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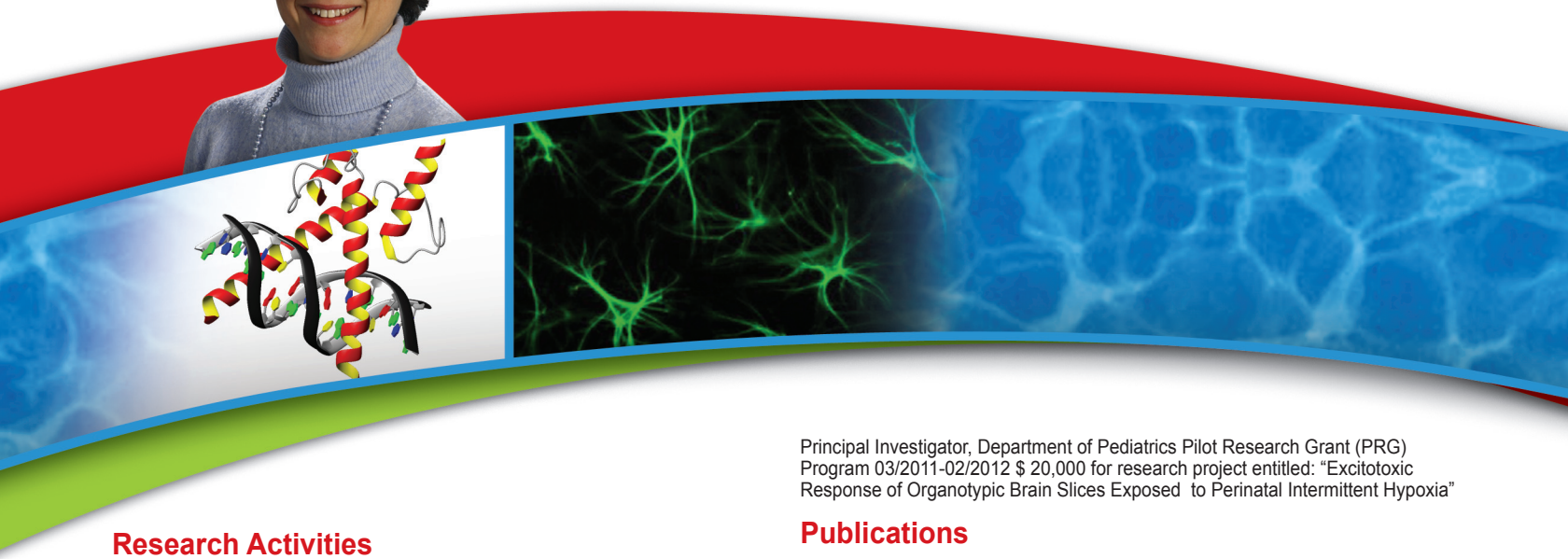

Research Activities

Sustained or intermittent oxygen restriction in the neural tissue frequently occurs in cerebrovascular disorders, pulmonary diseases, sleep apnea, and nervous system injury such as brain or spinal cord traumatic injury, resulting in excessive neuronal cell loss. The primary insult is usually followed by a secondary wave of injury mediated by various pathophysiological mechanisms, expanding the primary damage and compromising tissue ability to maintain function and respond to stress. Hypoxia induces stress-related pathways promoting angiogenesis, glycolysis, growth factors signaling, genetic instability, tissue invasion, oxidative stress and apoptosis, as part of a neural tissue stress response. The balance of these pathways may determine cellular fate and disease outcome. Additionally, neural tissue response to injury involves a significant glial response as well as the release of multiple neurochemicals, such as glutamate, that may be damaging to the surrounding tissue. Exposure to stress induces the expression of a highly conserved family of proteins, the heat shock proteins, a universal mechanism of cellular defense in various organisms. Constitutively expressed Hsps function as molecular chaperones and may play a role in preventing aggregation of damaged proteins, refolding proteins, or targeting them to degradation and may also prevent apoptosis. Alternatively, in response to increased accumulation of misfolded or ubiquitinated proteins, Hsps can induce apoptosis to remove dysfunctional cells. Thus, understanding the modulation of hypoxia-induced stress pathways in neurons and supporting tissue, may provide novel therapeutic strategies for diseases such as ischemia, neurodegenerative diseases, or traumatic injury to prevent delayed injury and improve recovery.

