Green – Papers I found interesting and relevant to Fadool lab

Blue – Everything else

# Papers

## Protective Effects of Hydrogen Sulfide Against the ATP-Induced Meningeal Nociception – Koroleva, K.

This paper discusses the current contradictions revolving around hydrogen sulfide as a neurotransmitter in relation to nociception. Previous studies have found that hydrogen sulfide acts as both a pro-nociceptor and anti-nociceptor. After experimentation exploring its effects on mast cells degranulation, ATP induced spiking of trigeminal nerve cells, agonists of pro-nociception such as alpha, beta-meATP, and calcium signaling in trigeminal neurons the study found contradictory findings as well. The authors hypothesized hydrogen sulfide plays roles in both pro- and anti-nociception depending on its concentration and location.

## Molecular Cloning and Functional Characterization of a Novel Receptor-activated TRP Ca2+ Channel from Mouse Brain -- Takaharu Okada

In this paper the role of TRP channels is studied, specifically with calcium increasing intracellularly. The experiments explored if intracellular calcium is increased by means of intracellular stores being depleted or if it being transported extracellularly by TRP channels. In addition, they looked into if TRP channels were activated by ATP. Results showed that TRP channels bring in extracellular calcium and have a high affinity for it. ATP is required for this process to occur and the activation to calcium uptake is not dependent on intracellular calcium depletion. The authors hypothesized that TRP activation could be due processes such as Gq protein, phospholipase C-beta, and protein kinase C, all of which are activated by ATP.

## Transient receptor potential canonical 5 mediates inflammatory mechanical and spontaneous pain in mice – Katelyn E. Sadler

The focus of this paper was TRPC5, a channel which has been identified to be a contributor to persistent and lingering pain. This was chosen instead of other TRP channels such as TRPA1 and TRPV4 because those channels are necessarily for normal tactile sensation, proprioception and acute, protective pain. The study found that TRPC5 inhibitors are viable for treating persistent pain and supported current drugs that are going through clinical trials (compounds GFB-887 and BI-1358894). This was shown through several experiments such as the usage of CFA, a persistent pain inducer, and paw incisions to show that TRPC5 inhibitors decrease the amount of time pain is present in a subject.

## Histamine Receptor H1-Mediated Sensitization of TRPV1 Mediates Visceral Hypersensitivity and Symptoms in Patients with Irritable Bowel Syndrome – Wouters, Mira M.

This paper talks about the usage of histamine receptor H1 (HRH1) as a potential sensitizer of TRPV1; the authors mention TRPV1 does not increase in expression in IBS rather it is sensitized as proven by previous studies. The treatment studied is Ebastine, an HRH1 antagonist. The study showed IBS patients experience less pain when treated with Ebastine over a 12-week period. They also found two pathways HRH1 regulates TRPV1 sensitization, the first being the phospohorylation of TRPV1 through phospholipase C or protein kinase C and the second being the sequestering (chelating) of phosphatidylinositol 4,5-biphosphate, a TRPV1 inhibitor. The authors make note that although Ebastine reduced pain in patients by 22% (about the same as other treatments), the study paves way for understanding the mechanism for IBS pain treatment through TRP channels and suggests further research into them could result in more effective treatments.

## Inhaled ethanol potentiates the cough response to capsaicin in patients with airway sensory hyperreactivity – Eva Millqvist

This short study was conducted to determine if ethanol plays a role in the sensitization of TRP channels in patients with sensory hyperreactivity (SHR). Patients that inhaled ethanol prior to capsaicin, a TRP agonist, showed an increased sensitivity when compared to those who inhaled saline solution. This effect increased with high concentrations of ethanol being inhaled. Like previous studies, the role of TRP channels in hyperreactivity, sensitivity and pain was emphasized and requires further research for treatment options.

## Ingestion of TRP channel agonists attenuates exercise-induced muscle cramps – Craighead, D. H

This clinical trial was to see if TRP channel agonists can result in a reduction of muscle cramping of subjects that voluntarily induced themselves with muscle cramps. Previous research showed that strong excitatory sensory stimuli result in a reduction of efferent neural output; this would be the premise of the study using capsaicin as their agonist. Results showed improved contraction time and force production when the agonist was taken before inducing a cramp along with decreased muscle soreness post-cramp. In addition, they found using a TRP channel agonist did not result in any negative consequences towards fine motor performance, in other words the agonist is suggested to only target large motor units, not small motor units in muscles.

## Modulation of Oral Heat and Cold Pain by Irritant Chemicals – Kelly C. Albin

This study looked into the effects of menthol, capsaicin, mustard oil and cinnamaldehyde in oral pain by using the tongue of participants coated in these compounds (for various times) and rating their pain levels after a thermode was applied at different temperatures. They found that menthol, unlike previous studies looking into other pain inducers, overcame the phenomenon called contact suppression. Their results showed that although exposed to menthol, a pain inducer, and a temperature probe exhibiting low temperatures, over time participants still experienced the same amount of pain. When looking at mustard oil and cinnamaldehyde, they saw increased heat pain, as expected, but also saw decreases in cold pain which they hypothesize is from the co-expression of TRPA1 and TRPV1 in sensory neurons along with different concentrations of agonists used compared to previous studies. Capsaicin testing showed a significant heat sensitization, similar to previous studies, but different results for heat sensitization over time. Previous studies showed desensitization of heat and cold 15 minutes after application of capsaicin but this study found sensitization is still present in that time frame. They hypothesize this could be due to capsaicin being able to bind in different binding sites of the TRPV1 channel.

