THE ROLES OF MAST CELLS AND THEIR PROTEASES DURING *CHLAMYDIA* INFECTION

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Introduction: *Chlamydia* is the commonest bacterial sexually transmitted infection (STI) and causes irreversible reproductive tract (RT) diseases. There is no effective strategy that prevent infection and, an improved understanding of the immune processes that clear infection is needed. Despite mast cells (MCs) being key immune cells widespread in the RT, their roles during STIs are largely unknown. Therefore, we investigated the roles of MCs and their granule-stored proteases during *Chlamydia* infection.

Methods: We used a mouse model whereby mice were given progesterone seven days before intra-vaginal infection with *Chlamydia muridarum*. Starting two days before infection (dbi), mice were daily intra-vaginally treated with cromolyn, a MC degranulation inhibitor (or vehicle), or with recombinant MC proteases (or vehicle). We also assessed infection in several knocked-out mice that are deficient in MC proteases (and wild type controls). At 3 and 14 days post infection (dpi), the levels of infection, immune factors/cells and pathology were evaluated.

Results: Inhibiting MC degranulation was protective against infection early (3dpi) in the vagina (*p=0.0069, t-test*) and in the uterus (*not significant, p=0.0728, Mann-Whitney*) but these effects were not maintained at later stages. Early treatments (2dbi to 2dpi) with protease serine member S31 (Prss31) were protective against infection in the vagina (*p=0.0052, Mann-Whitney*) at 3dpi and against pathology in the oviducts (*p=0.0177 and p=0.0018, t-test*) at 14dpi. Deficiency of Prss31 worsened infection in the vagina (*p=0.0456, t- test*) while deficiency of mouse mast cell protease 5 (mMCP5) was protective in the uterus (*p=0.0262, Mann-Whitney*) at 3dpi.

Conclusion: Our results suggest, for the first time, that MCs mediate immune responses to *Chlamydia* RT infection. While Prss31 appears protective, other MC proteases have different effects, highlighting the importance of studying them individually. Increased understanding of their specific roles could allow development of improved therapeutic strategies against *Chlamydia* infection and other STIs.

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