

## **AN AGED HOST PROMOTES RAPID EVOLUTION OF A VIRULENT COXSACKIEVIRUS SPECIES**

R. Gay (P)<sup>1</sup>, S. Belisle<sup>1</sup>, R. Bronson<sup>2</sup>, M. Beck<sup>3</sup>, S. Meydani<sup>1</sup>

<sup>1</sup>Nutritional Immunology Laboratory, JM USDA HNRCA at Tufts University, 711 Washington Street, Boston, MA, 02111 <sup>2</sup>Department of Biomedical Sciences, Tufts University School of Veterinary Medicine, 200 Westboro Road, North Grafton, MA, 01536 <sup>3</sup>Pediatrics and Nutrition, University of North Carolina-Chapel Hill, Room 3312 MBRB, CB #7224, Chapel Hill, NC, 27599

The recent emergence of new and more pathogenic viral diseases makes it essential that we elucidate the factors that promote viral evolution. Aging is associated with compromised immune function, increased oxidative stress, and susceptibility to viral infections. This suggests that the aged host may serve as unique reservoirs for viral infection. To test the effect of host age on virus evolution, we examined changes in the virulence, pathogenicity, and gene sequence in a normally avirulent strain of coxsackievirus B3 (CVB3/0) following a single passage through either young or old murine host. CVB3/0 infected old mice had significantly higher heart viral titers and incidence compared to CVB3/0 infected young mice. To determine if the higher titers in the old mice were due to a genetic change in CVB3/0, mice were infected with either CVB3/0, or CVB3/0 isolated from the hearts of previously infected old or young mice. Young and old mice infected with CVB3/0 that had been passed through an aged host, exhibited significantly higher heart viral titers, heart and liver pathology, and more mortality than young and old mice infected with CVB3/0. Sequence analysis of the virus isolated from mice infected with virus passed from old mice revealed 13 specific, stable, and reproducible nucleotide changes that matched nucleotides identified in the virulent CVB3/20 strain and are known to promote cardiovirulence. In contrast, only 1 nucleotide change, low viral titers, and no heart and liver pathology was observed in virus isolated from mice infected with virus passed from young mice. Our data demonstrate that the aged host environment promotes rapid evolution of a virulent pathogenic strain of CVB3 from a previously avirulent strain. Rapid viral evolution in the aged may pose an unexpected public health challenge in the light of the growing number of elderly world-wide.