PharmTox Weekly Buzz

(A publication of the UAMS Department of Pharmacology and Toxicology)

Week of December 6-10, 2021

Pharmacology and Toxicology Holiday Breakfast

The department kicked off the 2021 holiday season with pancakes and a virtual party with door prizes! A special thanks to professor Alexei Basnakian, who despite an electrical power surge, served up batches of his amazing blueberry pancakes! Also, thank you to professor and chair Nancy Rusch who generously provided the holiday meats, fruit cups and door prizes! We hope everyone enjoyed the party and best wishes for the holiday season!

Published Paper in PNAS for Dr. Chang

Professor Hui-Ming Chang had a paper published in the *Proceedings of the National Academy of Sciences (PNAS).* The publication also includes professor and chair of Internal Medicine, Edward Yeh, and Feng-Ming Yang, Ph.D., who was a postdoctoral fellow in Dr. Chang and Dr. Yeh's lab prior to their move to UAMS. "Regulation of TLR4 signaling through the TRAF6/sNASP axis by reversible phosphorylation mediated by CK2 and PP4" follows the 2017 publication in the *Journal of Clinical Investigation* about the on and off mechanism of a key switch for the immune system that resides in cells. That switch, TNF receptor-associated factor 6 (TRAF6) is locked by another molecule known as sNASP. When an immune response is triggered, this lock is de-activated by adding phosphate to sNASP. In this latest publication, the main result is that protein phosphatase 4 is a key to reactivating the sNASP lock. By removing the phosphate from sNASP, one could turn off the immune response by re-locking TRAF6 with sNASP.

Accepted Manuscript for Dr. Leung

Associate professor Ricky Leung and professor and vice chancellor Shuk-Mei Ho, had a manuscript accepted for publication in *Oncotarget*. "The androgen receptor inhibits transcription of GPER1 by preventing Sp1 and Sp3 from binding to the promoters in prostate cancer cells" looks at G-1, a GPERI agonist, shown to inhibit the growth of castration-resistant mouse xenografts, but not their parental androgen-dependent tumors. It is currently unknown how the androgen receptor (AR) represses GPER1 expression. The authors found that two GPER1 mRNA variants (GPER1v2 and GPER1v4) are transcriptionally repressed by the androgen-activated AR, and data from promoter assays suggested that both variants' promoters were inhibited by androgen treatment. Site-directed mutagenesis on Sp1/Sp3 binding sites revealed their role in basal expression of GPER1. Based on chromatin immunoprecipitation, Sp3 was found to bind to the promoters prior to the binding of Sp1 and RNA polymerase II. The binding of all three transcription factors was inhibited by DHT treatment. Concordantly, DHT treatment induced nuclear interactions between AR and Sp1 or Sp3. Taken together, these results indicate that AR represses transcription of GPER1 by binding to Sp1 and Sp3 independently to prevent transactivation of the GPER1 promoters.