Genetics Day Poster Submission

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Title: TORC1 INACTIVATION LIMITS VIRAL INFECTION THROUGH THE ALTERED REGULATION OF AGING-RELATED EFFECTOR PATHWAYS IN CAENORHABDITIS ELEGANS

Abstract: The COVID-19 pandemic had disproportionately negative effects on the survival of the aging population, highlighting the need for studying mechanisms of limiting viral infection. The process of aging results in the deregulation of most cellular process over time, resulting in many well-characterized hallmarks of aging. Several longevity pathways have been described that regulate these cellular processes via effector pathways that are highly evolutionarily conserved across species. One of these involves the target of rapamycin (TOR), which makes two separate complexes with individual RAPTOR and RICTOR proteins, forming TORC1 and TORC2, respectively. These complexes regulate distinct cellular functions; TORC1 governs effector mechanisms that are more likely immediately relevant for limiting viral infection, such as autophagy and stress responses. Caenorhabditis elegans (C. elegans) is a powerful genetic model for the study of aging due to its ease of ability to make genetic changes and shared conservation of longevity pathways with humans. Orsay virus (OV), a natural viral pathogen of C. elegans, is an emerging model system to identify the intersections between host-pathogen interactions, longevity signaling, and age-associated decline in adaptive responses to viral infection. Preliminary data from the laboratory has shown that C. elegans with inactivated TOR have lower OV viral loads, suggesting that the derepression of downstream effector pathways enables the cells to limit viral infection. In agreement with this, we found that inhibition of autophagy increased viral load and expression of the IPR, suggesting that the cells had lost their ability to limit viral infection. These data indicate that induction of autophagy is significantly involved as an effector pathway when TORC1 is inhibited. Future experiments will continue to test the involvement of downstream effector mechanisms of TORC1 and innate immune responses to OV infection in animals with inhibited TORC1. Altogether, these experiments will allow me to elucidate the role that longevity pathway component TORC1 and its downstream effector mechanisms play in limiting the cellular response to viral infection and in regulating host defense mechanisms.