

# TREATMENT FOR CENTRALLY MEDIATED ITCHING

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**Background:** Severe itch (or pruritus) is associated with multiple diseases such as liver disease, non-Hodgkin's lymphoma, psoriasis, and common eczema and is also a side effect of many treatments including analgesics (like morphine) and renal dialysis. Chronic pruritus is a top reason for dermatologist visits, yet there is no effective treatment for patients suffering from histamine-independent chronic pruritus. One major obstacle to effective treatment of itch is that no itch-specific genes suitable as drug targets have been identified. In addition, itching has been regarded as a less intense version of the body's response to pain, thereby making itch-specific therapy difficult to achieve without affecting pain responsiveness.

**Technology Description:** The invention encompasses novel methods for treating pruritus in humans and animals based on a newly defined itch mechanism. The studies identified the first itch-specific receptors, including gastrin-releasing peptide receptor (GRPR) and neuromedin B receptor (NMBR), as central mediators for the itch signal. Furthermore, Dr. Chen has demonstrated that responses to pain and itch represent independent signaling pathways and inhibition of the itch pathway can be used for pruritus treatment. Additionally, delivery of antagonists directed to the receptors using a genetic and pharmacologic approach can relieve itch. GRPR or GRPR/NMBR-double null mice treated with pruritic-inducing agents exhibited reduced scratching relative to wild-type mice. Wild-type mice treated with GRPR, NMBR or GRPR and NMBR antagonists exhibited virtually no scratching behavior in response to itch-inducing analgesics like morphine or other itch-inducing compounds. Antagonists were also able to relieve itch in mice with atopic dermatitis, suggesting that GRPR and/or NMBR antagonists can be used to treat both acute and chronic itch problems. Recent studies have demonstrated a distinct therapeutic approach involving the targeted ablation of spinal cord neurons expressing GRPR. Mice treated with a bombesin-saporin (GRPR ligand conjugated to a neurotoxin) exhibited complete itch relief but maintained normal pain responses and motor neuron function. Mice with chronic itch treated with bombesin-saporin also exhibited complete itch relief through ablation of GRPR spinal cord neurons.

## Key Advantages:

- Treatment for histamine-independent itch
- Targets central mechanism for virtually complete itch relief