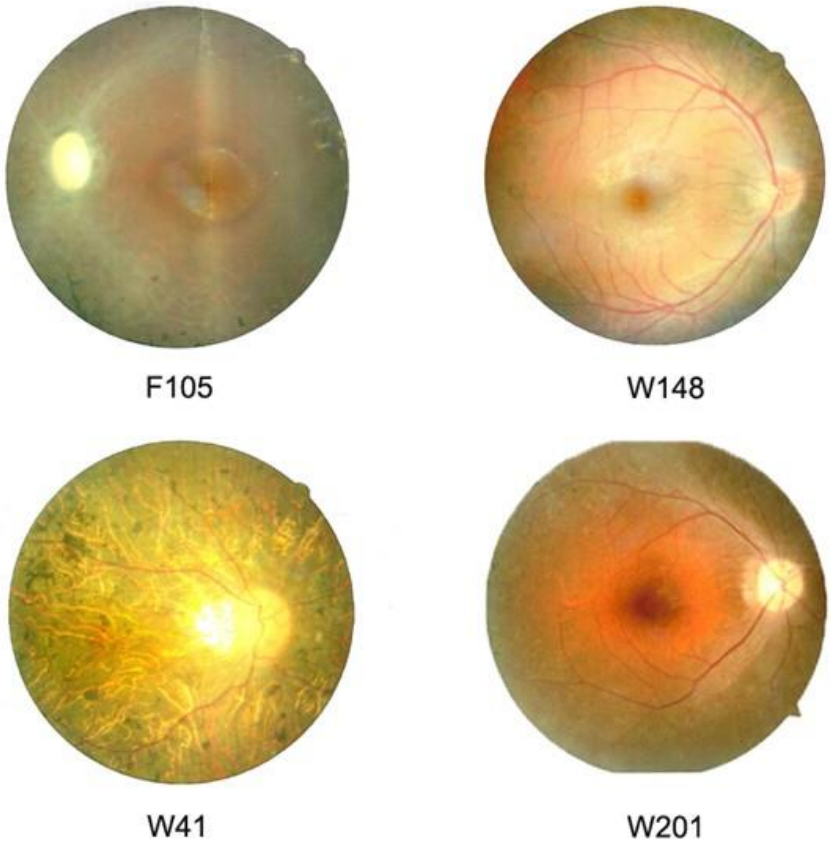
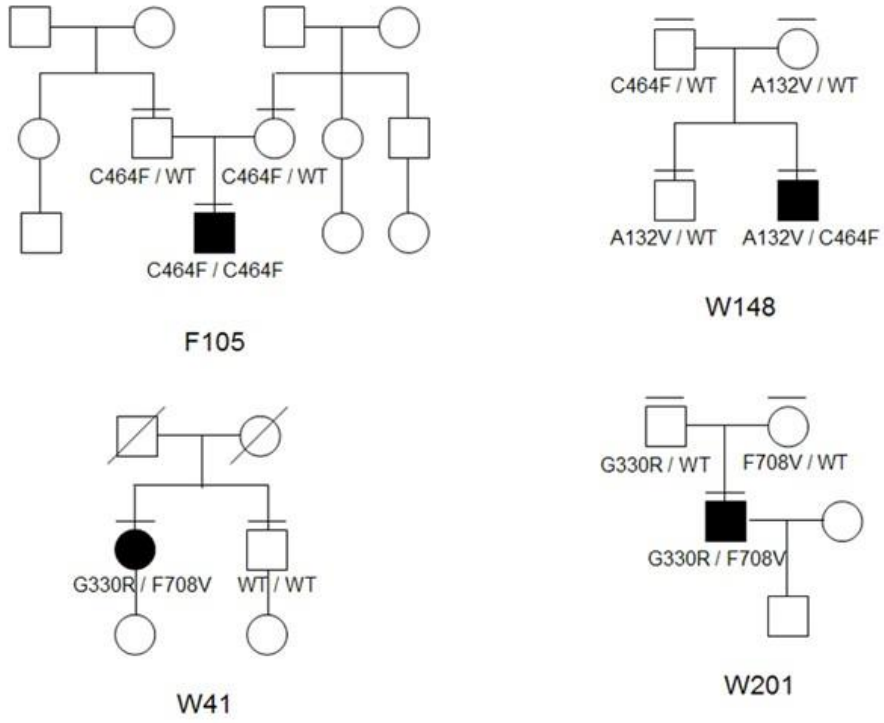
SUPPLEMENTARY INFORMATION

