FINAL REPORT

Pruriceptive role of neural and non-neural TRP ion channels in the skin
(NKFI-120187)

Background and aims

Pruritus i.e. itch generated in the skin, is the most common symptom in dermatology. Pruritogenic substances, or shortly pruritogens, can trigger acute itch sensation by activating a subpopulation of somatosensory neurons innervating the skin. In the sensory transduction of itch, members of the transient receptor potential (TRP) ion channels play a central role. Especially the role of the thermosensitive nociceptor TRPV1 and TRPA1 was characterized in histaminergic and non-histaminergic forms of itch, respectively. Although the understanding of acute itch transduction was made several advances in the recent years, the generation of chronic itch associated with medical conditions in which the presence of a well-defined puritogen cannot be clearly identified is less understood. It is assumed that in these conditions the surrounding, often inflamed tissue environment significantly contributes to the altered sensitivity or direct activation of the pruriceptive sensory fibers. In this project, we aimed at characterizing how TRP channels expressed by somatosensory neurons and by the neighboring non-neuronal cells in the skin can potentially contribute to intercellular signaling events resulting in pruritus.

Results of the project

TRPM3 mediates pain but not itch and it is inhibited by volatile anaesthetics

TRPM3 is a novel thermosensitive nociceptor TRP channel expressed by a subpopulation of somatosensory neurons. Together with TRPV1 and TRPA1, it has a crucial contribution to heat pain detection and plays a role in the development of inflammatory heat hyperalgesia. We investigated its functionality in non-neural cells of the skin and studied its role in the transduction of itch in.

Applying the endogenous TRPM3 agonist pregnenolon sulfate (PS) we found that HaCaT and primary isolated normal human epidermal keratinocytes (NHEKs), HCL-SG3 sweat gland cell line, SZ95 sebocytes and NIH3T3 fibroblast did not show any functional TRPM3 responses, although primary isolated human dermal fibroblasts responded to PS. Later pharmacological characterization revealed that the PS responses of the HDFs is independent of TRPM3, since they were not influenced by the TRPM3 blocker isosakuranetin and CIM0216, a hyperpotent exogenous agonist also failed to activate HDF. In good accordance, HDFs hardly expressed any TRPM3 transcript **(D25, D31)**.

In earlier studies, TRPV1 and TRPA1 were identified as key players in the transduction of pruritic stimuli in sensory neurons but the role of TRPM3 was not yet studied in itch. In collaboration with the laboratory of prof. Thomas Voets at KU Leuven, Belgium, we investigated the role of TRPM3 in mediating itch sensation *in vivo* and *in vitro*. Prof Voets' laboratory provided the facility and the animals used, and the experiments were designed and carried out by the members of our team. In the frame of our collaboration, Balázs Kelemen spent 6 month in the laboratory of prof. Voets carrying out *in vivo* studies. The project was approved by the Ethical Committee for Animal Experimentation of KU Leuven under the ID number P021/2018. We adopted and optimized the cheek model, a widely accepted paradigm in *in vivo* itch studies making possible the clear distinction between pruritic and nocifensive behavioral responses. In this model, itch in the cheek evokes scratching with the hind limb while pain initiates mainly wiping with the forelimb. Using this technique, we quantitatively compared the itch

and pain responses of trpm3+/+ and trpm3-/- mice for several pruritogenic and algogenic substances. We found that the activators of TRPM3 evoked only pain, but not itch. Moreover, both histamine and non-histaminergic pruritogens evoked a similar level of scratching in trpm3+/+ and trpm3-/- animals but trpm3-/- animals showed much less intense nocifensive responses for certain algogenic compounds. Moreover, investigating sensory neurons isolated from the trigeminal ganglia of the above animals, we have found that pruritogens activated the same percentage of neurons in both the trpm3+/+ and trpm3-/- animals. In good accordance, pruritogen evoked Ca^{2+} signals were not significantly affected by isosakuranetin, an antagonist of TRPM3. These results strongly argue for that neural TRPM3 is associated exclusively with pain transduction and it is not involved in the development of itch. Therefore, TRPM3 might be an important marker in the molecular distinction of itch and pain processing and it is a promising target to treat various forms of pain with an advantageous side effect profile. **(D11, D30, D37, D41, D43)**

