SLE Models

CrownBio
CONNECTING SCIENCE TO PATIENTS

Advance SLE agent development with robust *in vivo* models

Progress your systemic lupus erythematosus (SLE) agents to the clinic through our preclinical drug development platform. Utilize robust, spontaneous SLE models which more closely represent human disease.

- Select preclinical models with diverse mechanisms capturing many key characteristic clinical and pathologic features of SLE including:
  - MRL/Fas^{lpr} spontaneous model
  - NZB/W spontaneous model.
- Determine efficacy and response to treatment.
- Select qualified lupus lead agents.

MRL/Fas^{lpr} spontaneous model of SLE

- Spontaneous onset starting at 9-10 weeks of age, developing over 7-9 weeks.
- Major phenotype/characteristics:
  - dramatic lymphoproliferation and lymphadenopathy
  - splenomegaly
  - glomerulonephritis (subacute, proliferative) and proteinuria
  - skin lesions
  - expansion of $CD3^+CD4^-CD8^-$ T cells
  - no interferon signature.

NZB/W spontaneous model of SLE

- Spontaneous onset starting around 22-23 weeks of age, developing over 12-13 weeks.
- Major phenotype/characteristics:
  - splenomegaly
  - glomerulonephritis (subacute, proliferative) and proteinuria
  - persistence of long-lived autoreactive plasma cells
  - interferon signature.

Major endpoints for assessment:

- Body weight.
- Skin lesions (in MRL/Fas^{lpr}).
- Proteinuria.
- Spleen, kidney, and lymph node size/weight.
- Cytokine levels.
- Blood serum anti-dsDNA antibody levels.
- Blood urea nitrogen (BUN) levels.
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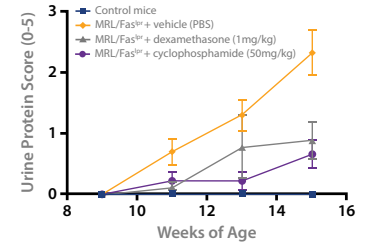
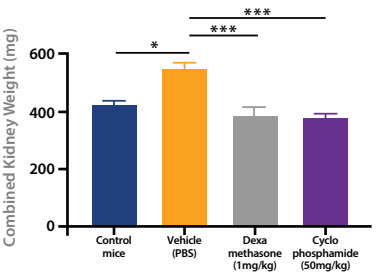
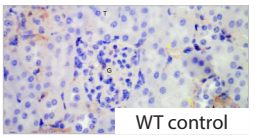
- FACS analysis of immune cell populations.
- Kidney histopathology and IHC staining for C3 and IgG levels.

Urine Protein Levels and Kidney Weight of MRL/MpJ-Fas^{lpr} Mice

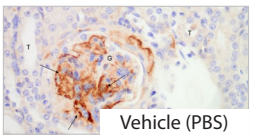




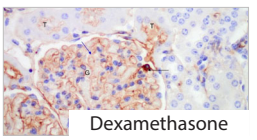
Kidney IgG Staining in the NZB/W Spontaneous Model of Lupus



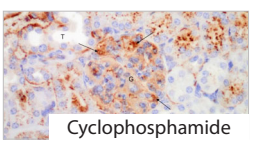
Panel A represents low IgG levels present in kidney glomeruli (G) of healthy control mice. No immunostaining is visible within the glomerulus. Surrounding renal tubules indicated as "T".



Panel B represents elevated IgG levels in glomeruli (G) of diseased kidneys from vehicle-treated NZB/W mice. Strong granular IgG immunolabeling is visible in most mesangial segments (black arrows).



Panel C represents IgG staining of kidney glomeruli (G) from dexamethasone-treated NZB/W mice. Focal immunolabeling is visible around only one nucleus within the glomerular tuft (black arrow).



Panel D represents kidney IgG staining in cyclophosphamide-treated NZB/W mice. Few foci of strong granular immunolabeling are visible within the mesangium (black arrows), but less than in vehicle-treated animals.