CLAIMS

1. A polypeptide, for use in suppressing or treating itch, wherein the polypeptide comprises:

(i) a non-cytotoxic protease, which protease is capable of cleaving a SNARE protein in an itch-specific DRG neuron or a pruriceptor;
(ii) a Targeting Moiety (TM) that is capable of binding to a Mas-related G protein-coupled receptor (Mrgpr) on the itch-specific DRG neuron or a pruriceptor, which Mrgpr is capable of undergoing endocytosis to be incorporated into an endosome within the itch-specific DRG neuron or a pruriceptor, and wherein said itch-specific DRG neuron or a pruriceptor expresses said SNARE protein; and
(iii) a translocation domain that is capable of translocating the protease from within an endosome, across the endosomal membrane and into the cytosol of the itch-specific DRG neuron or a pruriceptor;

with the proviso that the polypeptide is not a clostridial neurotoxin (holotoxin) molecule.

2. The polypeptide for use according claim 1, wherein the TM binds to a receptor selected from the group comprising MrgprX, MrgprA, or MrgprC or receptor analogues thereof.

3. The polypeptide for use according to claim 1 or 2 wherein the TM is selected from the group consisting of: a Bovine Adrenal Medulla (BAM) peptide, a Melanocyte Stimulating Hormone peptide (MSH), neuropeptides terminating in Y-G or Y-amide, a chloroquine (CQ), a peptide comprising $SLIGRLNH_2$, histamine, serotonin, capsaicin, cortistatin or truncations or peptide analogues thereof.

4. The polypeptide for use according to any of the previous claims wherein the TM is selected from the group comprising: BAM_{8-22}, a γ2-MSH, SLIGRL, NPAF, NPFF, a chloroquine (CQ), a histamine, or serotonin, capsaicin, cortistatin or truncations or peptide analogues thereof.

5. The polypeptide for use according to any of the previous claims wherein the TM binds to the MrgprX1 receptor.

6. The polypeptide for use according to any of the previous claims wherein the TM is BAM_{8-22} peptide or a truncation or peptide analogue thereof.

7. The polypeptide for use according to any preceding claim, wherein the itch is histamine-independent itch.

8. The polypeptide for use according to any preceding claim, wherein the use of an analgesic causes, or worsens the itch.

9. The polypeptide for use according to claim 8, wherein said analgesic is an opioid pain reliever.

10. The polypeptide for use according to any preceding claim, wherein the itch is chronic itch, preferably chronic itch resulting from a renal disease, a liver disease, cancer or a skin disease.

11. A polypeptide for use according to any preceding claim, wherein the non-cytotoxic protease comprises a clostridial neurotoxin L-chain or an IgA protease

12. A polypeptide for use according to any preceding claim, wherein the translocation domain comprises a clostridial neurotoxin translocation domain.

13. A nucleic acid encoding a polypeptide according to any of the previous claims for use in suppressing or treating itch.

14. A polypeptide comprising:

(i) a non-cytotoxic protease, which protease is capable of cleaving a SNARE protein in an itch-specific DRG neuron or a pruriceptor;
(ii) a Targeting Moiety (TM) that is capable of binding to a Mas-related G protein-coupled receptor (Mrgpr) on the itch-specific DRG neuron or a pruriceptor, which Mrgpr is capable of undergoing endocytosis to be incorporated into an endosome within the itch-specific DRG neuron or a pruriceptor, and wherein said itch-specific DRG neuron or a pruriceptor expresses said SNARE protein; and
(iii) a translocation domain that is capable of translocating the protease from within an endosome, across the endosomal membrane and into the cytosol of the itch-specific DRG neuron or a pruriceptor;

with the proviso that the polypeptide is not a clostridial neurotoxin (holotoxin) molecule, and wherein the TM is selected from the group consisting of: a Melanocyte Stimulating Hormone peptide (MSH), neuropeptides terminating in Y-G or Y-amide, a chloroquine (CQ), a peptide comprising SLIGRL-NH_2, histamine, serotonin, or truncations or peptide analogues thereof.

15. A nucleic acid encoding a polypeptide according to claim 14.