We also characterized pharmacological interactions of TRPM3 potentially influencing its sensory functions. Using HEK293T cells and sensory neurons isolated from mouse dorsal root ganglia expressing recombinant and native TRPM3, respectively, we discovered that volatile anaesthetics (VAs) inhibit TRPM3 activity evoked by either chemical agonist or increased temperature. We have characterized VAs with different chemical structures and identified halothane as the most effective blocker of TRPM3. VAs inhibited currents both mediated by the canonical pore of TRPM3 and by an alternative permeation pathway related to the voltage sensor domain. These results suggest that VAs do not act as classical pore blockers, rather inhibit a general conformational change related to channel opening evoked by various mechanisms. **(D1, D11, D18, D19, D23, D26)**

TRPV3 mediates inflammatory and pruritic responses in the skin

TRPV3 is a thermosensitive member of the TRP family. It is highly expressed in the epidermis and even was cloned from keratinocytes. Its gain-of-function mutations results in the development of dermatitits associated with itching, severely dry skin and hairless phenotype in rodents and causes Olmsted syndrome, a rare genodermatosis characterized by periorofacial hyperkeratosis, hypotrichosis, alopecia and severe pruritus in humans. Our earlier study indicated that chemical activation of human TRPV3 also inhibits hair growth. In the current project we intensely studied the role of TRPV3 in the development of pruritic inflammatory signaling in non-neural cutaneous cells.

Confirming previous studies, we also detected a high expression of TRPV3 in the epidermis of human skin in situ as well as in NHEKs in vitro. Activation of TRPV3 by chemical agonists evoked marked Ca^{2+} transients in NHEKs, and induced the activation of the NF-kB signaling pathway, which is a central regulator of inflammatory processes. Moreover, activation of TRPV3 induced the expression and release of inflammatory cytokines IL-1a, IL-6, IL-8 and TNFa. These data strongly argue for the role of TRPV3 in the development of pruritic dermatoses. **(D8)**

To better characterize the role of epidermal keratinocytes in the development of pruritic responses, we carried out whole transcriptome analysis (RNASeq) and investigated the expression of TRP channels and pruritus associated mediators and receptors in NHEKs. We identified the presence of several pruritogenic molecules, and sensory TRP channels among which TRPV3 and TRPV4 were expressed at relative high level. To reveal the potential role of TRP channels in the pruritic signaling, we treated the NHEKs with several pruritogens and investigated the expression and function of TRP channels. We found that activation of Toll-like receptor 3 (TLR3), which was earlier described as an essential receptor in the development of various forms of itch, selectively increased the expression of TRPV3 and potentiated TRPV3 mediated responses, but did not affect TRPV4 mediated signaling.

Other potentially pruritogenic inflammatory ligands (IL-4, histamine, TSLP, endothelin-1, etc.) did not affect TRPV3 expression. TLR3 activation is known to stimulate release of inflammatory citokines and the pruritic mediator endothelin-1 (ET1). Our results suggested that TLR3 evoked ET-1 release can be inhibited by ruthenium red, a non-selective TRPV3 antagonist arguing for the role of TRPV3 in TLR3 related pruritic signaling events. **(D12, D29, D33, D36, D40, D44)**

Further investigating the expression of TRPV3 in the human skin, we found that human sebaceous glands in situ and human SZ95 sebocytes in vitro also express functional TRPV3. The activation of TRPV3 in sebocytes also stimulated the synthesis of proinflammatory cytokines and inhibited the lipid (sebum) production of the cells suggesting that sebocytes can also contribute to dry skin associated itching dermatoses associated with TRPV3 activation. **(D5, D21, D22, D28)**

TRPV4 regulates dermal inflammatory/pruritic cytokine release and regenerative processes

Although HDFs did not express functional TRPM3 as mentioned above, we detected the expression of TRPV1, TRPV2, TRPV3, TRPV4 and TRPA1 transcripts, among which TRPV4 was expressed at the highest level. Using specific pharmacological tools, we proved that TRPV4 forms functional Ca^{2+} permeable channels in the membrane of HDFs. TRPV4 is known to be activated by mechanical stimuli and detects hyposmotic cellular environment. Hypotonic solutions evoked marked Ca^{2+} signals in HDFs which were effectively blocked both by the non-specific TRP blocker ruthenium red and by the TRPV4 specific antagonist HC047067. These results indeed indicate, that TRPV4 expressed by HDF cells functions as an osmosensor, sensing hyposmotic cues. Importantly, the chemical activation of TRPV4 not only evoked intracellular Ca^{2+} signals, but induced marked changes in the gene expression. TRPV4 activation highly upregulated the expression of IL-33, a known pruritic molecule as well as induced the expression and release of the inflammatory chemokine IL-8/CXCL8. Moreover, TRPV4 activation, among else, also increased expression of metalloproteinase genes MMP1 and MMP3 (whereas MMP11 was decreased) which may contribute to both inflammatory responses, as well as tissue re-modelling and regeneration. In good accordance with the above, TRPV4 activation seems to increase the invasiveness of HDFs as measured in an invasion assay monitoring penetration of the cells through a Matrigel covered membrane. Although TRPV4 activation did not alter the proliferation of NHEKs, supplementing the NHEK cultures with supernatant of HDF cells pretreated with TRPV4 agonist GSK10167920A increased the proliferation of keratinocytes compared with control cultures or cultures supplemented with non-treated HDF supernatants. These results suggest that dermal TRPV4 stimulates the synthesis of proinflammatory and pruritic cytokines and may regulate inflammatory and regenerative processes/tissue re-modelling in the skin which may affect barrier functions, as well. **(D13, D14, D25, D31, D32, D42)**

