Online Proceedings

POSTER SESSION 1

Commons East, Easel 71

11:00 AM to 1:00 PM

Spectroscopic Studies of Purified Rat TRPV1

Marium Raza, Senior, Biochemistry, Comparative History of Ideas

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Mentor: Sharona Gordon, Physiology and Biophysics

Mentor: Gilbert Martinez, Physiology and Biophysics

Transient receptor potential vanilloid-1 (TRPV1) ion channels are polymodal signal integrators of noxious stimuli including heat, vanilloids such as capsaicin, peptide toxins, acid, and inflammatory mediators. It is unknown whether activation of TRPV1 by different stimuli is achieved through the same structural mechanism or if different stimuli activate the channel through different structural mechanisms. Clinical trials using TRPV1 antagonists resulted in patients exhibiting hyperthermia, suggesting that TRPV1 plays a role in maintaining body temperature, and highlighting the need to ensure that therapeutics targeting the channel do not disrupt thermal homeostasis. Hence, knowledge of different structural mechanisms for channel activation would aid in the design of therapeutic agents targeting TRPV1. To address this, we have expressed a series of functional single-cysteine rat TRPV1 channels for spectroscopic analysis, with techniques such as electron paramagnetic resonance, double electron-electron resonance, and Förster resonance energy transfer spectroscopy. By probing several structural regions within TRPV1 we can determine which regions of the channels move during activation and whether those are the same for different noxious stimuli.

POSTER SESSION 4

Balcony, Easel 87

4:00 PM to 6:00 PM

Using Calcium Imaging to Create a Database of Functional TRPV1 Single-Cysteine Mutants for Future Structural Studies in Protein Targeting for Pain Relief

Margot T Maraghe, Senior, Biochemistry, Biology (Molecular, Cellular & Developmental)

Mentor: Sharona Gordon, Physiology and Biophysics

Mentor: Gilbert Martinez, Physiology and Biophysics

The transient receptor potential vanilloid 1 (TRPV1) ion channel is well known for its role in sensing numerous "noxious" stimuli. It responds to noxious heat, acid, capsaicin (the active compound that makes chili peppers "spicy"), and inflammatory signals, which can be perceived by the brain to be painful. When the TRPV1 channel senses a signal such as capsaicin, it goes from a closed, non-conducting state, to an open state that allows the passage of ions into the cell, generating an electrical signal. Since TRPV1 is activated by a variety of different stimuli one of our aims is to determine if the structural mechanisms that open the channel is the same or different for each stimulus, which could have important clinical implications. For example, failed clinical trials of some TRPV1 antagonists resulted in elevated body temperatures in patients, indicating that the body's ability to regulate body temperature is impaired when TRPV1 is completely inhibited. Hence, if TRPV1 can be inhibited in most cases, but still respond to temperature, it will be a better target. We aim to combine cysteine-scanning mutagenesis with spectroscopic techniques to map the structural changes of TRPV1 activation in response to different stimuli. Since introduction of mutations can result in impaired channel function, each mutant needs to be functionally verified. My research will be to generate a broad library of single-cysteine TRPV1 mutants and verify their function using calcium imaging. Mutants that preserve TRPV1 function can then be used for further spectroscopic studies.