

## Evaluation of class III semaphorins levels during polymicrobial sepsis

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**Aim:** To determine the circulating levels of class III semaphorins (SEMA3s) during polymicrobial sepsis.

**Methods:** Mice were subjected to sham operation or cecal ligation and puncture (CLP)-induced sepsis, as moderate (punctured twice with 21G) or severe (punctured twice with 19G) injury. At the initial phase (6h post-CLP) and during the late phases of sepsis (24h and 48h post-CLP), mice were anesthetized for blood collection, and plasma was obtained to quantify SEMA3s (3A to 3G) levels by ELISA.

**Results:** The mortality rate among mice subjected to moderate or severe sepsis at 48h post-CLP was 15.4% (2 non-surviving animals out of 13) and 44.4%, respectively (8 non-surviving animals out of 18). The plasma concentration of all class III SEMAs (3A to 3G) was altered during experimental sepsis, however, at different stages of the infection. SEMA3A, 3C, 3D, 3E (Sham:  $0.07 \pm 0.002$ ; CLP 21G:  $0.05 \pm 0.002$  and CLP 19G:  $0.06 \pm 0.004$  ng/mL;  $P < 0.05$ ) and 3F (Sham:  $2.21 \pm 0.09$ ; CLP 21G:  $1.55 \pm 0.09$  and CLP 19G:  $1.99 \pm 0.05$  ng/mL;  $P < 0.05$ ) showed a reduction in their circulating levels, especially in the late phase, i.e., after 48h of CLP induction. Furthermore, the plasma concentration of SEMAs was minimally affected by the severity of sepsis, suggesting that mice with severe sepsis exhibited statistically similar levels when compared to animals subjected to moderate sepsis. The sham surgery by itself did not change any SEMA levels compared with the naïve group.

**Conclusion:** This data reinforces the hypothesis of an immunomodulatory role of these secreted proteins, suggesting that maintaining increased circulating concentration of SEMAs may prevent the worsening of the pathophysiological condition of sepsis.