Supplementary Materials and methods

PINK1 gene conditional knockout in rats.Based on the design principle of single guide RNA (sgRNA), its recognition sequences were designed and constructed for the PINK1 gene in the non-conservative region of the sequence, and the corresponding primers were synthesized according to the designed sgRNA sequence and connected to the pcS-3G and pT7 plasmid expression vectors,pT7-sgRNA plasmids construction were completed and confirmed by DNA sequencing, respectively, for sequencing verification. sgRNA activity was detected. In addition, sgRNA with optimal specificity and high activity was selected to be transfected to the vector with a promoter plasmid for *in vitro* transcription. The RNA obtained by transcription was used for subsequent injection.

The selection of exon 2-8 for the PINK1 gene as the target of conditional knockout required the placement of locus of X-over P1 on both sides of the exon to achieve the conditional knockout. The two sgRNAs were designed in the non-conserved sequences downstream of intron1 and 3'UTR, respectively, and induced~ 7.5kb of genome deletion, so as to achieve the purpose of knockout of the target gene.First, PCR amplification and sequencing of rat tail target sites in SD rats were performed.The PCR and sequencing of rat tail DNA of SD rat Ensembl revealed that the target sequence of rat tail of SD rats was identical with that given by Genebank and Ensembl.The RNA, Cas9, and target vectors obtained in the previous screening experiments were microinjected into the fertilized rat eggs from SD rats to obtain the F0 generation rats. The positive rats of the F0 generation were verified using PCR and sequencing(Fig. S1). Due to the rapid cleavage rate in the early embryo, the F0 generation rats were obtained as chimeras. The F1 generation rats were obtained by mating the positive rats of the F0 generation with the wild-type (WT) rats. The PINK1 F1 generation rats were verified using PCR, Southern blot analysis, and sequencing to obtain positive F1 generation rats with stable genotypes(Fig. S2 andTableSI).The experimental operation was conducted by Beijing Biaosetu Gene Co., Ltd.

Methods for primary culture. One method is to cut up the isolated renal tubules and screen them for cell screening and culture. Another method is to select a medium for culture that promotes the growth of RTECs, while inhibiting other cells. Studies have shown that the primary culture of RTECs can be used to isolate renal tubules by Percoll density gradient centrifugation. Percoll (silica gel particles containing ethylenepyrroidone) does not damage the biofilm and destroy cells, it can be separated according to different states of cells, and it can be used to obtain active cells. However, this method also has some disadvantages: The renal tubules are obtained less segments, the extraction time of cells is lengthy, and cell viability is thus affected. It has been shown that the separation of the glomerulus and renal tubules can be performed by the grinding of renal tissue and the filtering of mesh, and the exclusion of glomerulus cells can be performed using 80- and 100-mesh screens, which can obtain more RTECs and make them purer(20). Therefore, in the present study, renal tissue grinding and sieve filtration were also used to isolate RTECs. The identification of RTECs was performed using the immunocytochemical method, due to the intermediate fibrous structure of epithelial cells contained epithelial cell-specific marker keratin components. Cytokeratin18 is specifically expressed in RTECs(Fig. S3). The cytoplasm and nucleus of the cell were observed using immunocytochemistry. The cells were washed gently with PBS after crawling and were fixed with 4% paraformaldehyde for 60min. After absorbing the paraformaldehyde, it was dried in the air for 5min. 30%H_2O_2 pure methanol (1:50) was added and soaked for 30min. Endogenous peroxidase was then inactivated and washed with PBS. Subsequently, 5%BSA sealing solution was then added and the excess liquid was absorbedat room temperature for 20 min. Rabbit anti-CK18 (1:200, ab133263,Abcam) was added and PBS was used as a negative control. The cells were then incubated at 37˚C for 1h and wash with PBS three times. Biotinylated goat anti-rabbit IgG was then added, at room temperature for 20min, washed with PBS three times, and reacted with SABC at 37˚C for 20min. The tablets were washed and developed using a DAB colour development kit (AR1002), slightly re-dyed with hematoxylin, and sealed with neutral gum.Under an optical microscope, RTECs exhibit a multilateral cobblestone shape, and the cells are closely connected. In the present study, the primary cultured RTECs were also multilateral cobble-like under an optical microscope(Fig. S4), and the cells were closely connected; it was thus confirmed that the cultured cells were RTECs.

Table SI.Primer sequence information.

Primer	Sequence(5’-3’)	Temperature (˚C)	Product size (bp)
EGE-WL-008-WT-F1	AGGACGCCAGAACAAGCAAGTATAG	63	WT:554
EGE-WL-008-WT-R1	TTGAACCCAGGCCCTATAGTAAGAC	63	
EGE-WL-008-WT-F1	AGGACGCCAGAACAAGCAAGTATAG	63	Mut:335
EGE-WL-008-WT-R	TTGCTGAACCCAAGGCTTCCTCTG	63	WT:7363