Urban vs Rural HIV-infected Persons Have Differential Gene Expression for Estrogen Signaling, Inflammation, and Cytokine Production Pathways

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Background. People aging with HIV (PAWH) are living longer with effective antiretroviral therapy and new HIV diagnoses are rising in older populations. Concurrent with trends in age, the epidemiology of HIV infection in the United States has shifted geographically and racially; the Southeast and African Americans now have the highest HIV incidence and prevalence. Although there are marked health disparities for rural and African American PAWH, limited data exist comparing aging phenotypes between rural and urban PAWH, and no data exist comparing mechanistic pathways between these populations. Among African American PAWH, we hypothesize that rural PAWH will be more likely than urban PAWH to have a molecular profile of advanced aging associated with chronic disease burden and shorter health span.

Methods. Demographics, clinical data, and RNA were collected from 14 matched pairs from rural (Wake Forest University, Winston-Salem, NC) and urban cohorts (ALIVE cohort, Johns Hopkins University, Baltimore, MD) matched on age, sex, Short Physical Performance Battery score, smoking status, and sample collection date. Raw sequences were examined for quality, aligned using STAR, and normalized using DESeq2. DESeq2 tested matched pair differential gene expression. Genes with an average read count threshold > 5, a genomic control adjusted P-value < 0.01 and a fold change > 1.3 were retained for further analysis using STRING, MCODE, and IPA to find functional and biological patterns.

Results. Of the 399 genes meeting significance criteria, 212 showed higher expression in the rural group; the remaining 187 genes showed lower expression in the rural group; the remaining 187 genes showed lower expression in the urban group. Flow cytometry revealed significant differences in surface markers among the cell types. iMG and iMGL displayed CD11b, C4D, CXCR4, CCR5 and lack of expression of CD4 and CX3CR1. In contrast, HMC3, C20, and PM were negative for CD11b, CD45, CX3CR1, CD4, CXCR4. Immunostaining showed that iMG and iMGL were positive for microglial markers TIMEM19 and P2RY12. RNA Seq analysis is currently underway to determine gene expression differences between the microglial cell lines and our microglia models. In preliminary results, iMG and iMGL were both readily infected with HIV, and comparison with other lines is ongoing.

Conclusion. There is no standard model available for defining the molecular and cellular events involved in HIV infection of microglia. Significant differences in microglial markers and in HIV receptor and coreceptor levels were noted in this study. iMG and iMGL appear to be viable microglial models susceptible to HIV infection.

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2520. Resource utilization in adolescents and young adults with HIV in the HIV Research Network

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Background. Adolescents and young adults (AYA) with HIV experience worse health outcomes than adults with HIV in the United States. Little is known about AYA patterns of utilization of costly healthcare resources.

Methods. We estimated utilization of outpatient, emergency department (ED), and inpatient care among 13–30 year-olds from 2006–2015. We stratified outpatient visits, ED visits and inpatient days per person-year (PY) by transmission mode (perinatal (PHIVY), non-perinatal (NPHIVY), age (13–17, 18–23, 24–30 years), CD4 strata (< 200, ≥200–499, ≥500 cells/µL) and presence or absence of viral load (VL) suppression (<, ≥ 400 copies/mL[c/mL]) combined with antiretroviral (ARV) use. We also quantified outpatient, ED, and inpatient care associated with specific AIDS-defining conditions.

