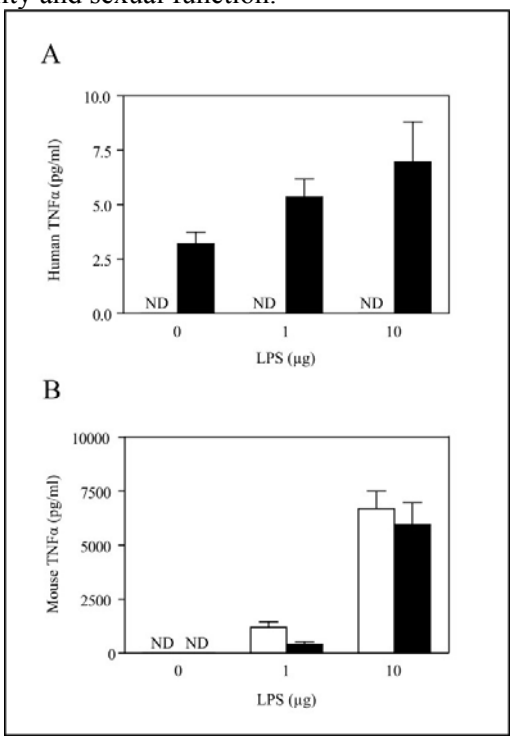
TNF-α Microinjected Mouse

Taconic offers a mouse model which overexpresses the human proinflammatory cytokine TNF-α. This model may be useful for evaluating new drug candidates as well as in basic research studies.

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]



TNF-α mice express low levels of human TNF-α, which is not significantly inducible by LPS challenge.[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:

- ~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:

1. Hayward MD, Jones BK, Saparov A, Hain HS, Trillat A, Bunzel MM, Corona A, Li-Wang B, Strenkowski B, Giordano C, Shen H, Arcamone E, Weidlick J, Vilensky M, Tugusheva M, Felkner RH, Campbell W, Rao Y, Grass DS, Buiakova O. (2007) An extensive phenotypic characterization of the hTNFα transgenic mice. BMC Physiol. 7:13

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