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**Session:** 280. Viral Pathogenesis
*Saturday, October 5, 2019: 12:15 PM*

***Background:*** Enterovirus (EV) and human Parechovirus (PeV) cause a range of illness including asymptomatic to systemic infections. The host immune response in children, especially the one induced by PeV, is largely unknown. The aim of this study was to determine the immune response induced by EV and PeV in cerebrospinal fluid (CSF) and plasma obtained from children with systemic infection.

***Methods:*** Left-over CSF and paired blood samples collected from children with laboratory confirmed EV and PeV central nervous system-infection were enrolled in this study. EV/PeV-negative CSF and paired plasma from children was used as controls. Level of cytokines and chemokines were measured using a customized 21-plex ELISA panel that included 16 cytokines and 5 chemokines (Millipore, CA). Additionally, clinical characteristics of all the patients were collected to determine the potential association between the immune response and pathogenicity.

***Results:*** Total of 74 samples were enrolled and divided into 3 groups, EV ($n$ = 27), PeV ($n$ = 23) and control group ($n$ = 24). Median age of all the three groups was 2 weeks (IQR 2–4 weeks).The key analytes which had a significant difference between each groups are show in the Table. In general, EV induced more robust cytokine secretion than PeV and control group. Anti-viral response such as IFN-g was remarkably absent in both CSF and plasma in PeV group compared with EV group ($P < 0.05$). Only IL-8 was significantly higher ($P < 0.05$) in EV CSF group compared with any other groups or sample types. Level of all the chemokines measured were much higher in all the three groups but significant difference was found between PeV CSF and plasma for IP-10 and MCP-1 chemokines ($P < 0.05$).

***Conclusion:*** In this study, we demonstrate that EV and PeV induces distinct immune response in children with systemic infections. While EV induces more robust inflammation, PeV-induced inflammation appears to be either weak or absent in CSF, but robust in plasma. The suppressed pro-inflammatory response might facilitate PeV growth and proliferation in CSF and might play a role in disease severity. Further studies are needed to fully understand the differential immune response induced by these two viruses.

**Table.** Comparison of cytokine levels (pg/ml) in different groups and sample types.

| Analytes (pg/ml) | EV CSF (n=23) Mean ± STD | EV Plasma (n=10) Mean ± STD | PeV CSF (n=27) Mean ± STD | PeV Plasma (n=14) Mean ± STD | Control CSF (n=24) Mean ± STD | Control Plasma (n=13) Mean ± STD |
|---|---|---|---|---|---|---|
| IFN-γ | 26.8 ± 34.83 | 25.1 ± 27.39 | 2.09 ± 1.06 | 11.5 ± 7.8 | 6.6 ± 16.3 | 21.4 ± 18.8 |
| IL-6 | 435.5 ± 696.8 | 40.5 ± 65.6 | 3.07 ± 2.15 | 21.4 ± 14.9 | 111.3 ± 403.04 | 36.3 ± 18.5 |
| TNF-α | 11.7 ± 13.8 | 94.1 ± 46.5 | 1.7 ± 1.78 | 84.2 ± 15.5 | 1.66 ± 1.7 | 74.4 ± 51.9 |
| IL-1Rα | 869.4±1421.08 | 1119.6±874.7 | 36.4 ± 32.18 | 3499.9±2291.4 | 129.3 ± 331.7 | 811.9 ± 1335.5 |
| Fractalkine | 176 ± 1.62 | 76.3 ± 34.24 | 154.6 ± 17.67 | 442.4 ± 562.3 | 132.2 ± 22.9 | 214.8 ± 326.9 |
| IL-8 | 1292.3±1760.4 | 31.9 ± 43.3 | 113.2 ± 53.6 | 31.9 ± 13.5 | 164.5 ± 235.6 | 38.09 ± 76.9 |
| IP-10 | 11521.8±5570.6 | 3900±4121.2 | 9474.1±3911.7 | 9765.8±2229.2 | 2953.7±4576.4 | 2600.6±3320.9 |
| MCP-1 | 6344.2±6332.3 | 2580.3±2344.8 | 3838.8±2192 | 7254±5021.7 | 1770.9±1174.7 | 1185.4±857.4 |
| RANTES | 339.1 ± 621.6 | 4187.3±1830.6 | 147.3 ± 312.3 | 3806±2166.5 | 227.6 ± 472.9 | 5816.3±3390.0 |

***Disclosures.*** **All authors:** No reported disclosures.

## 2783. Expansion of Monocytic Myeloid-Derived Suppressor Cells in Infants with Severe Respiratory Syncytial Virus (RSV) Infection

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***Background:*** RSV remains a leading cause for hospitalization of infants. The mechanisms associated with the ability of RSV to suppress the induction of an adequate immune response are not well understood and represent a challenge for vaccine development. Myeloid-derived-suppressor cells (MDSCs) have been shown to suppress CD8+ T cells in patients with malignancies. These immature myeloid cells are divided into three groups: granulocytic, monocytic, and undifferentiated. Of those, monocytic MDSCs (M-MDSCs) are considered to be key regulators of inflammatory responses during acute infections. Their potential role in the immunopathogenesis of RSV infection in infants is yet to be defined.

