24th International

C. elegans

Conference

June 24-28, 2023 | Glasgow, Scotland

ABSTRACT BOOK

GENETICS GSA G3 Genes | Genomes | Genetics

(TRPV1). Prolonged treatment with vanilloids triggered the desensitization of the TRPV1 leading to analgesic or antinociceptive effects. Following *C. elegans* genome sequencing, several genes encoding TRP ion channels, including TRPVs, were identified. Furthermore, several studies have shown that *C. elegans* TRPV orthologs (OSM-9 and OCR-2) are associated with behavioral and physiological processes, including sensory transduction. We have already shown capsaicin and eugenol targets *C. elegans* TRPV orthologs. The objective of this study was to perform proteomics to identify the proteins and pathways responsible for the induced phenotype.

Methods

N2 (Bristol) and other strains were obtained from the Caenorhabditis Genetics Center (CGC), University of Minnesota (Minneapolis, MN, USA). Strains were maintained and manipulated under standard conditions. Capsaicin or eugenol was dissolved in Type 1 Ultrapure Water at a concentration of 25 µM. *C. elegans* was isolated and washed and then expose to capsaicin or eugenol for 60 min. Then after, the nematodes were isolated, carefully washed, homogenized and protein were extracted, normalized, denature, reduced, alkylated, and digested with trypsin. Ultra-high-performance liquid chromatography/Quadrupole-Orbitrap mass spectrometry analysis operating in Data-Dependent Acquisition (DDA) mode was performed to identify and quantify proteins. Pathway analyses were performed using Metascape and the Reactome database.

Preliminary data

Capsaicin and eugenol can impede nocifensive response of *C. elegans* to noxious heat (32°C – 35°C) and the effect was reversed 6h post exposition. Additionally, we have identified the capsaicin target, OCR-2 and eugenol act redundantly with both OSM-9 and OCR-2. After we use proteomic investigations to performed *C. elegans* exposed to vanilloids. Preliminary results demonstrate that several specific processes were modulated following the pharmacological manipulation of *C. elegans* with capsaicin and eugenol. The inflammatory signaling pathways and the regulation of translation stand out from our bioinformatics analyses. These two processes are intimately linked to cell protection and survival mechanisms.

Novel aspect

Proteomics reveals inflammatory signaling pathways are triggered by the agonistic effects of capsaicin and eugenol on *C. elegans* vanilloid receptors.

1038V **The Ketone Body β-hydroxybutyrate ameliorates neurodevelopmental deficits in the GABAergic system of *daf-18/PTEN Caenorhabditis elegans* mutants.** Sebastián Giunti[1,2], María Gabriela Blanco[1,2], María José De Rosa[1,2], Diego Hernán Rayes[1,21]Instituto de Investigaciones Bioquímicas de Bahía Blanca, Departamento de Biología, Bioquímica y Farmacia (CONICET - UNS), [2]Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur

An increased Excitation/Inhibition (E/I) ratio in the brain is a hallmark of neurological disorders such as Autism Spectrum Disorder (ASD). Mutations in *PTEN,* a gene that encodes for the main negative regulator of the conserved PI3K/AKT pathway, are strongly associated with ASD. However, it is unclear how *PTEN* deficiencies can lead to E/I disequilibrium. The *C. elegans* neuromuscular system, where both excitatory (Cholinergic) and inhibitory (GABAergic) motor neurons regulate muscle activity, provides a proven simple model for studying E/I balance. We found that mutants in *daf-18* (ortholog for *PTEN)* exhibit phenotypes typical of animals with deficient GABAergic signaling. While cholinergic neuron morphology is normal, we observed defects that occur specifically in GABAergic neurites. This selective impairment accounts for the disruption of the E/I balance in *daf-18* mutants. In addition, we showed that the low activity of the transcription factor DAF-16 (ortholog for FOXO3A) during GABAergic neurodevelopment arises for the behavioral defects in *daf-18* mutants. Ketogenic Diets (KGDs), in which the production of ketone bodies (KBs) is forced, have been established as an effective treatment for disorders associated with E/I imbalances. The mechanisms underlying its effect are not understood. We found that exposure to the KB hydroxybutyrate (βHB) during early development improves GABAergic neurodevelopment in *daf-18* mutants. This effect depends on DAF-16/FOXO. Since the PI3K/AKT pathway is highly conserved, this study may provide universal information on the proven link between PTEN mutations and neurodevelopmental defects and, equally important, the mechanisms underlying KGDs positive effects on neuronal disorders characterized by E/I imbalance.

1039V **Reconstruction of *C. elegans* locomotion by optimal fluid control** Yongxing Wang, Thomas Ranner, Netta CohenUniversity of Leeds

C. elegans lives in a 3D environment whose locomotion however has been studied primarily through a microscope on a flat dish. There has been progress in developing a full 3D model of the worm, such as OpenWorm [1] or body midlines modelled as 3D curves [2,3]. Recent advances in imaging and midline reconstructions of worm's locomotion in 3D have opened up questions about the underpinning mechanics and neuromuscular control in 3D [4]. This dataset provides accurate body-midlines but