Next to HDFs, we have detected functional TRPV4 in human hair follicles, and keratinocytes isolated from the outer root sheath of the follicles, as well. If activated, TRPV4 inhibited hair growth, initiated apoptosis driven regression and induced catagen transformation of hair follicles, providing further evidence for its regulatory role in regeneration and proliferation. **(D2)**

TRPA1 acts in a protective manner in imiquimod-induced psoriasiform dermatitis

In frame of an international collaboration (Dept. of Pharmacology and Pharmacotherapy, Dept. of Dermatology at University of Pécs, and King's College London) we have described the protective role of TRPA1 in imiquimod-induced psoriasiform dermatitis. Our group identified that the pruritogenic imiquimod is a direct activator of TRPA1. **(D6)**

Human monocyte derived Langerhans cells (moLCs) express proinflammatory receptors linked to pruritus

Testing various conditions, among else preconditioned keratinocyte medium supplement and co-culturing with keratinocytes, we established and optimized the differentiation of Langerhans cells from CD14+ human monocytes isolated from peripheral blood. In these moLCs, we identified the expression of potentially pruritogenic histamine receptors (HRH1 and HRH4), TLR3 and heat sensitive members of TRP channels, namely TRPV1, TRPV2 and TRPV4. In functional studies, we found that TRPV4 stimulates the differentiation of moLCs (measured by surface expression of CD1a and CD207 Langerin), but it does not affect the further maturation of the differentiated cells. Moreover, activation of TRP channels upregulated the expression of TLR3 and inflammatory chemokines. **(D16, D17, D24, D27)**

Expression level of pruritogenic molecules correlates with disease activity in itching dermatomyositis

Pruritus is a common symptom of various dermatological disorders. We focused on dermatomyositis (DM), a less studied autoimmune disease with itching skin manifestations. We collected biopsy samples and carried out targeted gene expression analysis of lesional versus non-lesional skin of 17 patients affected with active DM. We showed, that itching index (5-d itch scale) in DM positively correlated with Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) score TNFα gene expression was significantly higher in lesional DM skin than in non-lesional DM skin. The normalized TNFα mRNA expression (i.e. gene expression in lesional skin normalized to non-lesional skin) was positively correlated with itch scale and its level was significantly higher in skin samples of patients with severe itch (itching score: 15-20) versus mild itch (itching score: 5-10). The normalized PPARγ gene expression negatively correlated with itch scale, and its level was significantly lower in patients with severe itch versus mild itch. Lesional IL-6 mRNA levels were associated with CDASI activity score. The mRNA levels of TRPV1-4 channels were not associated with 5-D itch score, but normalized TRPV1 and TRPV4 mRNA expressions were positively correlated with CDASI damage score. Interestingly, itching sensation of DM patients was not correlated with IL-33 mRNA levels measured in skin samples. These results argue for that higher cutaneous disease activity can generate pruritus. TNFα and PPARγ might play a causative, but opposite role in DM-associated itch. Furthermore IL-6, TRPV1 and TRPV4 channels might contribute to the cutaneous manifestations of DM. **(D45, D46, D47, D48)**

Additional results related to the project

As additional results of the optimization of cell cultures and hair follicle cultures, we have realized that the presence of the paracrine mediator adenosine might be beneficial for the cellular viability which was further characterized in microdissected hair follicles and keratinocyte cultures isolated from the other root sheath of human hair follicles. Our related results suggest that adenosine promotes the growth of human hair follicles in vitro and influences paracrine communication between epithelial and mesenchymal cells of the hair follicle. **(D3)**

