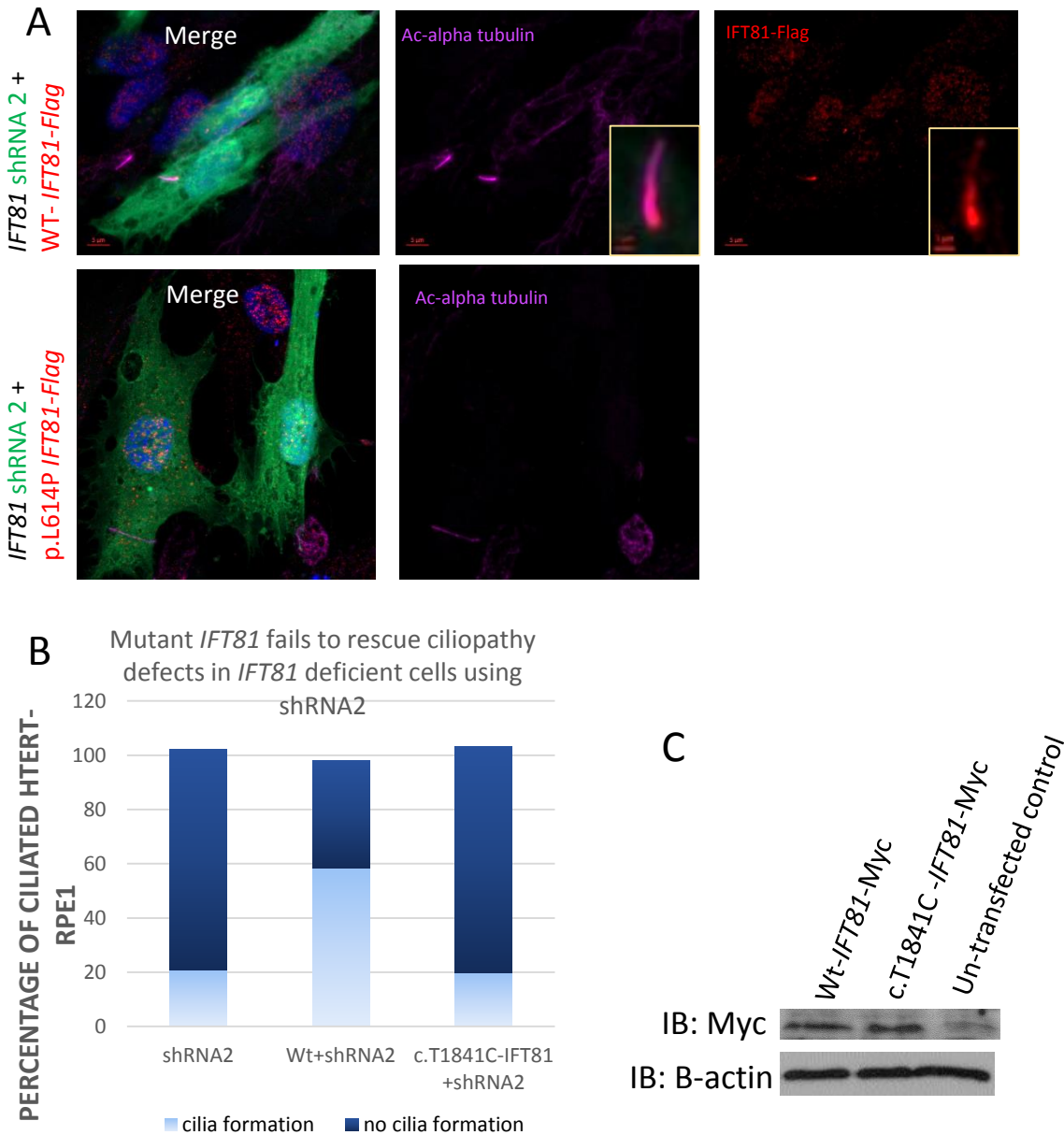
**Supplementary figure 1:** A and B: Left Macular atrophic lesions with pigment proliferation, characteristic of macular degeneration, can be seen in both eyes.

# Supplementary figure 2



Supplementary figure 2: The alternative candidate alleles in IRS1 gene follow a cis-segregation pattern.

## Supplementary figure 3



**Supplementary figure 3:** Lack of rescue potential of *IFT81* mutant in RPE subjected to shRNA 2 based knockdown of endogenous *IFT81*. A. Representative images displaying rescue of ciliogenesis in cells expressing shRNA2 by co-expression of WT *IFT81* (top panel). Co-expression of mutant *IFT81* does not rescue ciliogenesis (bottom panel). B. Quantification of cells co-expressing shRNA1 and WT or mutant *IFT81* and corresponding ciliated cell percentage. C. The expression level of *IFT81* wild-type and mutant protein in transfected 293T cell extract.

