

An Integrated Approach to Understanding Host-Pathogen Interactions

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The human herpesvirus, cytomegalovirus (CMV), is endemic within the global population and has a significant impact on morbidity and mortality. CMV causes disease upon immunosuppression and is a leading cause of birth defects. Therapeutic intervention for CMV infection has been focused on disrupting a single protein, specifically the viral DNA polymerase. Current compounds have been only moderately successful but are considered toxic and result in antiviral resistant strains. The long-term goal of this project is to identify key mechanisms that define and predict a non-permissive cell state for infection, and that can serve as targets for future therapeutic intervention, using comprehensive metabolic, proteomic, and genomic analyses and mechanistic computational modeling. Technologies developed by the Wisconsin CEGS will help elucidate p53 promoter occupancy and regulatory proteins affecting the PI3K-AKT-TSC2-mTOR signaling axis.