Dysregulation of autoreactive B cell responses in autoimmune diseases: from initial triggering to persistent activation

Neppelenbroek, S.

Stellingen behorend bij het proefschrift getiteld:

Dysregulation of autoreactive B cell responses in autoimmune diseases:
from initial triggering to persistent activation

1 Autoreactive B cells play an important role in the pathogenesis of autoimmune diseases, but fundamental mechanisms underlying their dysregulation remain incompletely understood.

2 The activated phenotype and clonal expansions of B cells targeting topoisomerase 1 (TOP1) in systemic sclerosis (SSc) suggest continuous antigen-driven triggering of these autoreactive B cells, which likely contributes to the development, progression and chronicity of SSc (this thesis).

3 The preferential recognition of TOP1-DNA complexes by a subset of anti-TOP1 autoantibodies in SSc influences the immunostimulatory properties of these antibodies and affects the activation of TOP1-reactive B cells (this thesis).

4 The recognition of microbial TOP1 by human anti-TOP1 autoantibodies support a role for microbes as source of antigen which stimulates the TOP1-reactive B cell response in SSc (this thesis).

5 The persistence of activated autoreactive B cells despite clinical disease control in rheumatoid arthritis is indicative for the absence of immunological remission. This ongoing immunological activity may be an important factor underlying the chronic nature of rheumatoid arthritis (this thesis).

6 The microbial cross-recognition of autoantibodies and the strong immunostimulatory capacity of microbial antigens form a deleterious combination, equipping autoreactive B cells with the ability to overcome tolerance mechanisms.

7 Immunological memory enables the immune system to effectively protect against previously encountered microbes, but also empowers autoreactive immune responses to chronically react to autoantigens in autoimmune diseases.

8 Advanced insights into the dysregulation of autoreactive B cells in autoimmune diseases are required to refine effective B cell-targeting strategies from broad depletion towards selective targeting of pathogenic B cell memory.

9 "Universities should be a playground for scientists." – Ben Feringa. An environment in which curiosity can be freely explored is essential for the generation of groundbreaking insights and solutions for the future.