TNF-α Microinjected Mouse (model 1006)

The TNF-α Microinjected Mouse carries a 3’-modified human TNF-α (Tumor Necrosis Factor alpha) transgene. It exhibits deregulated TNF-α expression, with constitutive expressed low levels of circulating human TNF-α and progressive development of severe inflammatory arthritis without experimental induction. The penetration of the arthritic condition is 100% with a consistent time of onset, making these mice excellent models to evaluate anti-arthritic compounds and study arthritis etiology and pathogenesis. This model additionally exhibits alterations in metabolic parameters and fertility and sexual function.¹

Potential Applications

- Evaluate anti-TNF-α antibodies and other agents for treatment of rheumatoid arthritis
- Study the role of TNF-α in the context of other pro-inflammatory cytokines such as IL-1 and immunosuppressive cytokines such as TGF β and their roles in mediating inflammatory disease progression
- Study the role of TNF-α in other disease areas, including bone homeostasis, obesity, metabolism and male sexual health.

Disease Progression in TNF-α Mice: Histopathological Progression

Forelimbs and hindlimbs were examined from TNF-α Microinjected Mice and control non-transgenic mice at 4 weeks and 8 weeks of age. With increasing age, a progressive increase in the severity of histopathological changes in the joints was observed:

4 week old TNF-α mice:
- Mild to moderate tenosynovitis
- Synovial cell hyperplasia associated with infiltration of neutrophils and macrophages
- Focal dissecting pannus occasionally noted

8 week old TNF-α mice:
- Moderate to severe tenosynovitis
- Increased synovial cell hyperplasia and accumulation of inflammatory infiltrates (neutrophils and macrophages)
- Dissecting pannus noted frequently accompanied by osteolysis revealing active arthritis (eroding cartilage and bone)

Gross Phenotypic Disease Observations

TNF-α Microinjected Mice and non-transgenic age-matched controls were visually observed to compare signs of disease progression:

TNF-α mice express low levels of human TNF-α, which is not significantly inducible by LPS challenge.¹
• ~5 weeks: normal appearance, no detectable symptoms
• ~9 weeks: mild disease; minor loss of flexibility in digits; minimal joint swelling and distortion
• ~14 weeks: moderate disease; moderate distortion and twisting of hindpaw and moderate swelling of joints
• ~20 weeks: severe disease, distortion and swelling of joints

The histopathology and gross observation data is specific to the TNF-α Microinjected Mice housed at Taconic. Onset and severity of phenotype may be influenced by environmental factors that may differ from facility to facility. A pilot characterization study may be helpful in determining the occurrence of disease in a specific facility.

Additional phenotypes of TNF-α mice

TNF-a mice display reduced body weight, increased metabolic rate and bone loss compared to wild type mice. Male TNF-a mice display sexual dysfunction.1

Ready for Your Experiments

Taconic’s TNF-α Microinjected Mouse is produced in Isolator Barrier Unit (IBU™) facilities under Murine Pathogen Free (MPF™) conditions and shipped in Taconic Transit Cages (TTC™). Current health reports are available at www.taconic.com. Barrier housing conditions are recommended for maintenance of the line.

References Cited:

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