CLAIMS

1. A composition comprising an iRNA agent for inhibiting the expression of an alpha-ENaC gene, wherein the iRNA agent comprises a sense strand and an antisense strand, wherein:

   nucleotides 2-19 (5’ à 3’) of the antisense strand comprise the nucleobase sequence of nucleotides 2-19 of SEQ ID NO: 1298 (5’ à 3’) (AUUUGUUCUGGUUGCACA);

   the nucleotide at position 1 (5’ à 3’) of the antisense strand forms a base pair with the sense strand;

   the sense strand comprises the nucleobase sequence of nucleotides 1-18 of SEQ ID NO: 1297 (5’ à 3’) (UGUGCAACCAGAACAAAU); and

   the antisense strand, the sense strand, or both strands comprise at least one modified nucleotide and/or at least one phosphate linker modification.

2. The composition of claim 1, wherein the antisense strand of the iRNA agent and the sense strand of the iRNA agent are each 19 to 23 nucleotides in length.

3. The composition of claim 1, wherein the iRNA agent comprises one or more 2′-modified nucleotides and/or one or more phosphorothioates.

4. The composition of claim 3, wherein the one or more 2′-modified nucleotides are independently selected from the group consisting of: 2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylarninopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), and 2'-O-N-methylacetamido (2'-O-NMA).

5. The composition of claim 3, wherein the sense strand and/or the antisense strand comprises a 3' overhang.

6. The composition of claim 3, wherein the sense strand and/or the antisense strand comprises a 5' overhang.

7. The composition of claim 3, wherein the iRNA agent comprises at least one blunt end.

8. The composition of claim 3, further comprising a buffer, diluent, penetration enhancer, carrier compound, and/or pharmaceutically acceptable carrier or excipient.

9. The composition of claim 3, wherein the composition is presented in unit dosage form.

10. The composition of claim 1, wherein the iRNA agent is ligated to one or more diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecogenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, Oligo Lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, epithelial receptor ligand, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

11. The composition of claim 3, further comprising one or more known agents effective in treatment of ENaC-related disorders.

12. The composition of claim 11, wherein the known agent is selected from the group consisting of: anti-inflammatory drug, bronchodilatory drug, antihistamine, anti-tussive drug, antibiotic, DNase drug substance, epithelial sodium channel blocker.

13. The composition of claim 3, wherein the iRNA agent comprises:
an antisense strand comprising a nucleotide sequence of nucleotides 1-19 of SEQ ID NO: 1298 and a sense strand comprising a nucleotide sequence of nucleotides 1-19 of SEQ ID NO: 1297.