Research highlights

**Caloric restriction mitigates age-associated hippocampal differential CG and non-CG methylation** (Hadad et al., Neurobiol Aging 2018 – Dr. Bill Freeman’s lab)

Brain aging is marked by cognitive decline and susceptibility to neurodegeneration. Calorie restriction (CR) increases neurogenesis, improves memory function, and protects from age-associated neurological disorders. Epigenetic mechanisms, including DNA methylation, are vital to normal central nervous system cellular and memory functions and are dysregulated with aging. The beneficial effects of CR have been proposed to work through epigenetic processes, but this is largely unexplored. We therefore tested whether life long CR prevents age-related hippocampal DNA methylation changes. Hippocampal DNA from young (3 months) and old (24 months) male mice fed ad libitum and 24-month-old mice fed a 40% calorie-restricted diet from 3 months of age were examined by genome-wide bisulfite sequencing to measure methylation with base specificity. Over 27 million CG and CH (non-CG) sites were examined. Of the ~40,000 differentially methylated CG and ~80,000 CH sites with aging, >1/3 were prevented by CR and were found across genomic regulatory regions and gene pathways. CR also caused alterations to CG and CH methylation at sites not differentially methylated with aging, and these CR-specific changes demonstrated a different pattern of regulatory element and gene pathway enrichment than those affected by aging. CR-specific DNA methyltransferase 1 and Tet methylcytosine dioxygenase 3 promoter hypermethylation corresponded to reduced gene expression. These findings demonstrate that CR attenuates age-related CG and CH hippocampal methylation changes, in combination with CR-specific methylation that may also contribute to the neuroprotective effects of CR. The prevention of age-related methylation alterations is also consistent with the longevity effects of CR working through an epigenetic mechanism.
Dr. Jian-xing Ma was awarded an R01 grant (renewal) from the NEI/NIH entitled “A new pathogenic mechanism for diabetic retinopathy” for the period of 2018-2022.

Dr. Bill Freeman was awarded a Veterans Affairs Merit grant, entitled “Dynamics of the brain epigenome with aging”.

Acting Editor-in-Chief of the International Neuromodulation Society journal (INS)

A message from the President of the International Neuromodulation Society:

"In terms of recent changes, as INS President-Elect Dr. Robert Levy prepares to begin his term as president in September, we are pleased to announce that Oklahoma University Professor Robert Foreman, PhD, will begin serving as acting editor of the INS journal Neuromodulation: Technology at the Neural Interface starting April 1, 2018. Dr. Foreman is a quintessential scientist who is widely recognized for his foundational work that provides insight into the mechanisms of pain and neuromodulation. He is also a respected leader within our organization, who serves as Section Editor for Basic Science on the editorial board of Neuromodulation: Technology at the Neural Interface; and has been INS treasurer; as well as past president of the North American Neuromodulation Society."
Aesculapian Award Recipient

Congratulations to Dr. Kennon Garrett for his recipient of the Aesculapian Award from the second year Medical students (class of 2020)

Milestones

Dr. Beverley Greenwood-Van Meerveld’s lab was well represented at the Experimental Biology 2018 in San Diego.

Dr. Beverley Greenwood-Van Meerveld herself gave a lecture sponsored by the American Physiological Society entitled Sex-Based Differences Following Early Adverse Life Events.

Additionally, two medical students, Jay Love and Jeff May, who each performed research rotations in the Greenwood lab presented their latest results.

Jay Love gave a platform presentation and a poster entitled Environmental enrichment reverses chronic stress-induced brain-gut axis dysfunction. His data revealed that pre-exposure of adult animals to short-term Environmental Enrichment prevents visceral and somatic hypersensitivity induced by chronic repetitive stress. Future experiments are designed to understand the basic underlying molecular mechanisms responsible for the positive effects of Environmental Enrichment on stress-induced visceral and somatic hyperalgesia and its implications in the treatment of brain-gut axis dysfunction.
Jeff May presented a poster on **Visceral organ cross-sensitization in a rodent model of early life stress.** Bladder pain syndrome (BPS) and irritable bowel syndrome (IBS) exhibit a high comorbidity, show a female predominance, and patients often report a history of early life stress (ELS). However, whether ELS serves as a risk factor for visceral organ cross-sensitization remains to be determined. Our data revealed that in adulthood intravesical infusion of protamine sulfate into the bladder in female rats previously exposed to ELS as neonates induces colonic hyperalgesia.

The Greenwood–Van Meerveld laboratory was also well represented at Digestive Disease Week 2018 in Washington DC

Krishna Manohar, a medical student who rotated in Dr. Greenwood-Van Meerveld’s lab, gave a platform presentation entitled **Microglia in the Central Nucleus of the Amygdala (CeA): Role in stress-induced visceral hypersensitivity.** Her data demonstrated that chronic stress produces an activation of amygdaloid microglial cells and increases visceral sensitivity, suggesting that targeting activated microglia in the CeA attenuates visceral hypersensitivity, illustrating that microglia in the CeA may play a significant role in the development IBS-related abdominal pain.

Ehsan Mohammadi gave a platform presentation entitled **Exploring an antihistamine combination therapy for diarrhea-predominant irritable bowel syndrome.**
Graduate student Accomplishments

Ashley Martin, a doctoral candidate in Dean Myers’ lab received a 2-year F31 National Research Service Award from the National Institute of Child Health & Human Development on her dissertation project studying the effect of maternal obesity on the fetal baboon hypothalamic appetitive neurocircuit development.

Dustin Masser, Ph.D. (Dr. Bill Freeman’s student) was awarded the Graduate College Outstanding Doctoral Dissertation Award for dissertation submitted in 2017 - $1000 award.

Congratulations and Farewell to Dr. Zhongjie Sun

Dr. Zhongjie Sun, former Physiology Professor and Vice Chair of Research at OUHSC, has joined the University of Tennessee Health Sciences Center as Chair of the Department of Physiology.
Farewell party for Dr. Zhongjie Sun – May 4, 2018

MAY YOU BE PROUD OF THE WORK YOU HAVE DONE
THE PERSON YOU ARE AND THE DIFFERENCE YOU HAVE MADE

All the best to
Dr. Sun and his
lab personnel

Kei
Yi
Jianguo
Zhongjie
Meijun
New faces

Dr. Ana Chucair-Elliot joined Dr. Bill Freeman’s group as a Staff Scientist.

Dr. Chucair-Elliot

Sarah Ocanas joined the Physiology Ph.D. program and will pursue her graduate studies in Dr. Bill Freeman’s lab.

About the newsletter

We hope you have enjoyed reading the OUHSC Physiology newsletter. This publication is intended to share with everyone the latest events and developments within the Department. We welcome articles, thoughts and suggestions for our future issues. Please do so by emailing Dr. Hui-Ying Lim (hlim@ouhsc.edu). Thank you!