Our group is focused on discovering novel antiviral mechanisms involved in regulating persistent and chronic viral infections such as the chronic Hepatitis B virus. Persistent and chronic DNA viruses in particular have developed many mechanisms to both manipulate and co-exist within the nucleus, evading the host immune system. During acute infections, CD8+ T cells eliminate virus-infected cells through direct killing and the production of antiviral cytokines; however, this is not achieved during chronic viral infections. In patients chronically infected with Hepatitis B virus, there is evidence showing that this effect is due to the loss of virus-specific CD8+ T cell function, though the mechanism(s) responsible for the CD8+ T cell failure is still not fully understood. Virus-specific CD8+ T cells isolated from the peripheral blood of chronically HBV-infected patients fail to proliferate, produce cytokines, and show elevated expression of checkpoint inhibitory molecules, a status defined as exhaustion. This CD8+ T cell dysfunction is hypothesized to be attributed to the high levels of persisting viral antigens composed of circulating soluble HBV surface antigen (HbsAg) and HBV e antigen (HbeAg). A better understanding of the mechanisms leading to viral persistence and T cell dysfunction is critical to guiding new therapeutic strategies aimed at treating such diseases.
Selected Publications

Site-specific association with host and viral chromatin by Kaposi’s Sarcoma-associated herpesvirus LANA and its reversal during lytic reactivation. [2]
Mercier A, Arias C, Madrid AS, Holdorf MM, Ganem D.

Occupancy of chromatin organizers in the Epstein-Barr virus genome. [3]
Holdorf MM, Cooper SB, Yamamoto KR, Miranda JJ.

Click here [4] for additional publications.

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