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Transient Receptor Potential (Trp) Channels Antagonist in Managing Atopic Dermatitis

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Short Commentary

Chronic atopic dermatitis (AD) is a distressing pruritic condition that has become increasing prevalent. Despite extensive research, children and adults still suffer from this devastating disease. The exact pathogenesis; interplay between the skin barrier innate defects, epidermal dysbiosis, immune aberrancy and relentless itch-scratch viscous cycle in chronic AD is still unresolved. Cognitive co-morbidities and the phenomena of allokinesis are not fully scientifically explained. Notable achievements were made in the domain of immune cascades dysfunction; with the advent and discovery of biologics. The complex nature of AD is still an interesting research area for pharmacologists, neurologists, cognitive scientists, microbiologists, gastroenterologists and dermatologists.

The TRP channels and its associated G Protein C Receptors and 5-Hydroxytryptamine receptors(HTR) (with different subtypes) may bring new insight to our understanding of this complicated skin disease. TRP receptors, namely TRPV1, TRPV3, TRPV4, TRPA1 and TRPM and serotonin receptors play a pivotal role in the pruritogenic pathway of this sensitive condition of AD.[1,2,3] TRPA 1 has a direct and initial activity in the transmission of nociceptive signals through neuronal depolarisation through calcium influx. Sensitive skin is believed to be mediated by TRP channels. TRP receptors existed on the surface of keratinocytes. Afferent neurones possess TRP receptors are widely distributed in skin epidermis synapsing with the dorsal horn of the spinal cord. Hypersensitivity and unprotected sensory endings of neurones in between keratinocytes activated TRP receptors by cationic change in the environment pH, temperature, various pollutants, natural agonists and allergens; relay transient signals to the cerebral cortex. In the synapses of the dorsal root ganglion, neurogenic together with non- neurogenic inflammations act through TRP, prostaglandins, NMDA, Bradykinin, Substance P, Nerve Growth Factors, Cytokines, Insulin, Noradrenaline, Histamine 1 to 4, Protease and Toll like receptors and its ligands propagate pruritic depolarization signals to the cerebral cortex. The subjective sensory symptoms of itch sometimes behaved in an uncontrolled manner and resulted in severe consequences.

Pruritogen-sensing G protein-coupled receptors, MrgprA3 and MrgC11 ligands associated itch is TRPA1 mediated. [1] IL- 31 was discovered to be closely assembled both anatomically and functionally with TRPA1 and TRPV1 in AD-induced pruritus.[1] Emerging evidence suggests that TRPA1 play a crucial role, besides TRPV1, in the induction of itch in the pruritogenic pathway.[2,3] TRPA1 like TRPV1 also participates in epidermal repair, homeostasis and pro-inflammatory activities. TRPA1 receptors and 5-Hydroxytryptamine 7 (HTR7) activation are required for the development of atopic dermatitis in mice. Morita and colleagues showed that HTR 7 receptor activation triggers serotonin and that SSRI evoked itch by promoting opening of the TRPA1 channels.[1] HTR 7 and TRPA1 are functionally coupled in eliciting itchiness.[1] TRPA1 antagonists and HTR7 are potential therapeutic targets in AD. TRPA1 and HTR7 are also distributed in the central nervous system including the brain; they are

important in our understanding of the hedonistic pathological itch -scratch cycle seen in AD. Serotonin, Dopamine, Noradrenaline and endogenous neuropeptides imbalance miswiring may explain the chronicity of the cognitive behaviour in severe AD patients.

TRPV3 is highly expressed in epidermal keratinocytes and is reported to have its highest density among other TRP.[3] Activation of TRPV3 release nitric oxide from keratinocytes which has significant effects on stimulated wound healing and keratinocyte migration. Gain-of-function mutation, TRPV3Gly573Ser, causes loss of hair and atopic-like dermatitis in mice with intense itching. TRPV3, like its relative TRPV1, thus participates in the mediation of proinflammation. This suggests that TRPV 3 may also be involved in the pathogenesis of itch in AD and hence should be further systemically studied pharmacologically.

In sum, apart from epidermal barrier dysfunction and an aberrant immunity, TRP channels and serotonin receptors activation in the central nervous system may all contribute to severe, chronic AD. The understanding of the TRP channels – inflammation – itch-scratch cycle with CNS connections provide one of the basic therapeutic model in the management of AD. Systematic evaluation of new AD pharmacological therapy should inform and educate practicing dermatologists on this. An integrated approach should enlighten the service providers and suffering patients and their families about these new discoveries in neuroimmunology.[4] Information on neuro-cognitive psychotherapies, biologics and other new evidence-based non-biologic pharmaceutical regimes should be made available to distressed chronic AD patients, hopefully, to enable them to choose the best management options for themselves.[4, 5]

REFERENCES

1. Morita, T., et al. HTR7 Mediates Serotonergic Acute and Chronic Itch. *Neuron*. **2015.** 1:87(1):124-138.
2. Chan, KTM., The pivotal Role of Transient Receptor Potential (TRP) Ion Channels in the Pathogenesis of Sensitive Skin. *Research Journal of Nervous System*. **2017.** 1(1):1.
3. Caterina, MJ., Pang, Z., TRP channels in skin biology and pathophysiology. *Pharmaceuticals*, **2016.** 9:77.
4. Sanders, KM., Nattkemper, LA., and Yosipovitch, G., Advances in understanding itching and scratching: A new era of targeted treatments. *F1000Res.* **2016.** 22: 5.
5. Leibovici, V., et al. Effects of virtual reality immersion and audiovisual distraction techniques for patients with pruritus. *Pain Res Manag*. **2009.** 14(4): 283-286.