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TITLE OF HIS PRESENTATION

Discovery of novel targets for the treatment of Complex Regional Pain Syndrome

RESULTS FOR THE TALENTUM PRIZE 2024 NOMINATION

Our research is the first to show that IgG autoantibodies, neuroinflammatory processes and signalling pathways in the central nervous system play key roles in Complex Regional Pain Syndrome, a primary chronic pain condition following minor injury. Our results have identified new therapeutic options for the treatment of this unmet medical need condition.

RESEARCH AREA

The causes of primary chronic pain conditions are not well understood, and include Complex Regional Pain Syndrome (CRPS) following minor tissue injury in the extremities, and fibromyalgia (FM), a widespread musculoskeletal pain without tissue damage after chronic psychosocial disstress. Despite intensive research, the pathophysiological mechanisms of these conditions are not known and since their treatment is not resolved, they represent unmet medical needs. In mice, passive transfer of immunoglobulin G (IgG) fractions from CRPS patients following small plantar incision results in the development of the main disease symptoms of prolonged, increasing pain and inflammation. Stress-induced pain models are used to explore FM-related mechanisms. In these translational disease models, which we have developed and characterized, we have identified inflammatory mechanisms, target molecules, and potential drug candidates in the dorsal root ganglia (primary sensory neurons) and pain-related brain regions using hypothesis-free transcriptomics and metabolomics, bioinformatics analysis, and immunohistochemistry techniques. We have demonstrated the efficacy of some novel treatment options for original development or repurposing that could open new directions in the management of these chronic primary pain conditions. A drug repurposing clinical trial based on our results is currently being conducted in Liverpool in CRPS patients.

TECHNIQUES AVAILABLE IN THE LAB

In vivo functional studies in rodent models of acute and chronic pain states: nociception assay and determination of inflammatory parameters. Other central nervous system comorbidities associated with chronic pain states (e.g. anxiety and depression) and behavioural tests for learning ability, memory in mice and rats; in vivo imaging (microCT, fluorescence and luminescence imaging), blood and tissue sampling; immunohistochemistry and histology (various tissue staining procedures, brain-spinal cord sectioning); analysis of transcriptomic and metabolomic data; statistical evaluations.

SELECTED PUBLICATIONS

Pohóczky, K., Kun, J., Szentes, N., Aczél, T., Urbán, P., Gyenesei, A., Bölcskei, K., Szőke, É., Sensi, S., Dénes, Á., Goebel, A., **Tékus, V.**, Helyes, Z. (2022). Discovery of novel targets in a complex regional pain syndrome mouse model by transcriptomics: TNF and JAK-STAT pathways. **Pharmacol Res 182:** 106347.

Helyes, Z., **Tékus, V.**, Szentes, N., Pohóczky, K., Botz, B., Kiss, T., Kemény, Á., Környei, Z., Tóth, K., Lénárt, N., Ábrahám, H., Pinteaux, E., Francis, S., Sensi, S., Dénes, Á., Goebel, A. (2019) Transfer of complex regional pain syndrome to mice via human autoantibodies is mediated by interleukin-1induced mechanisms. **Proc Natl Acad Sci U S A 116:** 1306713076.

Tékus, V., Hajna, Z., Borbély, É., Markovics, A., Bagoly, T., Szolcsányi, J., Thompson, V., Kemény, Á., Helyes, Z., Goebel, A. (2013) A CRPS-IgG-transfer-trauma model reproducing inflammatory and positive sensory signs associated with complex regional pain syndrome. **Pain 155(2):** 299-308.

Tékus, V., Horváth, Á. I., Csekő, K., Szabadfi, K., KovácsValasek, A., Dányádi, B., Deres, L., Halmosi, R., Sághy, É., Varga, Z. V., Adeghate, E., Kőszegi, T., Mátyus, P., Gábriel, R., Ferdinandy, P., Pintér, E., Helyes, Z. (2021) Protective effects of the novel amine-oxidase inhibitor multi-target drug SZV 1287 on streptozotocin-induced beta cell damage and diabetic complications in rats. **Biomed Pharmacother 134:** 111105.