

Name: Lisa Wu
PI Name: Denong Wang

Email: lisa.wu@sri.com
PI email: Denong.wang@sri.com

Mimicking concurrent viral infection and substance abuse in a cell culture model

Lisa Wu and Denong Wang

Tumor Glycomics Laboratory, SRI International Biosciences, Menlo Park, CA, USA

The adenosine deaminase acting on RNA-1 (ADAR-1)/interferon (IFN) pathway of the innate cytoplasmic immunity mounts rapid responses to many viral infections. However, ADAR-1 may also target characteristic RNA structures of certain host genes, notably the mRNA of serotonin receptor subtype 2C (5-HT_{2C}R). The ADAR-1-mediated 5-HT_{2C}R RNA editing plays roles in several pharmacologic and behavioral processes by altering serotonergic plasticity mediated by 5-HT_{2C}R. Thus, ADAR-1 immunity may have “Janus-like” effects that may be either beneficial or harmful; these effects need to be tightly modulated to sustain innate antiviral immunity while restricting undesired off-target self-reactivity. We present here a robust cell culture model that is highly sensitive to substance abuse in the presence of a viral infection. Specifically, we found co-treatment of the U87MG glioblastoma cell line (U87) with vaccine strains of measles viruses (e.g., MeV-vac2) and cocaine induced a unique pattern of cellular response characterized by suppression of the dendritic-like cell differentiation and enhancement of cell proliferation. Such striking cellular responses to the concurrent viral challenge and a cocaine dose highlight the combined effects of substance abuse and viral infection. Since this model mimics a clinical presentation in which a patient with substance use disorder (SUD) is challenged by a virus or vaccine that could increase the risk of developing a mental illness, it may be explored to screen for the ADAR-1-modulators that may alter serotonergic plasticity to treat SUD-associated mental illness.