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In vitro Interaction between RA Domain-containing Proteins and Ras Family GTPases

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Ras genes code for small GTPases that act as molecular switches, cycling between an inactive GDP-bound state and an active GTP-bound state. They are activated in response to a wide variety of extracellular stimuli and regulate pathways that control multiple biological processes, allowing a cell to respond to its microenvironment. Ras genes are found mutated in 20 to 25% of human tumors. The goal of this project is to investigate the interaction between Ras family GTPases, with bound GDP or GTP, and RAS-associating (RA) proteins using HIS- and GST- tagged proteins. Interactions were analyzed by pull down assays with the GST-proteins and detecting the bound HIS-tagged proteins by immunoblotting. Preliminary results failed to detect any interactions. The results will be beneficial for understanding the properties and functions of Ras family GTPases.

Ontogenetic Differences in the Vertical and Horizontal Distribution of *Thysanoessa spinifera* along the Monterey Bay Submarine Canyon

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Euphausiids, small shrimp-like crustaceans also known as krill, form an integral part of marine food webs. The vertical and horizontal distribution of furcilia larvae (F1-F5), juveniles, and adults of the neritic krill, *Thysanoessa spinifera*, were sampled using stratified oblique plankton tows (0-100m and 100m-200m) conducted along the edges of the Monterey Bay Submarine Canyon (MBSC). Early larvae (F1-F3) were more abundant in the upper layer (0-100m) and later furcilia (F4-F5), juvenile and adult stages were more abundant in the deeper layer (100m-200m). The results indicate that maximum abundance of *T. spinifera* are highest at stations nearest the canyon edge.

Are they Hot or Not? An Investigation of the Trophy Mate Phenomenon

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An important part of male-male competition is mate choice among males, and when any object is competed over it becomes a sign of prestige, hence the "trophy mate" phenomenon (rich older men dating young beautiful women). This study investigates the

role played by peer judgment in the selections of potential short term sexual partners and attempts to understand how sex affects that behavior. Subjects completed an internet survey where they viewed photos of the opposite sex and rated each photo on how likely they would be to have a one night stand with that person. Finally, they listed the age and sex of other people in the room with them while they took the survey. We hypothesize that males will become more choosy of females when other males are present, but there should be no audience effect on females.

The Impacts of Wildfire on Water Quality in Southern California

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Wildland fires are necessary for ecosystems to facilitate plant reproduction and so cannot be prevented. We would like to know in what ways burned areas are impacted – predicting the hydrologic effects of wildfires in southern California could prevent some common post-fire impacts. Water samples were collected from both burned and non-burned environments and analyzed for isotope and other chemical data. The results indicate that some elements such as Na are not affected by wild land fires, so such tests are no longer necessary. We are now focusing on other elements (K and DOC) and flow rates to help us better understand the impacts of wildland fires. This data can determine water quality which will help identify the response water sources have to specific disturbances.

Modeling Feedback of the Tumor Suppressor p53

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In response to DNA damage, the tumor-suppressor protein p53 binds to DNA and induces expression of genes responsible for cell cycle arrest or apoptosis. It also stimulates expression of MDM2, which antagonizes p53 by targeting it for proteasomal degradation and by blocking its DNA-binding domain. A recent study revealed the importance of damage-induced MDM2 auto-degradation. Additionally, MDM2 can only regulate p53 when found as a heterodimer with MDMX, a protein that significantly increases the half-life of MDM2. We have developed an updated model of p53 regulation that incorporates this new information. Mass action-based nonlinear differential equations were used to describe the altered dynamics of p53, MDM2, and MDMX in response to a generalized damage signal. Computer simulation results support the hypothesis that increased MDM2 turnover may be the critical factor for p53 activation.

Correlation of Glial and Neuronal Changes Measured Immunohistochemically with Brain Imaging After Traumatic Brain Injury

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Traumatic brain Injury (TBI) affects thousands of individuals each year, yet little is known about the resulting neural pathology. An animal model employing a controlled cortical impact (CCI) is being used to study experimental neurotrauma: a craniotomy is performed and an infarct induced with an air pressurized piston. The degree of injury ranges from mild to severe, depending on whether a hematoma is produced. Brain samples from CCI animals were compared to sham and intact control animals using two methods: immunohistochemistry (IHC) and histology. The degree of neurodegeneration was proportional to the severity of TBI. All neuronal damage was isolated to the ipsilateral brain, although contralateral neuronal atrophy was seen in severe CCI animals. Mild and severe CCI both triggered a secondary inflammatory response as manifested by proliferation of OX-42 positive microglia and GFAP-positive astrocytes.