***Methods:*** Single-center, prospective cohort study in previously healthy infants hospitalized with severe RSV lower respiratory tract infection (LRTI) and age-matched healthy controls (HC). Nasopharyngeal swabs for RSV detection and blood samples for cell immunophenotyping were analyzed at enrollment (D1), 1-month (D30), and 6-months (D180) follow-up visits. Disease severity was assessed using a clinical disease severity score (CDSS), duration of supplemental O2, and duration of hospitalization.

***Results:*** We enrolled 39 infants with RSV LRTI (median [IQR] age: 3.3 [1.5–5.2] months) and 5 HC (5.9 [4.5–7.2] months). Infants with RSV infection demonstrated an expansion of M-MDSCs during the acute infection (D1) that resolved to numbers comparable to those in HC at follow-up visits (Figure 1A). In addition, numbers of CD8+ T cells were significantly reduced during the acute infection (D1) in RSV-infected infants, but also returned to the HC baseline on D30 and D180 (Figure 1B). Finally, the increase in M-MDSCs numbers and decrease in CD8+ T-cell numbers were associated with worse clinical outcomes as defined by duration of supplemental oxygen (>1 day), hospitalization (>48 hours), and clinical disease severity score (CDSS, > 9) (Figure 2).

***Conclusion:*** These findings suggest that an expansion of M-MDSCs may play a role in T-cell suppression in children with severe RSV disease. As new vaccines are being developed, it is critical to elucidate the immune suppressive mechanisms associated with RSV infection.

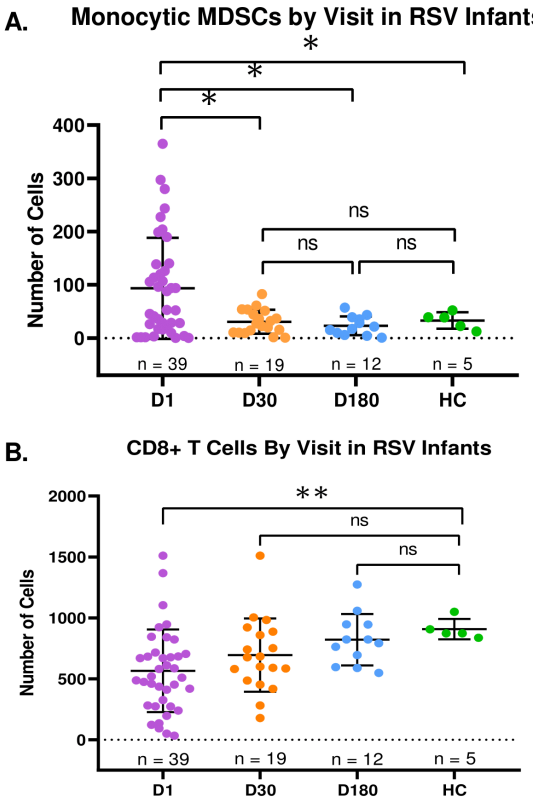


**Figure 1.** Number of **(A)** monocytic myeloid-derived suppressor cells (M-MDSCs) and of **(B)** CD8+ T cells in infants hospitalized with RSV LRTI (D1), and at follow up of 1-month (Day 30) and 6-months (Day 180) post hospitalization, and healthy controls (HC). (p<0.05).

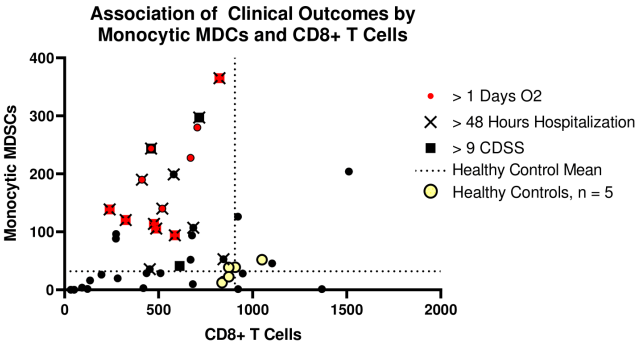


**Figure 2.** RSV infants profiled by numbers of monocytic myeloid-derived suppressor cells (M-MDSCs) and CD8+ T cells. Stratified by the mean number of CD8+ T cells and M-MDSCs of age-matched healthy controls (HC, dotted lines). RSV infants with higher number of M-MDSCs and lower number of CD8+ T cells (left upper quadrant) showed worse parameters of clinical disease severity. Healthy controls are plotted as a reference (yellow dots).

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## 2784. Increased Frontal Lobe Volume and Density in Macaques Exposed to Zika Virus In Utero

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