During the above detailed experiments, several techniques were optimized e.g. antibodies and western blot conditions to detect thermosensitive TRPV1-4 channels or silencing of TRPV3 expression using siRNA technique. These results were also exploited in parallel experiments on other cell types, among else podocytes, by which we also investigated the "skin-specificity" of our results. During these experiments, we have shown that podocytes express TRPV3 protein and transcripts at relatively low

level compared to keratinocytes and sebocytes. Furthermore, the functionality of the TRPV3 in podocytes is also questionable: although nonspecific TRPV3 agonists evoked prominent Ca^{2+} signals, these signals were not inhibited either by TRPV3 agonists or by TRPV3 silencing. In contrast, similar to HDFs, we found TRPV4 as the dominant, functionally expressed isoform of heat sensitive TRPV channels in podocytes. **(D10, D20, D39)**

In parallel experiments we started to investigate TRP channels in the cells of the dental pulp and their role in the development of pulpitis and related pathophysiological sensation, like pain, hyperalgesia and allodynia. In this experiments we extensively utilized the methodological advances of the current project, like optimized culturing and treatment conditions, molecular detection and functional investigation of TRP channels. As we did in keratinocytes, we studied the expression and functionality of sensory TRP channels and investigated the effect of inflammatory pathogenic signals. Similar to keratinocytes, we found that TLR3 activation is a very effective inductor of inflammatory responses. Interestingly, in human dental pulpal cells, TLR3 seemed to increase the expression of TRPA1, and not TRPV3 as found in keratinocytes. **(D35, D38)**

During the project, we reviewed the state-of-the-art and published a review paper about the neuro-endocrine control mechanisms of sebaceous glands and sebocytes. We also published a book chapter discussing the role of endogenous factors that can influence skin pH. In these reviews we discussed, among else, the role of TRP channels and our previous results in the field which have also significant consequences regarding the development of cutaneous disorders and itch. Moreover, we got an additional invitation to write a review about the role of TRP channels in itch and pain. This submitted review is planned to be published in a book entitled *Itch and Pain: Similarities, Interactions, and Differences*, edited by Gil Yosipovitch, Hjalte H. Andersen, and. Lars Arendt-Nielsen. The book is planned to be published by IASP press, the publisher of the International Association for the Study of Pain (IASP). We considered this invitation as a great honor and appreciation of our work. **(D7, D9, D2)**

Training achievements

The results of the projects provide a solid base for PhD thesis supervised by senior researchers of the project. Closed and expected PhD defenses related to the project:

Lidia Ambrus (2019): Role of TRPC6 and heat-sensitive TRPV channels in regulation of human podocytes. Supervisor: Tamás Bíró – successfully defended thesis

Erika Lisztes (2019): Új, komplex mechanizmusok felderítése a hajnövekedés szabályozásában – fókuszban a külső gyökérhüvely keratinocyták. Supervisor: Tamás Bíró – submitted thesis

Balázs Kelemen (2020, expected): Thesis about the pruriceptive role of TRPM3 and its regulation by volatile anaesthetics. Supervisor: Balázs István Tóth – expected thesis

Anita Vladár (2021, expected): Thesis about the pruriceptive role of epidermal TRPV3 and its regulation by TLR3 signaling. Supervisor: Balázs István Tóth – expected thesis

Detailed list of disseminations related to the project

Published papers and manuscripts accepted for publication related to the project

D1. Kelemen B, Lisztes E, Vladár A, Hanyicska M, Almássy J, Oláh A, Szöllősi AG, Pénzes Zs, Posta J, Voets T, Bíró T, Tóth BI (2020) Volatile anaesthetics inhibit the thermosensitive nociceptor ion channel transient receptor potential melastatin 3 (TRPM3). Biochem Pharmacol. 174:113826. IF: 4.82

D2. Tóth BI, Szöllősi AG, Bíró T (2020) TRP channels in itch and pain. In: Yosipovitch G, Arendt-Nielsen L (eds): *Itch and Pain: Similarities, Interactions, and Differences. IASP Press* ACCEPTED FOR PUBLICATION – *INVITED REVIEW, UNDER PUBLICATION*

D3. Lisztes E, Tóth BI, Bertolini M, Szabó IL, Zákány N, Oláh A, Szöllősi AG, Paus R, Bíró T (2019) Adenosine promotes human hair growth and inhibits catagen transition in vitro – Role of the outer root sheath keratinocytes. *J Invest Dermatol.* ACCEPTED FOR PUBLICATION, MS ID: JID-2019-0272.R2 IF: 6.290*

D4. Szabó IL, Herczeg-Lisztes E, Szegedi A, Nemes B, Paus R, Bíró T, Szöllősi AG (2019) Transient receptor potential vanilloid 4 is expressed in human hair follicles and inhibits hair growth in vitro. *J Invest Dermatol. 139(6)*:1385-8 IF: 6.290*

