

CLAIMS

1. A method for targeted editing of target RNA in a cell based on LEAPER technology, wherein the target RNA is an RNA containing a G to A mutation in a USH2A gene transcript, comprising:

introducing a construct comprising an adenosine deaminase recruiting RNA (arRNA) for editing the target RNA or a construct encoding the arRNA into the cell, wherein the arRNA comprises a complementary RNA sequence that hybridizes to the target RNA, and wherein the arRNA is capable of recruiting adenosine deaminase acting on RNA (ADAR), thereby the target adenosine in the target RNA is deaminated.

2. The method according to claim 1, wherein the target RNA is a pre-mRNA.

3. The method according to claim 1 or 2, wherein the length of the arRNA is about 151-61 nt, ~~131-66 nt, 121-66 nt, 111-66 nt, 91-66 nt, or 81-66 nt.~~

~~4. The method according to claim 3, wherein the length of the arRNA is any natural number selected from 66nt-131nt.~~

~~54. The method according to any one of claims 1-4, wherein the length from the targeting base to the 3' end in the arRNA is ≥ 7 nt, ≥ 10 nt, ≥ 15 nt, preferably 16-55nt, 20-50nt, 25-45nt, 25-35nt, or 25-30nt, and/or, wherein the length from the targeting base to the 5' end in the arRNA is ≥ 25 nt.~~

~~6. The method according to any one of claims 1-5, wherein the length from the targeting base to the 5' end in the arRNA is ≥ 25 nt, ≥ 30 , ≥ 35 , ≥ 45 , preferably 46-90nt, 50-85nt, 55-80nt, 60-75nt, or 65-70nt.~~

~~7. The method according to any one of claims 1-6, wherein a targeting base is introduced into the arRNA to pair with the target A in the target sequence, and the preference order of the targeting base from high to low is C, A, U, or G.~~

~~85.~~ The method according to any one of claims 1-~~74~~, wherein the target RNA is an RNA comprising a transcribed human USH2A gene NM_206933.2(USH2A)_c.11864 G>A (p.Trp3955Ter) mutation site.

~~96.~~ The method according to any one of claims 1-~~85~~, wherein the arRNA is selected from the group consisting of: SEQ ID NO: 23, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 2, SEQ ID NO: 3, and SEQ ID NO: 4.

~~10. The method according to any one of claims 1-9, wherein the arRNA is selected from the group consisting of: SEQ ID NO: 7, SEQ ID NO: 8, and SEQ ID NO: 9.~~

~~117.~~ The method according to any one of claims 1-~~106~~, wherein the construct is a linear nucleic acid, a viral vector, or a plasmid, particularly, the viral vector is an adeno-associated virus (AAV) vector or a lentiviral vector, more particularly, the AAV vector is introduced into the cell by infection after being packaged into an AAV2, AAV5 or AAV8 capsid.

~~12. The method according to claim 11, wherein the viral vector is an adeno-associated virus (AAV) vector or a lentiviral vector.~~

~~13. The method according to claim 12, wherein the AAV vector is introduced into the cell by infection after being packaged into an AAV2, AAV5 or AAV8 capsid.~~

~~14. The method according to claim 13, wherein the AAV vector is introduced into the cell by infection after being packaged into an AAV8 capsid.~~

~~158.~~ The method according to any one of claims 1-~~147~~, wherein the cell is an optic nerve cell or auditory nerve cell of a mammalian.

~~169~~. An arRNA for targeted editing of the target RNA containing a G to A mutation in a USH2A gene transcript, comprising or consisting of a sequence selected from the group consisting of: SEQ ID NO: 23, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 2, SEQ ID NO: 3, and SEQ ID NO: 4.

~~1710~~. A construct or delivery vector comprising the arRNA according to claim ~~169~~, particularly, the construct or delivery vector is a plasmid, virus, liposome, or lipid nanoparticle, more particularly, the construct or delivery vector is an adeno-associated virus (AAV) or a lentivirus, even more particularly, the adeno-associated virus (AAV) is AAV2, AAV5, or AAV8.

~~18. The construct or delivery vector according to claim 17, which is a plasmid, virus, liposome, or lipid nanoparticle.~~

~~19. The construct or delivery vector according to claim 18, which is an adeno-associated virus (AAV) or a lentivirus.~~

~~20. The construct or delivery vector according to claim 19, wherein the virus is AAV2, AAV5, or AAV8.~~

~~2111~~. A cell obtained by the editing method according to any one of claims 1-~~158~~.

~~2212. The arRNA according to claim 9 or the construct or delivery vector according to claim 10~~ A method for treating Usher type II syndrome in an individual, comprising use in correcting a G to A mutation associated with Usher type II syndrome in a cell of ~~the an~~ individual ~~by the method according to any one of claims 1-15.~~

~~2313. The method-use~~ according to claim ~~2212~~, comprising introducing wherein the arRNA according to claim ~~16-9~~ or the construct or delivery vector according to ~~any one of claims 17-2010~~

is introduced into a subject.

~~24~~14. The ~~method-use~~ according to claim ~~23~~13, wherein the arRNA according to claim ~~16~~9 or the construct or delivery vector according to ~~any one of~~ claims ~~17-20~~10 is introduced into the subretinal space of the subject.

~~25~~15. Use of the arRNA according to claim ~~16~~9 or the construct or delivery vector according to ~~any one of~~ claims ~~17-20~~10 in the preparation of a medicament for treating Usher type II syndrome.