Supplementary Figures

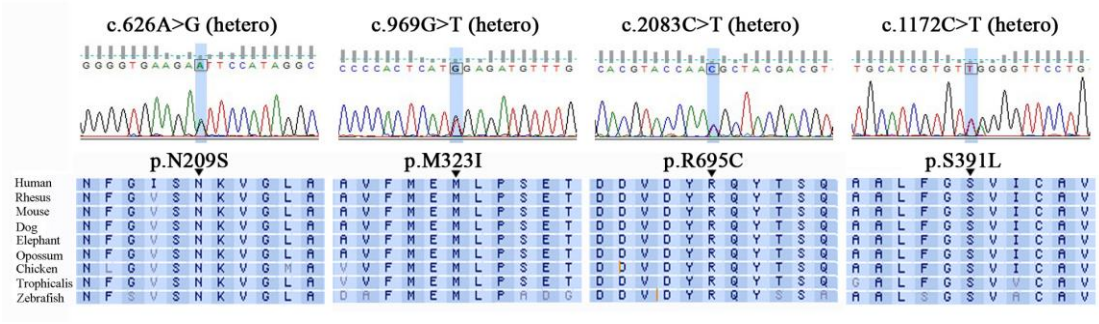


Supplementary Fig. 1. Fundoscopy of the four additional patients with distinct SLC7A14 mutations

Patients with the s mutation displayed typical manifestations in their fundi including peripheral or pan-retina bone-spicule pigmentation, optic disc pallor and arterial attenuation. F105 had a homozygous mutation; W148, W41 and W201 carried two compound mutations.