## TRPV1and TRPA1stimulation induces MUC5B secretion in the human nasal airway in vivo – Lisa Alenmyr

This study focused on TRP agonist induced symptoms on MUC5AC and MUC5B as they are mucus producing proteins in the respiratory tract. Through immunostaining, they found that TRPV1 agonists, such as capsaicin, olvanil and anandamide, result in MUC5B expression in submucosal glands, whereas MUC5AC is not expressed. Previous studies noted that co-expression/production of MUC5AC and MUC5B increase nasal polyposis and allergic rhinitis (in the absence of MUC2 and MUC18 expression), are found in chronic rhinosinusitis patients, and are found in patients with asthma and chronic obstructive pulmonary disease, rendering its understanding their expressions impactful. They also hypothesized that TRPV1 would have a regulatory role in ciliated epithelial cells due to its calcium regulation. When testing calcium signaling through ciliary beat frequency, they found TRPV1 activation through capsaicin did not increase CBF, implying it does not have a role in its regulation. The authors concluded there is not enough research to make conclusions about TRP roles in mucosal secretion.

## Effects of TRP channel agonist ingestion on metabolism and autonomic nervous system in a randomized clinical trial of healthy subjects – Stephanie Michlig

This study looked into the effects of different agonists of TRP channels, specifically for TRPA1, TRPV1 and TRPM8. The agonists used were Capsaicin, cinnamaldehyde and a cooling flavor such as menthol. They measured fat and carbohydrate oxidation, heart rate variability, blood pressure, heart rate and facial temperatures for this experiment to determine the metabolic effects of these agonists. They found that cinnamaldehyde produces a significant change in energy expenditure and both cinnamaldehyde and capsaicin increased fat oxidation after meals. It was determined that the TRPA1 agonist (cinnamaldehyde) was not associated with upregulation of brown adipose tissue function, uncoupling protein 1 gene expression, or catecholamine secretion; it was also hypothesized that its properties could be affecting the sympathetic nervous system by inducing adrenaline secretion, or induces vasodilation through inhibition of calcium channels that cause vasorelaxation and decreased heart pressure.

## The TRPC2 channel forms protein-protein interactions with Homer and RTP in the rat vomeronasal organ – Thomas G Mast

Purpose of the study was to the chaperone effects of RTP1 and REEP1 on the protein expression of TRPC2. The study also wanted to explore if there was a Homer protein interacting with the TRPC2 and IP3R3 joined proteins. They found that RTP1 and REEP1 act as chaperone proteins for the TRPC2 complex by increasing its membrane expression in cells, whereas if it was expressed without the chaperone proteins, it would be mostly located closer to the nucleus. They also found TRPC2 is interacting with Homer 1b/c and can be forming a complex between them and IP3R3. They conclude that Homer could play a critical role for binding TRPC2 and IP3R3 that could increase the channels’ functions but requires further experimentation.

# Relevant Websites

## <https://www.ncbi.nlm.nih.gov/books/NBK92823/>

Has information on the introduction of TRP channels, how to conduct experimentation on them, what conditions they are activated in and information on the different antibodies or lines of culture (mice or cell lines) that can be used for experimentation.

## <https://www.uniprot.org/uniprot/P19334>

Contains information on the structure, expression, topology, location, function and much more.

## https://www.britannica.com/science/transient-receptor-potential-channel

A brief yet descriptive summary of TRP channels along with how they work and other introductory information.

## https://thebiogrid.org/210769/publication/trp-channels-in-insect-stretch-receptors-as-insecticide-targets.html

Website on the usage of TRP channels as an insecticide target with the organism being studied.

## https://www.genecards.org/cgi-bin/carddisp.pl?gene=TRPM5

Has lots of information for the TRPM5 protein such as antibodies available, protein products (purified protein, etc.) and research information regarding the protein.

## https://www.nature.com/subjects/transient-receptor-potential-channels

Catalog of research papers on TRP channels published by nature that are open access.

## <https://www.guidetopharmacology.org/GRAC/FamilyIntroductionForward?familyId=78>

Has information about the different types of TRP channels with not only a diagram for the family tree but also a figure for structural features for the family members.

## <https://www.medchemexpress.com/Targets/TRP%20Channel.html>

Page on the different inhibitors, activators, mediators, antagonists and agonists for TRP channels along with purchasing options.

## <https://neuros.creative-biolabs.com/category-transient-receptor-potential-trp-channels-90.htm?gclid=EAIaIQobChMI3u7Km8_e8wIVl4jICh3SMQ18EAMYASAAEgKkAfD_BwE>

A website that sells TRP channel mitosis inhibitors or cell lines for different TRP proteins that can be used in experimentation. They sell a TRPA1 recombinant cell line that can be used for GPCR screening.

## <https://www.alomone.com/c/trp-channels-ion-channels>

Another website to purchase activators, inhibitors, antibodies, etc. Also has “explorer kits” that contain these products in a package and are grouped into different fields such as TRPA1 blocker, activator and other similar kits depending on the purpose of your research.