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C. elegans

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ABSTRACT BOOK

GENETICS GSA G3 Genes | Genomes | Genetics

Δ6 fatty acid desaturase, *fat-3*, exhibits a strong phosphine resistance phenotype. Exposure to phosphine is known to increase the generation of reactive oxygen species that can peroxidise conjugated double bonds of the fatty acid tails of membrane lipids. We propose that the *fat-3* mutation decreases lipid peroxidation by decreasing the number of double bonds in membrane fatty acids. Raising wild-type C*. elegans* at 15°C, increases membrane desaturation to maintain membrane fluidity. We found that rearing wild-type *C. elegans* at 15°C, followed by equilibration to 20C and prior to fumigation at 20C, increased sensitivity to phosphine relative to controls of the same developmental stage that had been reared at 20C. We found that the *fat-3* mutant, like wild-type, was more susceptible to phosphine when reared at 15°C. This suggests that membrane desaturation in response to rearing at 15°C occurs independently of *fat-3*. This study highlights the contribution of cellular fatty acid desaturation to phosphine toxicity and presents a practical strategy to control phosphine resistant individuals via modulation of fatty acid composition of membranes with a 15°C temperature shift before fumigation.

1255V **CDC-48 influences SKN-1 activity in response to pathogen infection** Carolaing Gabaldonmicrobiology and molecular genetic, university of texas health science center at houston

In Caenorhabditis elegans, bacterial infections produce an imbalance in the amount of ROS in the cell, causing oxidative damage in molecules. Attempts to counteract the damage occur by transcriptional activation of detoxification programs in response to high levels of oxidative stress. In our lab, we observe the effects of infection on the host by exposing C. elegans to the human pathogens Enterococcus faecalis and/or Pseudomonas aeruginosa, which are ingested and colonize the lumen of the intestine.

The infection triggers the expression of the transcription factor SKN-1, a protein that is activated by ROS and is involved in the activation of detoxification genes such as gst-4 (glutathione Stransferase 4) and gcs-1 (glutamate-cysteine ligase), which encode proteins that promote the survival of the animal. An RNAi screen looking for genes whose loss prevented SKN-1 activation on pathogen discovered cdc-48. CDC-48 is involved in targeting ubiquitinated substrates for proteolysis and helps maintain cellular proteostasis. Specifically, loss of cdc-48 by RNAi failed to cause the activation of SKN-1 reporter genes following infection with E. faecalis or P. aeruginosa. Congruently, the levels of SKN-1 in the nucleus were observed to be significantly decreased. Additionally, the absence of cdc-48 during infection renders C. elegans significantly more susceptible to the pathogen.

My current focus is to understand the mechanism by which CDC-48 influences SKN-1 and this is an active area of ongoing investigation. In conclusion, CDC-48 affects the activation and nuclear localization of SKN-1 to affect survival on human pathogens such as E. faecalis and P. aeruginosa.

1256V **Biological activities of essential oils on *Caenorhabditis elegans*: from molecular targets to anthelmintic therapeutic strategies** Guillermina Hernando, Ornella Turani, Noelia Rodriguez Araujo, Cecilia BouzatInstituto de Investigaciones Bioquímicas de Bahía Blanca, Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS)-CONICET, 8000 Bahía Blanca, Argentina.

Plants, herbal preparations and essential oils are used for health and medical functions since ancient times. Essential oils (EOs) have been extensively applied for human and veterinary health; their active agents have been isolated and incorporated into many current pharmaceutical preparations. Our study involves the use of *Caenorhabditis elegans* as a model of parasitic nematodes due to its simplicity and easy maintenance in the laboratory. We start from the hypothesis that EOs of aromatic plants used for aromatherapy or as food additives have anthelmintic action. We developed behavioral and molecular assays in wild-type worms, and analyzed mutant strains lacking receptors involved in locomotion to identify the pharmacological targets mediating the anthelmintic activities. We also explored the combination of current anthelmintics together with the addition of EOs purified compounds as a strategy to reduce resistance. In paralysis assays on agar plates, all tested EOs inhibited with different potencies *C. elegans* locomotion as well as egg hatching. The major compounds present in the tested EOs, trans-cinnamaldehyde (TC), geraniol, citronellol and linalool, were active at *C. elegans*. The combination of TC with the commercial anthelmintics levamisole and monepantel showed synergistic paralysis effects, while its combination with piperazine or ivermectin produced antagonic effects. Mutant worms lacking the levamisole-sensitive nicotinic receptor (L-AChR), GABA and glutamate receptors were partially resistant to these compounds. By single-channel recordings from *C. elegans* muscle cultured cells we deciphered how L-AChRs are modulated by TC. The analysis revealed that TC acts as an allosteric inhibitor of L-AChRs with key roles in nematode locomotion. Overall, we identified essential oils and their components as novel anthelmintic drugs and revealed their main pharmacological targets. Our results propose EOs as sources of natural compounds with promising polypharmacological profiles for anthelmintic therapeutics, and provide data on the efficacies of combinations that emerge as strategies to reduce drug resistance in nematodes.

1257V **Mechanism of oleic acid in alleviating violacein-induced toxicity in *Caenorhabditis elegans*** Jessica Antonio, Kyoung-hye YoonYonsei University Wonju College of Medicine

Oleic acid (OA) is an 18-carbon monounsaturated fatty acid that has been shown to alleviate numerous kinds of toxicity and