

## VIROLOGY

### **Qin Yan, Ph.D.**

The Yan laboratory is interested in epigenetic regulation by histone demethylases in cancer and stem cells. Aberrations in epigenetic processes often lead to cancer and other human diseases. In particular, we focus on the JARID1/KDM5 histone demethylase family. These enzymes can remove tri- and dimethyl marks from lysine 4 in histone H3 (H3K4me3/2), the epigenetic marks for transcriptionally active chromatin. We have previously identified KDM5A/RBP2 (Retinoblastoma Binding Protein 2) as one of the first known H3K4me3 histone demethylases. To understand the in vivo function of this enzyme, we generated an RBP2<sup>-/-</sup> mouse model, which is the first knockout mouse model for lysine demethylases. Furthermore, we showed that loss of this enzyme inhibits tumorigenesis in two mouse cancer models. We have also generated a mouse knockout model for a related H3K4me3 histone demethylase, KDM5B/PLU-1. KDM5B is highly expressed in mammary and prostate tumors and contributes to the stemness of melanoma cells. We are currently studying how these enzymes regulate oncogenesis, using highly integrated mouse genetic, molecular biological, cell biological, and biochemical approaches. As these enzymes play critical roles in drug resistance and the maintenance of cancer stem cells, they are strong candidates of drug targets for cancer therapy.

### **José Costa, M.D.**

Dr. Costa is interested in elucidating how the somatic cells of a multicellular organism are induced to evolve, an activity that should in principle be forbidden by the cooperation intrinsic in a multicellular organism. This interest stems from the fact that most common cancers in the human are formed by an evolutionary process that converts normal cells into tumor cells.

### **Don Nguyen, Ph.D.**

The goal of the Nguyen lab is to study thoracic malignancies that can spread aggressively to multiple distant organs with limited opportunity for effective therapeutic intervention. Metastatic lung cancer cells are believed to acquire complex biological properties by deregulating pleiotropic genetic or epigenetic programs and interacting with their micro-environment. Our laboratory is interested in uncovering the molecular and biological determinants of metastasis by different lung cancers, including lung adenocarcinoma. In this endeavor, we utilize a variety of approaches, such as animal modeling, cell culture assays, bioinformatics, and clinical validation. Finally, in the hopes of exploring new therapeutic possibilities, we are using biological insights gained through our experimental approach to try to better understand the link between the eventual resistance of some cancers to systemic therapy and metastatic relapse.

### **Narendra Wajapeyee, Ph.D.**

The focus of the Wajapeyee lab is to understand the mechanisms of genetic and epigenetic regulation of cancer-causing genes and to translate this understanding for early detection and treatment of human cancers. More specifically, the lab has the following major ongoing projects: 1) role of epigenetic regulation in cancer progression and identifying cancer stage specific epigenetic signature; 2) identification of gene specific regulators of epigenetic silencing; 3) understanding the mechanism of cellular senescence; and 4) role of microRNAs in senescence and cancer.

### **Jack Rose, Ph.D.**

The Rose laboratory has developed vaccine platforms based on recombinant viruses that can be engineered to express high levels of foreign antigens. One of the major platforms is based on recombinant vesicular stomatitis virus (VSV), a cattle virus that induces potent immune responses in a wide variety of animal species. The virus has been attenuated so that it no longer causes disease and then engineered to express protective antigens from other viruses or bacteria. Immunization with such vectors protects animals from infection and disease caused by numerous pathogens, including influenza virus, respiratory syncytial virus, simian immunodeficiency virus (SIV), Ebola virus, and Yersinia pestis, the bacterium that caused the notorious bubonic plagues.

Research projects in the Rose laboratory are focused on further development and testing of the VSV vaccine platform as well as other platforms such as alphavirus replicons that are packaged by the VSV glycoprotein into infectious, virus-like particles. Major research projects are underway to develop new approaches to HIV/SIV vaccines, influenza vaccines, and vaccines to protect from emerging viruses for which no vaccines currently exist.

### **Michael Robek, Ph.D.**

Some viruses, such as HIV and the hepatitis B (HBV) and C viruses, establish chronic infections that persist for the lifetime of their hosts and are associated with a large degree of worldwide mortality. The Robek laboratory studies the host-pathogen interactions related to HBV infection. Our lab is exploring three unique therapeutic approaches to treat this disease: 1) we are investigating the relationships between HBV and cellular signaling pathways, as these may be exploited pharmacologically to block virus replication; 2) we are characterizing the ability of novel immunoregulatory proteins to inhibit HBV replication and prevent liver damage; and 3) we are studying new methodologies for therapeutic vaccination to boost the immune response to HBV in people who are chronically infected with the virus.