D5. Szántó M, Oláh A, Szöllősi AG, Tóth KF, Páyer E, Czakó N, Pór Á, Kovács I, Zouboulis CC, Kemény L, Bíró T, Tóth BI (2019) Activation of TRPV3 Inhibits Lipogenesis and Stimulates Production of Inflammatory Mediators in Human Sebocytes – A Putative Contributor to Dry Skin Dermatoses. *J Invest Dermatol. 139(1)*:250-3. IF: 6.290*

D6. Kemény Á, Kodji X, Horváth S, Komlódi R, Szőke É, Sándor Z, Perkecz A, Gyömörei C, Sétáló G, Kelemen B, Bíró T, Tóth BI, Brain SD, Pintér E, Gyulai R (2018) TRPA1 Acts in a Protective Manner in Imiquimod-Induced Psoriasiform Dermatitis in Mice. *J Invest Dermatol. 138(8)*:1774-84. IF: 6.290

D7. Bíró T, Oláh A, Tóth BI, Szöllősi AG (2018) Endogenous Factors That Can Influence Skin pH. *Curr Probl Dermatol. 54*:54-63.

D8. Szöllősi AG, Vasas N, Angyal Á, Kistamás K, Nánási PP, Mihály J, Béke G, Herczeg-Lisztes E, Szegedi A, Kawada N, Yanagida T, Mori T, Kemény L, Bíró T. (2018) Activation of TRPV3 Regulates Inflammatory Actions of Human Epidermal Keratinocytes. *J Invest Dermatol. 138(2)*:365-74. IF: 6.290

D9. Szöllősi AG, Oláh A, Bíró T, Tóth BI (2018) Recent advances in the endocrinology of the sebaceous gland. *Dermatoendocrinol. 9(1)*:e1361576.

D10. Ambrus L, Kelemen B, Szabó T, Bíró T, Tóth BI (2017) Human podocytes express functional thermosensitive TRPV channels. *Br J Pharmacol. 174(23)*:4493-4507. IF: 6.81

Manuscripts in preparation and further planned publications

D11. Kelemen B, Pintho S, Lisztes E, Vladár A, Hanyicska M, Oláh A, Szöllősi AG, Bíró T, Voets T, Tóth BI: TRPM3 transmits pain but not itch in the mouse cheek model. – *working title. Planned submission by 31 Dec 2019*

D12. Vladár A, Lisztes E, Kelemen B, Hanyicska M, Oláh A, Szöllősi AG, Bíró T, Tóth BI: TRPV3 mediates proinflammatory and pruritic effect of TLR3 activation on human keratinocytes. – *working title. Planned submission by 31 May 2020*

D13. Lisztes E, Szöllősi AG, Almohammadi S, Kelemen B, Vladár A, Hanyicska M, Oláh A, Bíró T, Tóth BI: TRPV4 regulates inflammatory and regenerative processes in human dermal fibroblasts. – *working title. Planned submission by 31 August 2020*

Citable abstracts

D14. Lisztes E, Kelemen B, Vladár A, Hanyicska M, Bíró T, Tóth BI (2019)Regulatory function of TRPV4 on the dermal component of inflammatory skin conditions. *J. Invest. Dermatol.139(9S) Supplement 2*:S324

D15. Kelemen B, Lisztes E, Hanyicska M, Vladár A, Pinto S, Voets T, Bíró T, Tóth BI (2019) Pruriceptive role of TRPM3. *J Invest Dermatol. 139(9S) Supplement 2*:S283

D16. Pénzes Zs, Alimohammadi S, Gyetvai Á , Guba D, Bíró T, Szöllősi AG (2018) Human monocyte-derived Langerhans cells express multiple proinflammatory receptors linked to pruritus. *Eur. J. Immunol. 48 (Suppl. 1)*:140 P-210

D17. Alimohammadi S, Gyetvai Á, Pénzes Zs, Guba D, Bíró T, Szöllősi AG (2018) Expression and role of pruritic receptors on monocyte-derived Langerhans cells J Invest Dermatol *138(5):*S164.

