

**TITLE:** Hierarchical clustering to identify cytokine patterns in hospitalized patients with community-acquired pneumonia (CAP)

**AUTHOR LIST:** Timothy L Wiemken PhD; Robert R Kelley PhD; Rafael Fernandez-Botran PhD; Paula Peyrani MD; Rodrigo Cavallazzi MD; Jose Bordon MD PhD; Julio Ramirez MD

### ***Background***

Patients with severe CAP usually have an exaggerated cytokine response. Studies to modulate cytokine response and improve outcomes have been inconclusive. We hypothesize that the host response to pneumonia may be characterized by distinct cytokine patterns, which can be harnessed for personalized therapies. Here, we use hierarchical clustering methods to examine if patterns of cytokines in the plasma and sputum in hospitalized patients with CAP can be defined.

### ***Methods***

This was an ancillary study of the prospectively collected database from the Community Acquired Pneumonia Inflammatory Study Group (CAPISG). The following cytokines were measured on the day of admission: interleukin (IL)-1 $\beta$ , IL-1 receptor antagonist (IL-1ra), IL-6, CXCL8 (IL-8), IL-10, IL-12p40, IL-17, interferon (IFN) $\gamma$ , tumor necrosis factor (TNF) $\alpha$ , and CXCL10 (IP-10). Hierarchical agglomerative clustering algorithms were used to evaluate clusters of patients within the plasma determinations and sputum determinations.

### ***Results***

A total of 13 patients were included in this pilot study. Distinct cytokine patterns were identified when cytokines were clustered according to values in the plasma, sputum, plasma/sputum combined, and the ratio of plasma to sputum levels.

### ***Conclusions***

Distinct cytokine patterns in plasma and sputum can be identified in hospitalized patients with CAP. This characterization of the local and systemic inflammatory response may help to better discriminate patients for enrollment into clinical trials of immunomodulatory therapies.