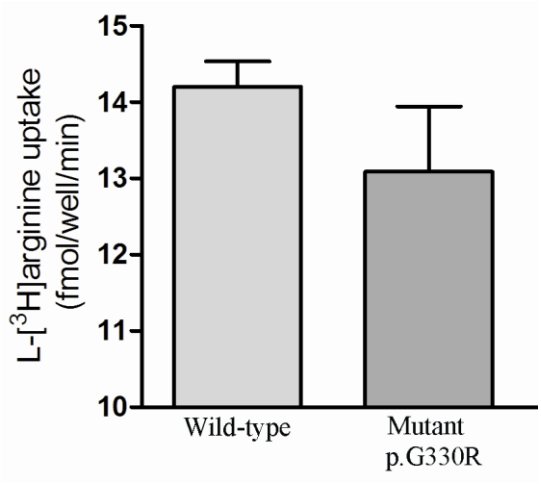


Supplementary Fig. 2. Pedigrees with SLC7A14 mutations



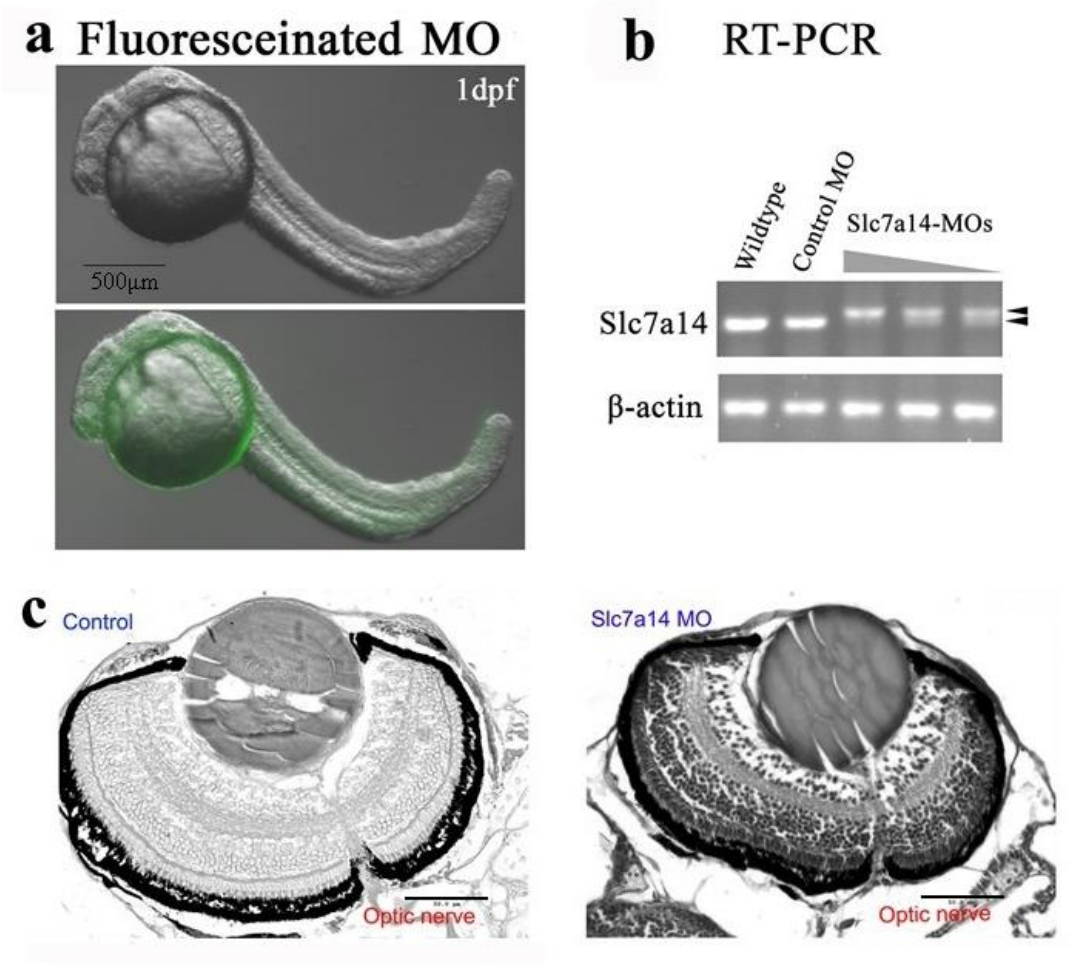
Supplementary Fig. 3. Identified mutations in the SLC7A14 gene.

Sequence chromatograms illustrated the causal lesions identified in five unrelated arRP patients. Each mutation leads to alteration of a highly conserved amino acid residue.



Supplementary Fig. 4. L-[3H]arginine uptake in photoreceptor cells with either wild-type or mutant *Slc7a14* gene.

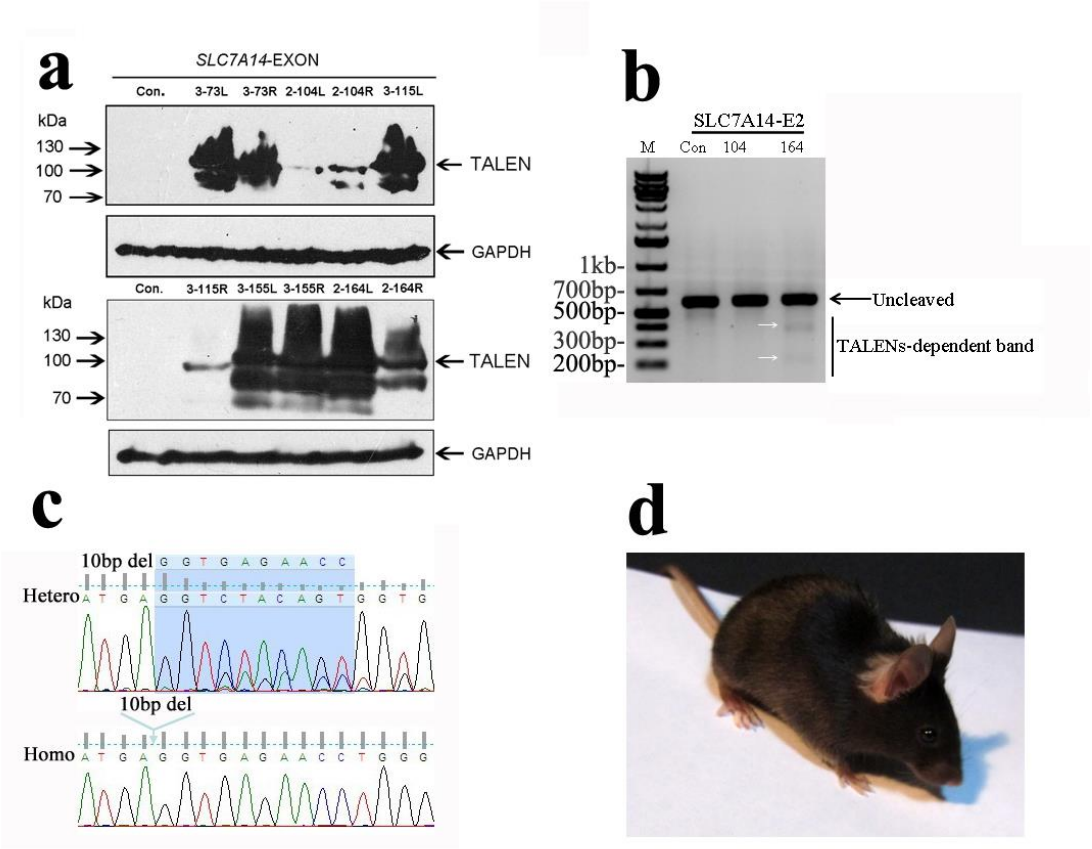
Four independent experiments (N=4) were performed and the results were analyzed using Student's t-test. Bars in the graph represent standard errors of the mean (SEM). No significance was observed.