D18. Kelemen B, Kulin F, Lisztes E, Posta J, Voets T, Bíró T, Tóth BI (2018) Volatile anaesthetics inhibit thermosensitive TRPM3 ion channels. *Biophysical Journal 114 (Suppl. 1)*:

Presentations on national and international conferences

D19. Kelemen Balázs, Kulin Flóra, Radnóti Enikő, Vladár Anita, Posta János, Thomas Voest, Bíró Tamás, Tóth István Balázs (2017): Illékony anesztetikumok gátolják a TRPM3 ioncsatorna működését. *Conference: ÉFM2017 A Magyar Élettani Társaság, a Magyar Kisérletes és Klinikai Farmakológiai Társaság és a Magyar Mikrocirkulációs és Vaszkuláris Biológiai Társaság közös Vándorgyűlése, 2017. Június 13-16., Debrecen – poster presentation*

D20. Ambrus Lídia, Kelemen Balázs, Szöllősi Attila Gábor, Oláh Attila, Vladár Anita, Szabó Tamás, Bíró Tamás, Tóth István Balázs (2017): Hőérzékeny tranziens receptor potenciál vanilloid (TRPV) csatornák kifejeződése 7uman podocitákon. *Conference: ÉFM2017 A Magyar Élettani Társaság, a Magyar Kisérletes és Klinikai Farmakológiai Társaság és a Magyar Mikrocirkulációs és Vaszkuláris Biológiai Társaság közös Vándorgyűlése, 2017. Június 13-16., Debrecen – poster presentation*

D21. Balázs Kelemen, Magdolna Szántó, Attila Oláh, Attila Gábor Szöllősi, Ilona Kovács, Christos C. Zouboulis, Tamás Bíró, Balázs István Tóth (2017): Activation of TRPV3 inhibits lipogenesis and stimulates production of inflammatory mediators in human sebocytes, *Conference: "42th Symposium on hormones and Cell Regulation (European Society of Endocrinology – ESE) Ion Channels in Hormonal Homeostasis: Transient Receptor Potential Channels and Calcium Signaling" 2017 október 04-07. Mont Ste Odile, Franciaország – poster and oral presentation*

D22. Attila Oláh, Magdolna Szántó, Balázs Kelemen, Attila Gábor Szöllősi, Ágnes Pór, Ilona Kovács, Christos C. Zouboulis, Tamás Bíró, Balázs István Tóth (2017): TRPV3 decreases lipogenesis and promotes production of inflammatory mediators in human sebocytes *Conference: MIT 2017 – Magyar Immunológiai Társaság Vándorgyűlése, Velence, 2017. Október 18-20. – poster presentation*

D23. Balázs Kelemen, Flóra Kulin, Erika Lisztes, János Posta, Thomas Voets, Tamás Bíró, Balázs István Tóth: Volatile anaesthetics inhibit thermosensitive TRPM3 ion channels. *Conference: BJP2018, 62nd Annual Meeting of the Biophysical Society, 2018. Febr. 17-21. San Francisco, CA, USA – poster presentation*

D24. Pénzes Z. , Alimohammadi S. , Gyetvai Á,, Guba D. , Bíró T. , Szöllősi A.G. Human monocyte-derived Langerhans cells express multiple proinflammatory receptors linked to

pruritus. *Conference: 15th International Symposium on Dendritic Cells, 10–14 June 2018, Aachen, Germany – poster presentation*

D25. Herczeg-Lisztes Erika, Kelemen Balázs, Vladár Anita, Puskás Zsófia, Gyetvai Ágnes, Bíró Tamás, Tóth István Balázs (2018): A termo- és ozmoszenzitív TRP ioncsatornák kifejeződése és szerepe humán dermális fibroblasztokon. *Conference: 48. Membrán-transzport Konferencia, Sümeg, 2018. május 15-18. – poster presentation*

D26. Kelemen Balázs, Vladár Anita, Lisztes Erika, Posta János, Kulin Flóra, Thomas Voest, Bíró Tamás, Tóth István Balázs (2018): Az illékony anesztetikumok gátolják a TRPM3 ioncsatornát. *Conference: 48. Membrán-Transzport Konferencia 2018. május 15-18., Sümeg – oral presentation*

D27. Shahrzad Alimohammadi, Ágnes Gyetvai, Zsófia Pénzes, Dorina Guba, Tamás Bíró, Attila Gábor Szöllősi: Expression and role of pruritic receptors on monocyte-derived Langerhans cells. *Conferences: IID 2018 (5th International Investigative Dermatology (IID) Meeting, 2018. 05.16-19., Orlando, Florida, USA) – poster presentation*

D28. Oláh Attila, Szántó Magdolna, Tóth Kinga Fanni, Kelemen Balázs, Szöllősi Attila Gábor, Pór Ágnes, Kovács Ilona, Christos C. Zouboulis, Bíró Tamás, Tóth István Balázs (2018): A TRPV3 ioncsatorna aktivációja csökkenti a faggyúlipid-termelést, és gyulladásos választ vált ki humán szebocitákban. *Conference: A Magyar Élettani Társaság 82. Vándorgyűlése, Szeged, 2018. június 27-30. – poster presentation*