Various projects currently under investigation in our laboratory include:
- Cellular models in intermittent and sustained hypoxia.
- Alterations in neural tissue response to excitotoxicity after long term intermittent or sustained hypoxia, in a model of brain organotypic slices.
- Signal transduction pathways underlying cellular metabolism and adaptation to hypoxia/ischemia and oxidative stress.
- The role of stress response and heat shock protein induction in the modulation of cellular survival after spinal cord injury, and prevention of secondary traumatic injury.

Grants

Principal Investigator,
Department of Pediatrics Research Bridge Support 07/01/2011 – 06/31/2012 79, 000 $ as a departmental support to support research aimed at generating preliminary data that will allow grants submissions for funding 7/01/2012 – 06/31/2014 – 127,400 $ /yr.

Co-Investigator, 5% effort NIH/ National Institute of Allergy and Infectious Diseases R01AI075212 - 08/08/2008-07/30/2012 Direct costs $ 1,397,000 for research project entitled: "Modulation of Neutrophil Apoptosis by Akt-Hsp27 Signalosome" (Madhavi J. Rane, Ph.D., P.I., Gozal-Co-PI)

Principal Investigator, Department of Pediatrics Pilot Research Grant (PRG) Program 03/2011-02/2012 $ 20,000 for research project entitled: "Excitotoxic Response of Organotypic Brain Slices Exposed to Perinatal Intermittent Hypoxia"

Publications

* Sedoris K.C., **Gozal E**, Ovechkin A.V., Theile A.R. and Roberts A.M. Interplay of Endothelial and Inducible Nitric Oxide Synthases Modulate the Vascular Response to Ischemia-Reperfusion in the Rabbit Lung. Acta Physiologica. 204 (3): 331-343 (2012) * Co-mentored graduate student. PMID: 21827639

Schurr A. and **Gozal E**. Aerobic production and utilization of lactate satisfy increased energy demands upon neuronal activation in hippocampal slices and provide neuroprotection against oxidative stress. Special issue: "The link between brain energy homeostasis and neuronal activity", Front. Pharmacol. doi: 10.3389/fphar.2011.00096, 2012. Front Pharmacol. 2011;2:96. Epub 2012. PMID: 22275901

Dixon J.T., **Gozal E.** and Roberts A.M. Platelet-mediated vascular dysfunction during Acute Lung Injury. Arch. Physiol. Biochem. 118(2):72-82 (2012). PMID: 22439828

Roberts AM, Lominadze D, Dassanayaka S, Sachleben Jr. LR, Juniel C, **Gozal E.** Pulmonary Microvascular Constriction and Oxidative Stress in the Intact-ventilated Mouse Lung during Acute Inhibition of Nitric Oxide Synthase Presented at: Experimental Biology Meeting 2011, April 9 - 13, Washington, DC . Abstracted in: FASEB J., 2011.

Dixon JT, **Gozal E**, Sachleben Jr. LR, Lominadze D, Juniel CL, Roberts AM. NFkB signaling and inducible nitric oxide synthase activity during pulmonary ischemia-reperfusion increase colocalization of fibrinogen/fibrin and platelets at sites of vascular leakage in rabbit lung. Presented at: Experimental Biology Meeting 2012, April 21 – 25, San Diego, CA, Abstracted in: FASEB J., 2012.

Jagadapillai R, Mellen N, Sachleben, Jr. LR., **Gozal E.** Ceftriaxone enhances glutamate transporters expression and improves cell viability in rat hippocampal slices exposed to intermittent hypoxia. Presented at: 41th Annual Meeting of the Society for Neuroscience, October13-17, 2012, New Orleans, LA. Abstracted in: J. Neuroscience Vol. 37, Abstract # 332.22

External Professional Activities:

Grant review:
12/2012 NIH/NIGMS, Minority Biomedical Research (MBRS) program, Special Emphasis Panel/Scientific Review Group 2013/01 ZGM1 TWD-7.

Journal of Pharmacy and Pharmacology
Toxicology Letters
International Journal of Molecular Sciences
Life Sciences
PLoS ONE
Molecular Neurobiology