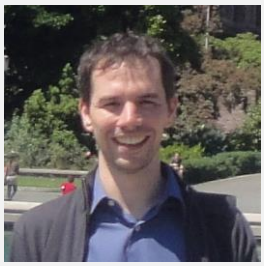
ImmunoTools *special* Award 2014



Federico Remes Lenicov, PhD

INBIRS – Facultad de Medicina, UBA,
Paraguay 2155 – Piso 11, Buenos Aires C1121ABG, Argentina

Semen modulates the specific immune response against sexually-transmitted pathogens

It is well known that semen is able to suppress a number of immune responses mediated by both the innate and adaptive immune system. The immunosuppressive actions of semen induce a state of non-responsiveness to sperm antigens and promote a tolerogenic response to paternal alloantigens favoring maternal acceptance of the conceptus at implantation. The mechanisms underlying the suppression of the immune response mediated by semen appear to be related to the presence of extremely high concentrations of TGF-beta and PGE2 in the semen.

It is reasonable to speculate that the immunosuppressive effects mediated by semen can influence the course of the immune response against HIV and other sexually transmitted agents favoring the spreading of the infectious process. Surprisingly, the impact of semen on the immune response against sexually transmitted infectious diseases has not been defined yet.

In previous studies, we have shown that human seminal plasma can induce tolerogenic properties in dendritic cells, such as increased ability to produce IL-10, TGF-beta and expand the population of regulatory T cells. Since dendritic cells are the cells in charge of initiating and coordinating the adaptive immune response, we hypothesize that semen can alter the immune response against sexually-transmitted pathogens by acting on these cells.

In our current project, we are studying the influence of semen in the specific immune response induced by an intravaginal (ivag) immunization protocol in mice. To this end, we are using 6-8-week-old female Balb/C mice inoculated intravaginally with recombinant Vaccinia virus expressing HIV-gp160 (VV HIV-1 EnvIIIB) (107 pfu), in the presence or absence of seminal vesicles content. We analyse lymphocytes and antigen presenting cells from both iliac lymph nodes and spleen cells, measure TNF-α or IFN-γ in cells supernatants by ELISA and intracytoplasmic flow cytometry, TGF-beta and IL-10 expression by RT-qPCR, and IFN-γ producing cells by ELISPOT. We also quantified antibodies in blood by ELISA.

In the first place, we demonstrated that the content of seminal vesicles content does not compromises the infectivity of recombinant Vaccinia virus HIV-1 EnvIIIB. Afterwards, we showed that intravaginal inoculation in the presence of seminal vesicles content increases viral titers in ovary, although both conditions showed similar IgG antibody responses. In addition, we found that inoculation of seminal vesicles content compromised the inflammatory response induced by the intravaginal immunization, since it reduced production of IFN-gamma and TNF-alpha levels in lymphocytes from the spleen as well as from the draining lymph nodes. Inoculation of seminal vesicle content also decreased TGF-beta and IL-10 production by lymphocytes, further suggesting that an inflammatory response was compromised.

So far, our results suggest that semen might be able to modulate the immune response against sexually transmitted pathogens in a regulatory profile, favoring the establishment of infectious diseases.