TRPV4 ion channels as a target in systemic pruritic diseases

Unmet Need
Pruritus, or an itching sensation, is one common symptom shared by hepatobiliary diseases, intrahepatic cholestasis of pregnancy (between 0.2% of 2% of all pregnancies) chronic kidney disease (55% prevalence globally), and pruritic psoriasis. Pruritus can be debilitating, as the constant itching sensation disrupts sleep and lowers the overall quality of life. Treatments for pruritus in the hepatobiliary conditions are better established than for kidney diseases but are not always effective and have adverse side effects. There is a need for a treatment of pruritus that can help with all these diseases.

Technology
Duke inventors have developed a treatment for pruritus. This is intended to be used by clinicians to help alleviate chronic pruritus in patients with hepatobiliary diseases, chronic kidney disease, or psoriasis. Specifically, Duke inventors discovered that skin cells display the common receptors for itch and are activated by elevated levels of lysophosphatidylcholine (LPC) found in patients suffering from these conditions. One receptor, TRPV4 on skin cells, was shown to be a principal modulator of pruritus. Duke inventors have identified a battery of molecules that can be used to modify the activation of this receptor to alleviate pruritus. This has been demonstrated in an in vivo murine model of pruritus where inhibition of TRPV4 abrogated pruritus and elucidated the mechanism of cellular activation. This was further validated in a rhesus macaque model of pruritus wherein injection of LPC elicited an itch response. In addition, they showed that microRNA-146a, which is released from skin cells treated with LPC, elicits an itch response in the
Other Applications

This technology could also be used as a disease marker for pruritic disorders. Duke inventors found that LPC was elevated in human patients suffering from the hepatobiliary condition primary biliary cholangitis with pruritus compared to patients that did not experience pruritus. Further, quantification of mirRNA-146a in serum of patients can also be used to identify pruritic disorders. This could be extended to other disorders wherein pruritus plays a role in disease classification.

Advantages

- Identifies multiple targets for the treatment of pruritus.
- Provides a common target for treating pruritus in multiple diseases.
- Identified biomarkers for the incidence of pruritus.
- Provides another modality for the treatment of pruritus.