Supplementary Fig. 5. Confirmation of MO injection in zebrafish Larvae.

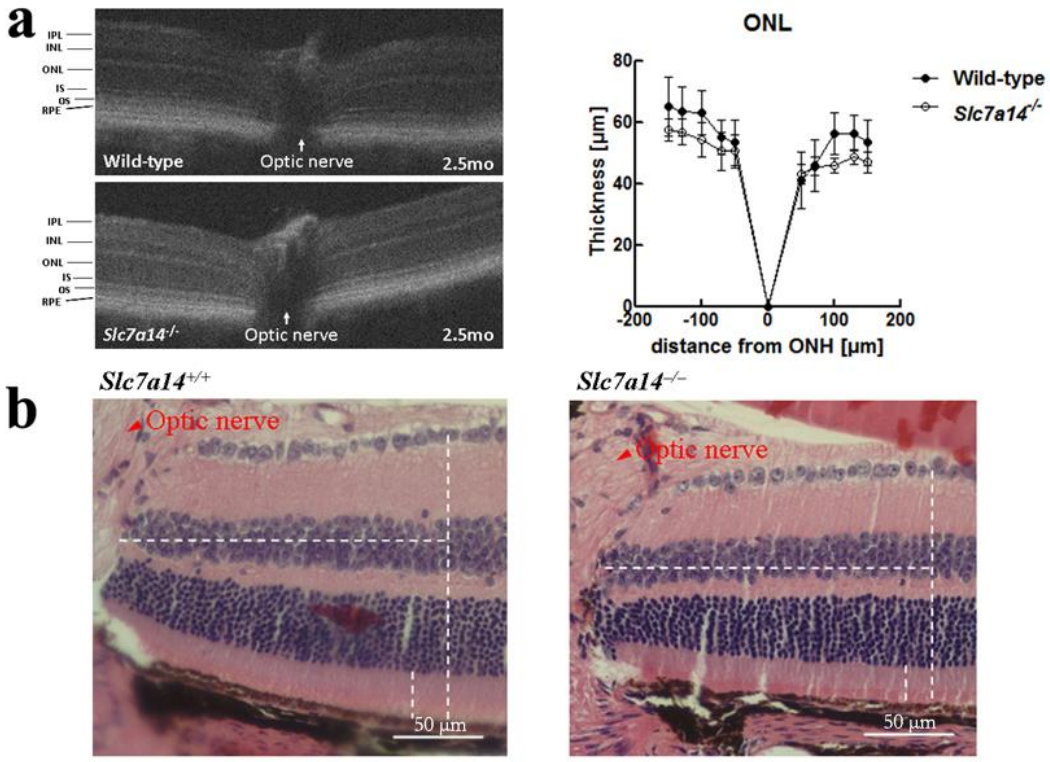
(a) After injection of fluoresceinated standard control MO and *Slc7a14* MO solution, fluoresceins were observed in 1dpf Larvae. Scale bar, 500μm. (b) RT-PCR confirmed splicing change in Slc7a14-MO injected larvae. Three doses (1nL of 0.25nM, 0.15nM, 0.05nM) of MOs were tested. (c) Immunohistology demonstrated no significant changes of retinal structure in the Slc7a14-MO zebrafish. Each section was shown with optic nerve. Scale bar, 50μm.

