1154. Host and Pathogen Genetics Modulate HSV-1 Severity

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Session: 134. Viral Infections: Pathogenesis
Friday, October 10, 2014: 12:30 PM

Background. HSV-1 infection has a wide severity spectrum in the immunocompetent host, from asymptomatic seropositivity to frequent orolabial lesions. To gain insight into virus and host genotype contributions to disease phenotype, we evaluated HSV-1 genotypes and immunity in mono- (MZ) and dizygotic (DZ) twins.

Methods. HSV-1 seropositive twin pairs collected daily oral swabs for quantitative HSV-1 PCR and kept symptom diaries for 60 days. Associations of shedding rates were assessed by estimating correlations. We categorized the viral strain as identical or different in each pair with DNA available for genotyping from both. The identity and breadth of HSV-1 antigens recognized by circulating CD4 T-cells were determined using a complete HSV-1 ORF (open reading frame) set. CD4 T-cell responses were scored as present or absent to each ORF. We used a bootstrap method to estimate the distribution of agreements in ORF responses between individuals.

Results. We enrolled 29 MZ and 22 DZ twin pairs. The overall shedding rate was 10.3% of days (median 9.3%; range 0-47%). There was a positive correlation between shedding rates within twin pairs ($r = 0.33$, $p = 0.015$) but not among unrelated individuals ($r = -0.086$; $p = 0.5$). Genotyping showed that 15/14 twin pairs had the same/different HSV-1 strain, respectively. The correlation for shedding rates in all twin pairs was higher in those with the same virus ($r = 0.55$, $p = 0.033$) vs different ($r = -0.169$, $p = 0.56$). 8 MZ pairs were analyzed for CD4 T-cell responses. The median number of ORFs recognized per person was 19 (range 6-35). The bootstrapped mean percent agreement in ORF response between unrelated pairs was 71% ($5^{th}/95^{th}$ percentile, 67%/75% respectively). The percent agreement between the original 8 pairs of MZ twins was 77% ($p = 0.003$ for difference from bootstrapped dataset).

Conclusion. A relationship between HSV-1 shedding and host genotype is supported by our observation of a higher correlation in HSV-1 shedding between twin pairs than between unrelated individuals and similar CD4 T-cell responses between MZ twins. These data and the higher correlation in shedding rates among twins with the same vs different virus suggests that both viral and host genetics contribute to HSV-1 severity.

Disclosures. **A. Wald**, Aicuris: Consultant, Consulting fee; Genocea: Investigator, Research support; Agenus: Investigator, Research support; Vical: Investigator, Research support