

MOUSE MODELS OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

NZB/W F1 MOUSE MODEL OF SLE

Characteristics

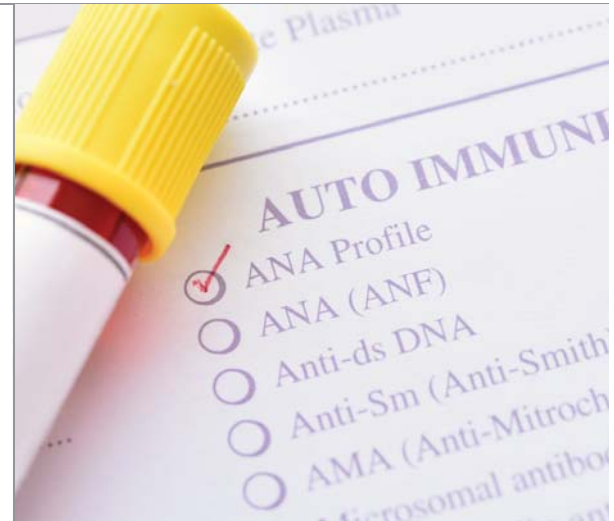
- Most commonly used preclinical model for SLE
- Model developed by Helyer and Howie in 1963 and subsequently transferred to Jackson Laboratories
- Develops anti-dsDNA (auto) antibodies at ≥ 16 weeks of age
- Develops 3+ proteinuria after 20 weeks of age
- NZM lines: Genetic susceptibility loci (sle1,2,3)

Clinical Measures

- Proteinuria
- Weekly body weights
- Anti-dsDNA antibody ELISA
- Glomerular filtration rate
- IDEXX clinical analyzer

FLOW CYTOMETRY

- B cells, T cells, dendritic cells, NK cells, NKT cells, apoptosis
- Experienced with multicolor (up to 10 color) panel design
- Validation with human (PMBCs), rat and mouse cells (whole blood, splenocytes and lymph node cells)



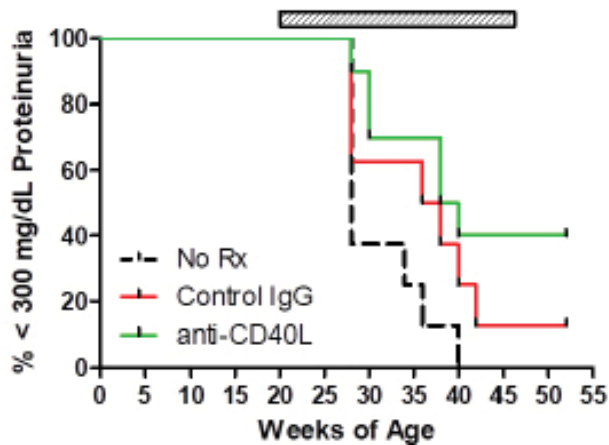
HISTOPATHOLOGY

- Glomerulonephropathy
- Dilated tubules
- Degenerate tubules
- Lymphocyte aggregates



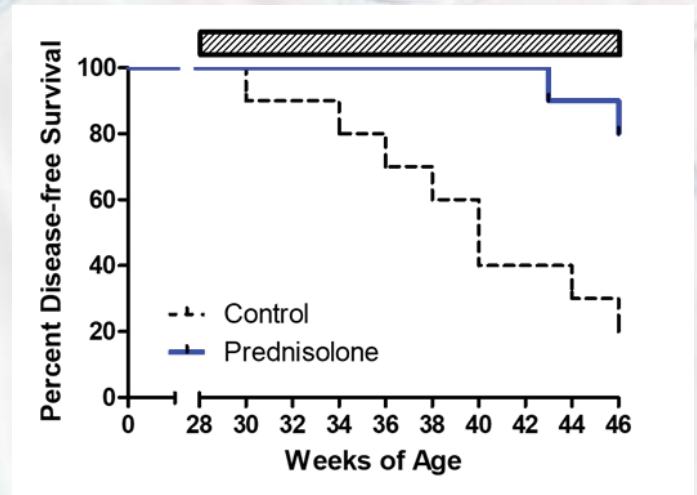
NZB/W F1 SLE MOUSE PREVENTION STUDY

- N=10/group with proteinuria = 0+ at 20 weeks of age
- Dose once every two weeks from 20 - 46 weeks of age
- Measure body weights once weekly and proteinuria once every two weeks
- Humane survival end points: $\geq 3+$ proteinuria on two consecutive weeks

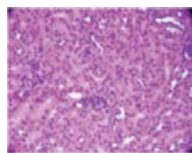


NZB/W F1 SLE MOUSE REMISSION STUDY

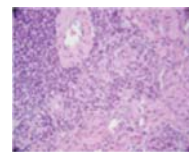
- NZB/W F1 female mice with moderate proteinuria (1 - 2+) were entered into groups at 28 weeks of age (n = 10/group) and initiated treatment (bar)
- Proteinuria was measured once every two weeks (the following week to confirm a $\geq 3+$ reading)
- Humane survival end points: $\geq 3+$ proteinuria on two consecutive weeks



NZB/W F1
Proteinuria = 3+ at 46 weeks of age



MRL/lpr
Proteinuria = 3+ at 15 weeks of age



Both mice reached the same humane endpoint, but lymphocyte aggregates were noticeably more severe in MRL/lpr mice (mean score = 3) compared to NZB/W F1 mice (mean score = 2)

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IT'S PERSONAL.

Driven to expedite your journey.



"With more than 200,000 cases per year in the U.S., Biomere realized long ago the importance of a validated model for SLE. In 2011, we collaborated with Dr. Betty Diamond at the Feinstein Institute to develop small molecule therapeutics for lupus. Biomere continues to offer validated rodent lupus models to investigate mechanisms and characteristics of this systemic disease."

- Chris H., Program Director