# Supplementary figure 4

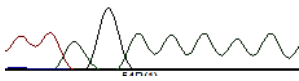
## *IFT81* WT CDNA

```
AGCCCTTTAGAAAAACTATAATT
AGCCCTTTAGAAAAACTATA:TTT
AGCCCTTTAGAAAAACTATAATT
AGCCCTTTAGAAAAACTATAATT
AGCCCTTTAGAAAAACTATA:TTT
```

```
170 180
AGCCCTTTAGAAAAACTATAATT
```

mutated baG>AG>AA1)  
P F R K N Y N L

```
54R(2) Fragment base #163. Base 163 of 213
T T A G A A A A A
A A T J T T T T
```



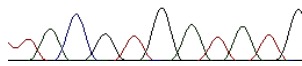
Against shRNA1

```
TCITTTTTACGCGATAIGATAGATGCCT
TCITTTTTACGCGATAIGATAGATGCCT
```

```
190 200
TCITTTTTACGCGATAIGATAGATGCCT
```

Mutmutated base T>A  
L F Y V I . . M P

```
1053R(1) Fragment base #106. Base 106 of 243
T A C G T G A T A T G
T A C G T G A T A T G
```



Against shRNA2

## *IFT81* mutant CDNA

```
AGCCCTTTAGAAAAACTATAA:
AGCCCTTTAGGAAGAACTATAA:
AGCCCTTTAGAAAAACTATAA:
AGCCCTTTAGGAAGAACTATAA:
AGCCCTTTAGGAAGAACTATAA:
AGCCCTTTAGGAAGAACTATAA:
AGCCCTTTAGGAAGAACTATAA:
AGCCCTTTAGGAAGAACTATAA:
```

```
370 380
AGCCCTTTAGGAAGAACTATAA:
```

mutated baG>AG>Ad))

```
Screen R (2) Fragment base #372. Base 372 c
T T A G A A A A A
A A T J T T T T
```



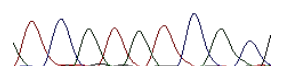
Against shRNA1

```
GGCATCTATCATTCCCGTAAAAAA
GGCATCTATCATTCACGTAAAAAA
GGCATCTATCATTCACGTAAAAAA
GGCATCTATCATTCACGTAAAAAA
GGCATCTATCATTCACGTAAAAAA
GCATCTATCATTCACGTAAAAAA
```

```
1360 1370 1380
GGCATCTATCATTCACGTAAAAAA
```

mutMutated base C>A

```
Autl1 1053 Screen R Fragment base #334. Base 334 o
T C A T A T C A C
A A T A T A T A
```



Against shRNA2

**Supplementary figure 4:** Synonymous base changes to make shRNA-resistant *IFT81* wild-type and mutant CDNA

## Supplementary figure 5

### A. Experiment methodology

293T cells co-transfection

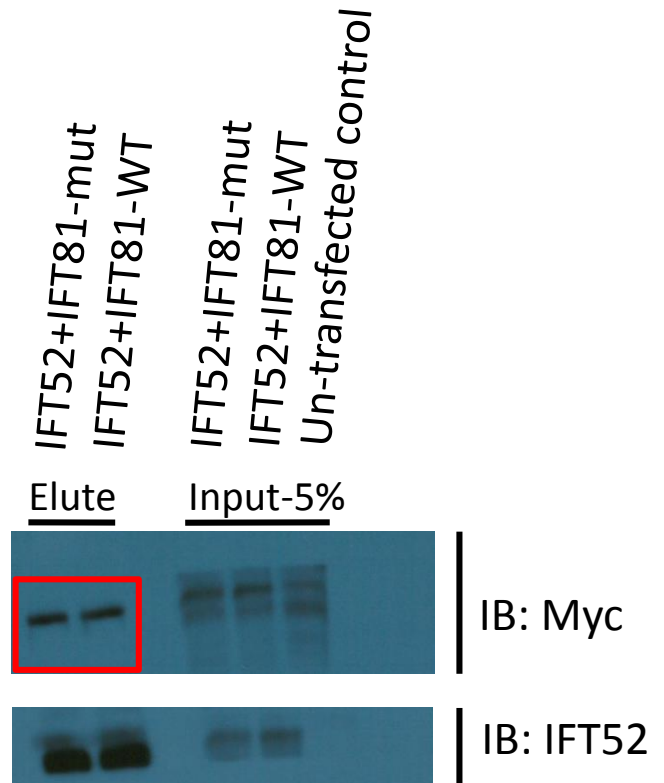


↓  
IP against GFP (IFT52)

↓  
Soft-Elution  
TCA

IB: Myc (IFT81)  
IB: anti-IFT52

### B. Experiment methodology



**Supplementary figure 5:** A. Experimental Methodology for Immunoprecipitation and western blotting to confirm interaction with of WT and c.1841T>C mutant allele with IFT52. B. The c.1841T>C mutant allele does not significantly alter the interaction of IFT81 with IFT52/46 sub-complex.