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## Regulation and function of immune suppressive myeloid cells in systemic autoimmunity

Trine N Jorgensen

Lerner Research Institute, USA

Systemic lupus erythematosus is an autoimmune disease characterized by elevated production of auto-reactive antibodies and systemic inflammation. Nine out of ten patients suffering from SLE are female. Sex hormones have been extensively studied for their potential effects on disease pathogenesis. It is thus known that testosterone protects while estrogens exacerbate disease development. We have recently described a population of Gr1+CD11b+ cells that are upregulated in male lupus-prone (NZB x NZW)F1 mice. These cells are driven by testosterone in a dose-dependent manner, as revealed by castration and hormonal reconstitution studies. Interestingly, although Gr1+ cells from both male and female prepubescent (NZB x NZW)F1 mice are immunosuppressive, the suppressive capacity is driven by different mechanisms and only male-derived cells remain immunosuppressive after puberty. In support hereof, adult 9 week old male mice depleted of Gr1-expressing cells develop increased levels of antibodies to both thymus-dependent antigens (NP-CGG) and nuclear auto-antigens, while a similar depletion strategy in age-matched females had no effect on either NP-specific antibody production or the spontaneous appearance of anti-nuclear autoantibodies. Further studies revealed that Gr1+ cell depletion in adult (NZB x NZW)F1 male mice resulted in increased levels of TFH and GC B cells after immunization. We conclude that a population of testosterone-driven Gr1+ cells present in (NZB x NZW)F1 lupus-prone male mice exert a hitherto unappreciated role in controlling activation of the adaptive immune system and the development of lupus-like disease. Manipulation of these cells represents an interesting new target for immunotherapy in autoimmune disorders with a female predominance.

### Biography

Trine N Jorgensen obtained her PhD from The University of Southern Denmark in 2002. She completed her Postdoctoral studies at the University of Colorado, Denver Health Sciences Center studying the importance of sex hormones and type I interferon signaling in lupus. In 2007, she joined the faculty at the Lerner Research Institute at the Cleveland Clinic as an Assistant Professor. She has published more than 25 papers and reviews in reputed journals and serves as an ad hoc reviewer for numerous scientific journals.

[jorgent@ccf.org](mailto:jorgent@ccf.org)