D29. Vladár Anita, Herczeg-Lisztes Erika, Kelemen Balázs, Bíró Tamás, Tóth István Balázs (2018): Epidermális TRP csatornák szerepe a viszketés kialakulásában szerepet játszó szignalizációs folyamatokban. *Conference: A Magyar Élettani Társaság 82. Vándorgyűlése, Szeged, 2018. június 27-30. – poster presentation*

D30. Kelemen Balázs, Silvia Pinto, Thomas Voest, Bíró Tamás, Tóth István Balázs (2018): A TRPM3 ioncsatorna pruriceptiv szerepének vizsgálata. *Conference: A Magyar Élettani Társaság 82. Vándorgyűlése, Szeged, 2018. június 27-30. – poster presentation*

D31. Herczeg-Lisztes Erika, Kelemen Balázs, Vladár Anita, Puskás Zsófia, Gyetvai Ágnes, Bíró Tamás, Tóth István Balázs (2018): Termo- és ozmoszenzitív ioncsatornák vizsgálata humán dermális fibroblasztokon: fókuszban a TRP fehérjék. *Conference: A Magyar Élettani Társaság 82. Vándorgyűlése, Szeged, 2018. június 27-30. – poster presentation*

D32. Herczeg-Lisztes Erika, Kelemen Balázs, Vladár Anita, Hanyicsak Martin, Gyetvai Ágnes, Bíró Tamás, Tóth István Balázs: A termo- és ozmoszenzitív TRPV4 ioncsatorna kifejeződése és szerepe humán dermális fibroblasztokon. *Conference: Magyar Dermatológiai Társulat 2018-as vándorgyűlése (2018.11.29-12.1. Budapest, Magyarország) – poster presentation*

D33. Vladár Anita, Herczeg-Lisztes Erika, Kelemen Balázs, Bíró Tamás, Tóth István Balázs: Epidermális TRP csatornák szerepe a viszketés kialakulásában szerepet játszó szignalizációs folyamatokban. *Conference: Magyar Dermatológiai Társulat 2018-as vándorgyűlése (2018.11.29-12.1. Budapest, Magyarország) – poster presentation*

D34. Posta János, Kelemen Balázs, Herczeg-Lisztes Erika, Vladár Anita, Thomas Voest, Bíró Tamás, Tóth István Balázs Az illékony anesztetikumok gátolják a TRPM3 ioncsatornát? *Conference: TOX'2018 Magyar Toxikológusok Társasága Lillafüred, 2018. október 17-19. – poster presentation*

D35. Herczeg-Lisztes E, Molnár D, Kelemen B, Vladár A, Hanyicska M, Bohács J, Bágyi K, Bíró T, Marincsák R, Tóth IB. Gyulladás hatása a hőérzékeny tranziens receptor potenciál ioncsatornák kifejeződésére humán dentális pulpális sejtekben. *Conference: 49. Membrán-Transzport Konferencia, 2019 május 14-17, Sümeg – poster presentation*

D36. Vladár A, Herczeg-Lisztes E, Kelemen B, Hanyicska M, Bíró T, Tóth IB Epidermális TRP csatornák szerepe a viszketés kialakulásában szerepet játszó szignalizációs folyamatokban *Conference: 49. Membrán-Transzport Konferencia, 2019 május 14-17, Sümeg – poster presentation*

D37. Kelemen Balázs, Silvia Pinto, Lisztes Erika, Vladár Anita, Hanyicska Martin, Thomas Voets, Bíró Tamás, Tóth István Balázs: A TRPM3 ioncsatorna szerepe a viszketés és a fájdalom kialakulásában. *Confernce: 49. Membrán-Transzport Konferencia, 2019 május 14-17, Sümeg – oral presentation*

D38. Lisztes Erika, Molnár Dóra, Kelemen Balázs, Vladár Anita, Hanyicska Martin, Bohács Judit, Bágyi Kinga, Bíró Tamás, Marincsák Rita, Tóth István Balázs Gyulladást indukáló mikrobiális szignálok hatása a termoszenzitív tranziens receptor potenciál (TRP) ioncsatornák expressziójára humán dentális pulpális sejtekben. *Conference:FAMÉ 2019 - Magyar Kísérletes És Klinikai Farmakológiai Társaság, Magyar Anatómus Társaság, Magyar Mikrocirkulációs És Vaszkuláris Biológiai Társaság, Magyar Élettani Társaság Közös Vándorgyűlése, 2019 06.05-08, Budapest – poster presentation*