Supplementary Fig. 6. Representative images of the MO-injected zebrafish. Comparing with the control MO-injected zebrafish, Slc7a14-knockdown led to dramatically smaller eye size. Scale bar, 1000μm.



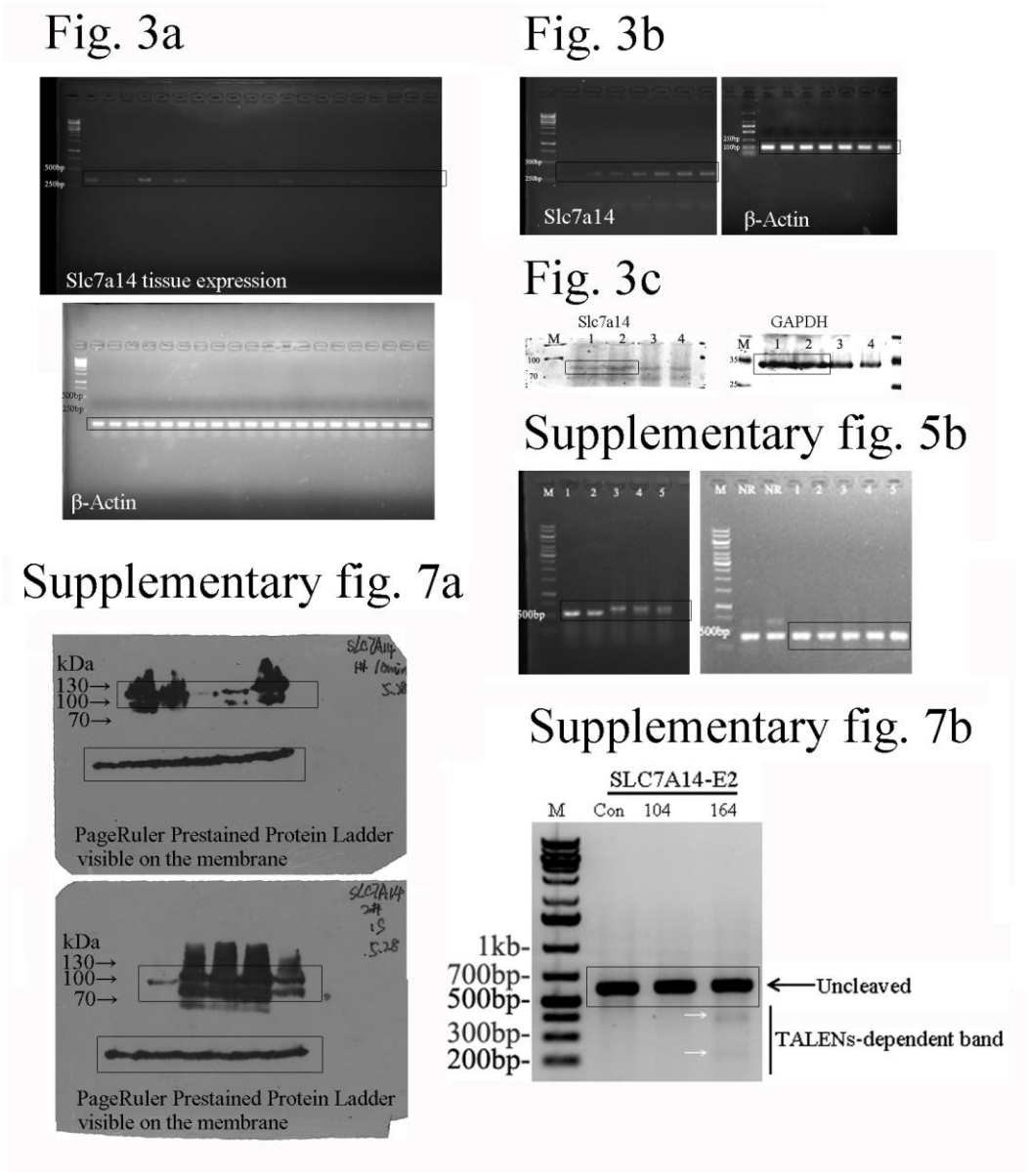
Supplementary Fig. 7. Slc7a14-deficient mice

(a) Western blot confirmed the TALEN expression in the transfected C6 cells. Each lane represents an independent experiment. (b) MSDase assay demonstrated the activity of TALEN pair E2-164. (c) Genotyping of the KO mice revealed a 10bp deletion. Upper image, heterozygous; lower image, homozygous. (d) The *Slc7a14*-deficient mice were viable, fertile and did not show noticeable physical abnormalities.



