



Molecular Genetics
UNIVERSITY OF TORONTO

DEPARTMENTAL SEMINAR SERIES

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Systematic Genetic Analysis of the Epstein-Barr Virus B-cell Lytic Switch

HOST Dr. Lori Frappier

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Epstein-Barr virus (EBV) uses a biphasic lifecycle, switching between latent and lytic phases to persistently infect most adults. Latency enables EBV to evade immune responses to over 70 viral lytic proteins and used by most of the 200,000 EBV-associated cancers/year. EBV reactivation is increasingly implicated in autoimmune diseases, including multiple sclerosis, and in the tumor microenvironment. However, mechanisms that regulate EBV reactivation have remained incompletely understood. We used CRISPR-Cas9 human genome-wide screens to define host factors that control the viral B-cell lytic switch. These highlighted MYC and the LSD1/CoREST/ZNF217 complex as key repressors of the lytic switch, who control expression of a pro-lytic viral lncRNA, which in turn controls higher order viral genome structure through long-range DNA interactions.