D39. Hanyicska Martin, Kelemen Balázs, Lisztes Erika, Vladár Anita, Szabó Tamás, Bíró Tamás, Tóth István Balázs: A TRPV4 ioncsatorna biológiai szerepének vizsgálata humán podocytákon. *Conference: FAMÉ 2019 - Magyar Kísérletes És Klinikai Farmakológiai Társaság, Magyar Anatómus Társaság, Magyar Mikrocirkulációs És Vaszkuláris Biológiai Társaság, Magyar Élettani Társaság Közös Vándorgyűlése, 2019 06.05-08, Budapest – poster presentation*

D40. Vladár Anita, Kelemen Balázs, Hanyicska Martin, Herczeg-Lisztes Erika, Bíró Tamás, Tóth István Balázs: A TLR3 aktivátor polyinosinic:polycythaidic sav (poly(I:C)) fokozza a inflammatórikus TRPV3 ioncsatorna expresszióját normál humán epi-dermális keratinocitákon. *Conference: FAMÉ 2019 - Magyar Kísérletes És Klinikai Farmakológiai Társaság, Magyar Anatómus Társaság, Magyar Mikrocirkulációs És Vaszkuláris Biológiai Társaság, Magyar Élettani Társaság Közös Vándorgyűlése, 2019 06.05-08, Budapest – poster presentation*

D41. Kelemen Balázs, Silvia Pinto, Lisztes Erika, Vladár Anita, Hanyicska Martin, Thomas Voets, Bíró Tamás, Tóth István Balázs: A TRPM3 ioncsatorna szerepe a viszketés és a fájdalom érzékelésében. *Confernce: FAMÉ 2019 - Magyar Kísérletes És Klinikai Farmakológiai Társaság, Magyar Anatómus Társaság, Magyar Mikrocirkulációs És Vaszkuláris Biológiai Társaság, Magyar Élettani Társaság Közös Vándorgyűlése, 2019 06.05-08, Budapest – oral presentation*

D42. Erika Lisztes, Balázs Kelemen, Anita Vladár, Martin Hanyicska, Tamás Bíró, Balázs István Tóth: Regulatory function of TRPV4 on the dermal component of inflammatory skin conditions. *Conference: 49th Annual Meeting of ESDR, Bordeaux, France – poster presentation*

D43. Balázs Kelemen, Erika Lisztes, Martin Hanyicska, Anita Vladár, Silvia Pinto, Thomas Voets, Tamás Bíró, Balázs I. Tóth: Pruriceptive role of TRPM3. *Conference: 49th Annual Meeting of ESDR, Bordeaux, France – poster presentation*

D44. Anita Vladár, Erika Lisztes, Balázs Kelemen, Martin Hanyicska, Rita Marincsák, Tamás Bíró, Balázs István Tóth: Expression of the inflammatory ion channel TRPV3 is induced by TLR3 activation in human keratinocytes *Conference: MIT 2019, Magyar Immunológiai Társaság Vándorgyűlése, Bükfürdő, 2019.10.16-18. – poster presentation*

D45. Anett Vincze, Erika Herczeg-Lisztes, Katalin Szabó, Katalin Hodosi, Melinda Nagy-Vincze, Tamás Bíró, Katalin Dankó, István Balázs Tóth, Zoltán Griger: Pruritonegic

mediators in skin samples of patients with dermatomyositis. *Conference: Global Conference on Myositis, Berlin, 2019.03.27-30. – oral presentation*

D46. Griger Zoltán, Vincze Anett, Herczeg-Lisztes Erika, Szabó Katalin, Hodosi Katalin, Nagy-Vincze Melinda, Bíró Tamás, Tóth István Balázs, Dankó Katalin: Pruritogén mediátorok vizsgálata dermatomyositisben. *Conference: Magyar Allergológiai és Klinikai Immunológiai Társaság 47. Kongresszusa, Kecskemét, 2019.05.9-11. – oral presentation*

D47. Anett Vincze, Erika Herczeg-Lisztes, Katalin Szabó, Katalin Hodosi, Melinda Nagy-Vincze, Tamás Bíró, Katalin Dankó, István Balázs Tóth, Zoltán Griger: Pruritonegic mediators in skin samples of patients with dermatomyositis. *Conference: European League Against Rheumatism, Madrid, 2019.06.12.15. – poster presentation*

D48. Vincze Anett, Herczeg-Lisztes Erika, Szabó Katalin, Hodosi Katalin, Nagy-Vincze Melinda, Bíró Tamás, Tóth István Balázs, Dankó Katalin, Griger Zoltán: Pruritogén mediátorok vizsgálata dermatomyositisben. *Conference: Magyar Reumatológusok Egyesületének 2019. Évi Vándorgyűlése, Eger, 2019.09.26-28. – oral presentation*