Results. Among 4,450 AYA (PHIVY: 15%; NPHIVY: 85%), mean (SD) follow-up was 2.8 years (2.5) [PHIVY: 4.2 years (3.1); NPHIVY: 2.5 years (2.3)]. Mean age was 21.4 years (PHIVY: 16.9 years; NPHIVY: 22.3 years) and female sex was 28% (PHIVY: 52%; NPHIVY: 23%). Among PHIVY, most person-time (PT) was spent between ages 13–23 years (13–17 years: 43%; 18–23 years: 45%), CD4 ≥ 500/µL (61%), and VL < 400 c/mL (69%). Among NPHIVY, most PT was spent between ages 24 and 30 years (56%), CD4 ≥ 500/µL (54%), and VL < 400 c/mL (66%). PT spent while prescribed ARVs and VL ≥ 400 c/mL was 30% (PHIVY) and 24% (NPHIVY) among those prescribed ARVs (Figure 1). Rates of ED visits and inpatient days were higher during PT spent at older ages (18–23 years, 24–30 years), lower CD4 (< 200, 200–499/µL), and among those prescribed ARVs (Figure 1). Rates of ED visits and inpatient days were higher during PT spent at older ages (18–23 years, 24–30 years), lower CD4 (< 200, 200–499/µL), and among those prescribed ARVs (Figure 1). Rates of ED visits and inpatient days were higher during PT spent at older ages (18–23 years, 24–30 years), lower CD4 (< 200, 200–499/µL), and among those prescribed ARVs (Figure 1). Rates of ED visits and inpatient days were higher during PT spent at older ages (18–23 years, 24–30 years), lower CD4 (< 200, 200–499/µL), and among those prescribed ARVs (Figure 1). Rates of ED visits and inpatient days were higher during PT spent at older ages (18–23 years, 24–30 years), lower CD4 (< 200, 200–499/µL), and among those prescribed ARVs (Figure 1).

Conclusion. Among AYA with HIV, more ED visits and inpatient days were observed during time spent at older ages, lower CD4 counts, and VL ≥ 400 c/mL. While AIDS-defining conditions were rare, associated resource utilization was substantial. Interventions to improve retention in care, virologic suppression, and immune response may improve outcomes, and thus decrease costly resource utilization, for AYA with HIV as they transition to adulthood.

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2521. Prevalence and Associated Factors of Protective Antibody Responses against Diphtheria, Tetanus, and Pertussis among HIV-Infected Thai Adolescents Stable on Combination Antiretroviral Treatment

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Background. To assess the prevalence and associated factors of protective antibodies against diphtheria, tetanus, and pertussis among HIV-infected adolescents stable on combination antiretroviral treatment (cART).

Methods. A multicenter seroprevalence study was conducted. Perinatally HIV-infected Thai adolescents (11–25 years) who had previous evidence of severely immune suppression (CD4 < 15% or < 200 cells/mm³), were currently stable on cART (CD4 > 350 cells/mm³ for > 6 months or CD4 > 200 cells/mm³ with viral suppression [VS; HIV RNA < 50 copies/ml], for > 12 months) and had completed a 5-dose series of diphtheria, tetanus, whole cell pertussis (DTwP) vaccine during childhood were enrolled. Adolescents who received immunosuppressive agents or blood components within 6 months were excluded. Protective antibodies for diphtheria, tetanus, and pertussis were defined as diphtheria toxoid IgG ≥ 0.1 IU/mL, tetanus toxoid IgG ≥ 0.1 IU/mL, and anti-pertussis toxin IgG ≥ 5 IU/mL, respectively. Logistic regression analysis was performed to identify factors associated with protective antibody response to each antigen.

Results. Of 150 adolescents, 47% were male, a median age was 19 years. Forty (27%) and 0 (0%) adolescents had ever received tetanus, diphtheria (Td) or tetanus, diphtheria, acellular pertussis (Tdap) vaccine during adolescence, respectively. A median duration since the last dose of DTwP/Td vaccine was 12 years. At enrollment, 67% of adolescents were on NNRTI-based cART regimens, a median cART duration was 13 years. A median CD4 was 29%, and 90% had VS. Prevalence of protective antibodies against diphtheria, tetanus, and pertussis were 37%, 82%, and 52%, respectively. Proportion of adolescents with protective antibodies and geometric mean concentrations of antibodies to all antigens declined over time after the last immunization (Figures 1–3). Associated factors of protective antibodies to diphtheria, tetanus and pertussis are shown in Table 1.

Conclusion. Although having completed a 5-dose series of DTwP during childhood, significant proportion of our perinatally HIV-infected adolescents had no protective antibodies to those antigens, particularly diphtheria and pertussis, when entering adolescence. Tdap vaccination is a crucial strategy to prevent such diseases in the future.

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2522. Prescription Drug Use Among Women with HIV Who Are of Childbearing Potential

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