Supplementary Fig. 8. OCT results of 2.5-month-old *Slc7a14*-KO mouse

(**a**) Compared to age-matched wild-type mice, the 2.5-month-old *Slc7a14*$^{-/-}$ mice had a thinner outer nuclear layer (2.5-month age, n=3). Due to the limited number of the mice (n=3), we were unable to perform any statistical analyses. Bars represent SEM. Bonferoni test, no statistical significance. (**b**) HE staining of a histological section of retina shows a thinner retina in the *Slc7a14*$^{-/-}$ mice. Each retinal section shows the optic nerve as an internal reference. Scale bar, 50μm.



Supplementary Fig. 9. Data of full blots.

Boxes indicate lanes used in the labeled figures.

Supplementary Tables

Supplementary Table 1. List of the 15 homozygous variants after adopting filtering

Chr	***Location***	***Gene symbol***	***Variant***	***In homo region>1Mb***
1	248813827	*OR2T27*	c.359A>G,	No
12	53681883	*ESPL1*	c.4304A>T,	No
19	36349333	*KIRREL2*	c.235G>A,	No
19	38877754	*GGN*	c.148T>C,	No
2	219319657	*USP37*	c.2936T>C,	No
7	87022264	*CROT*	c.1599C>A,	No
9	125512575	*OR1L6*	c.449G>A,	No
X	154128188	*F8*	c.6226G>A,	No
11	47609867	*FAM180B*	c.433G>A,	No
11	5537592	***UBQLNL***	c.80C>G,	**Yes**
2	21257717	***APOB***	c.875C>G,	**Yes**
6	64422984	***PHF3***	c.5500C>T,	**Yes**
8	27295006	***PTK2B***	c.1520A>G,	**Yes**
X	118586003	***SLC25A43***	c.722G>A,	**Yes**
3	170201230	***SLC7A14***	c.988G>A,	**Yes**

Supplementary Table 2. Primer sets for *SLC7A14* amplification

Exon	Forward primer	Reverse primer	Tm	Length
1	GAGAAGGCTGCACTGGGTC	TGATGATCCACTTTTCTGCC	58	565bp
2	CAGAAGTGAGGTTGGAAGAGG	AAGGATGGATAGATTCATAGAGAAAG	58	576bp
3	CCTCGGCCTCCCAGTTTAC	GGTGATAAAGAGGGTGCTGTG	58	468bp
4	TGCGTGTTTAGCACGAGTTC	GGCTACAGGGGACAAAAGAC	58	413bp
5	GTGAATGGATCCAAACTGCC	GATACATAACAAGGTCCACAGTCC	58	468bp
6	TAAATTGGTGGAGCAGGACC	CCATAGAACCAGCCAGATTTC	58	1132bp
7	TGTGGATGCAGTGTTGTCAG	GGTGGTTGCACCTAAGATGG	58	856bp

Supplementary Table 3. Primers for site-directed mutagenesis

Primer	Sequence
hSLC7A14-full-F	GGAGCTCGCCACCATGAGTGGCTTCTTCAC CTCGCTG
hSLC7A14-full-R	GGGTACCGCTCTGGAGAGTAATCTAACTCA TC
hSLC7A14-mut-F	GTTTGTGGCTCATAGGTTCTATGCTGC
hSLC7A14-mut-R	GCAGCATAGAACCTATGAGCCACAAAC
hCAT2-NheI-F	GCTAGCATGATTCCTTGCAGAGCCGC
hCAT2-XhoI-R	CTCGAGTTAGAATTCACTTGTCTTTTCATG
hSLC7A14-fusion-F	GGATCCGCCTACACCTACAGCTATG
hSLC7A14-fusion-R	GGTACCGAAGGAGCAAGACACAGA