The Role of Complement Activation in Antibody Treatment of Cryptococcal Infection

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Antibodies have several properties that make them ideal therapeutic candidates, such as complement activation and interaction with Fc receptors on immune cells. However, much remains to be understood about how these properties relate to antibody efficacy against disease. We are using *Cryptococcus neoformans*, a fungus that causes life-threatening meningoencephalitis in immunosuppressed patients, to identify the properties of different human IgG isotypes responsible for effectiveness against this pathogen. IgG2 and IgG4 are protective against *C. neoformans* in mice, while IgG1 and IgG3 are not. The protective isotypes do not activate complement, suggesting that complement activation may be unfavorable to passive antibody protection against *C. neoformans*. We have created two recombinant antibodies, each with a mutation in the nonprotective IgG1, to determine if i) this antibody becomes protective if complement activation is reduced (P331S) and ii) the effect of enhancing antibody-mediated complement activation (E333S).

Evaluation of Mentoring and Positive Youth Development for At-Risk Populations

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Low socioeconomic status youth are at high risk for engaging in health compromising behaviors. The Community Outreach for Prevention Education (COPE) program is a community-based health promotion program designed to address the needs of at-risk

youth. Volunteer college students, with faculty supervision and support, developed, implemented, and evaluated optimal intervention strategies to reduce risk factors and increase protective factors to build and strengthen the youth's resiliency. A number of studies have documented the varied benefits youth derive through participation in programmatic mentoring. However, not all mentors or mentoring programs are equally effective. Risk factors associated with health compromising behaviors and strategies for effective prevention and intervention are reviewed. Preliminary results suggest that risk exposures among youth can be moderated and/or buffered by effective program practices, related to screening, training, and ongoing support, with a focus on individual strengths and environmental protective factors.

Context Fear and MAPK Activation in the Anterior Cingulate Cortex

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The anterior cingulate cortex (ACC) is important for the expression of context fear and for the consolidation of context fear memories. Post-training lesions of the ACC or inhibition of the mitogen-activated protein kinase (MAPK) signaling pathway impair context conditioning. The current studies were conducted to better characterize the relationship between MAPK activation in the ACC and context fear conditioning. Phosphorylation of MAPK was found to occur strongly in the ACC within 15 minutes after training. This suggests that activation of this kinase is important for the initial acquisition of context fear. To confirm and extend these findings, MAPK activation will be inhibited by infusing the ACC with UO126, a MAPK inhibitor, prior to training (memory acquisition) or before a memory test (memory retrieval). The results will contribute to our understanding of the role of the MAPK pathway in memory acquisition and retrieval.

Phase Mapping of Wavefront-obstacle Interactions in Rat Neonatal Myocyte Cells

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Ventricular fibrillation is the leading cardiac abnormality that leads to sudden death. Patients with a history of myocardial infarctions have a higher occurrence of cardiac arrhythmias due to the formation of scar tissue. The scar tissue acts as an obstacle, breaking electrical wavefronts, called reentry activity that can generate self-sustaining and rotating electrical waves. We believe that the dominant mechanism causing fibrillation and related arrhythmias are directly related to the morphologies of anatomical inhomogeneities. Using neonatal rat myocyte cells, photolithographic methods, voltage sensitive fluorescent dye, an optical imaging system, and imaging processing techniques, we were able to study the 2D phase mapping of electrical wave propagations. We mathematically modeled the contributions from different morphologies of anatomical

inhomogeneities to distorting electrical wavefronts. This work will provide insight into the understanding of 3D electrical wavefront-obstacle interactions, and thus the general mechanism of cardiac arrhythmias.

Kainate-induced Hippocampal Cell Death Requires γ -8 Protein

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Kainic acid (KA) induces epileptiform seizures in mice and causes hippocampal cell death. This cell death has been thought to be mediated through activation of kainate receptors (GluR5, 6). However, KA induces a larger current mediated by AMPA receptors (GluR1-4) in *Xenopus* oocytes. This occurs only when transmembrane AMPA receptor regulatory proteins (TARPs), such as γ -8, are co-expressed with GluR subunits. These findings suggest that KA-induced excitotoxicity may in large part be caused by the over-activation of AMPA rather than kainate receptors. We injected γ -8 knock-out (KO) and wild-type (WT) mice with KA and examined the hippocampi for pyramidal cell death. We found that KA caused cell death and pyknosis in CA1 and CA3 regions of the wild type and γ -8 heterozygous controls, but not in γ -8 KO mice. These findings suggest that KA induced excitotoxicity is mediated through the activation of AMPA/TARP heteromers.

Characterizing Mirror Mode waves in the Magnetosheath of Jupiter

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Mirror mode waves have been observed in the magnetosheaths of Earth, Jupiter, Saturn, and near comets. These structures are described by the mirror instability equation. Their generation depends upon a combination of a high plasma- β and a temperature anisotropy of plasma ions. Mirror mode waves are pressure balanced structures that are stationary in the frame of the flowing plasma. This study focused on two types of mirror mode fluctuations: spikes and dips in the field magnitude. We examined their spatial distribution in the magnetosheath of Jupiter. From an automatic program developed to identify mirror mode, we found that spike waves are localized predominantly in the sub-solar region of the magnetosheath, and dip waves are found in the dawn-dusk flanks. Plasma data describing the properties of particles in the magnetosheath are being investigated to determine how these waves arise.