NanoBiotec
Min samples, Max info

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Model: Collagen Induced Arthritis (CIA)

A commonly used model for human rheumatoid arthritis (RA). Arthritis is initiated by intradermal injections of Collagen Type II emulsified in Complete Freund's Adjuvant. This causes immune response generating antibodies against Collagen Type II. There is both a T cell and B cell component to the pathology. The pathological features of CIA model shared with RA include a proliferative synovitis with infiltration of polymorphonuclear and mononuclear cells, cartilage destruction, bone resorption, pannus formation and fibrosis. Additionally, susceptibility to both CIA and RA is linked with genes encoding MHC class II molecules, which indicates the role of CD4+ T cells in these two diseases. Similar to RA in humans, CIA models abundantly express proinflammatory cytokines, including tumor necrosis factor (TNFα) and interleukin (IL)-1β.

Methods and readouts:

- length: 5-6 weeks
- dosing paradigms: prophylactic or therapeutic
- dosing routes: po, ip, sc, iv, infusion pump
- positive controls: dexamethasone
- assessments: arthritis score, hind paw thickness, body weight
- circulating or tissue level biomarker analysis (profiling of cytokines and other protein or genes)

- collagen antibody levels
- flow cytometric analysis of cell populations in spleen/lymph node
- histological/IHC assessment of joints
- PK/PD blood collections

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Model: Adjuvant-induced RA (AIA)

Complete Freund's adjuvant is used to initiate induction of arthritis. This model is the original model of RA, has been extensively used to pre-clinical screening of new anti-arthritis compounds and has successfully predicted activity and toxicity in multiple new therapeutics.

After a single injection of the adjuvant, a robust and easily measurable polyarthritis develops. The joint pathology seen in AIA animals shares the cartilage degradation, bone reportion and cellular influx seen in human RA. This model is also T cell and neutrophil dependent with no requirement for B cells. Cytokines of both the Th1 and Th17 cells (eg. IL-1, IL-6, IL-17A, IL-21) play a role in the joint pathology. As this model is generally less severe than CIA and is transient (normally resolving after a month), lower doses of test compounds can be effective in this model. The pathology is not limited to the extremities since the spine, GI tract, skin and even the eyes can be affected.

Methods and readouts:

- type: mono-arthritis or polyarthritis
- length: 2-4 weeks
- dosing paradigms: prophylactic or therapeutic
- dosing routes: po, ip, sc, iv, infusion pump
- controls: dexamethasone, Enbrel, morphine
- assessments: arthritis score, hind paw thickness, body weight
- pain assessments (von frey, thermal)

- circulating or tissue level biomarker analysis (proteins or genes)
- histological/IHC assessment of joints
- PK/PD blood collections

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Model: Experimental Autoimmune Encephalomyelitis (EAE)

Experimental Autoimmune Encephalomyelitis (EAE) is a widely-accepted model of demyelinating diseases, such as **multiple sclerosis**. This model is produced by administering a myelin basic protein peptide (MBP) fragment that induces an autoimmune response directed to the myelin sheath surrounding motor neurons. Demyelination of neurons within the CNS leads to impaired locomotor function and mirrors symptoms of the human disease. As with multiple sclerosis in humans, the condition in rodents appears in relapsing-remitting cycles and are characterized by loss of nerve conduction and chronic progression of disability.

Methods and readouts:

- Chronic EAE model: induced by subcutaneous injection of myelin oligodendrocyte glycoprotein (MOG)/CFA, followed by ip injection of pertussis toxin
- Adoptive transfer EAE model: recipient mice will skip the immunization phase. The donor mice will be immunized first (same as the chronic EAE model). After immune response to the MOG is developed, spleen cells are harvested. Activated encephalitogenic T cells are transferred to recipient mice to induce EAE.
- Disease duration: up to 5-7 weeks for scoring. Tissues are usually collected at the peak of the disease (14-18 dpi).
- Disease scores and body weight over time.
- PK/PD blood collections
- Histopathological evaluation (by IHC) in brain and spinal cord
- Flow cytometric analysis of leukocytes in blood, bone marrow, brain and spinal cord
- T cell in vitro assays (^{3}H-thymidine proliferation assay, naïve T cell differentiation assay)
- Cytokine/chemokine assay

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Model: Type IV Hypersensitivity Reactions

Delayed-type hypersensitivity (DTH) reactions, also known as type IV hypersensitivity reactions, are mediated by soluble or cell-associated antigens primarily involving CD4+ or CD8+ T cell activation. These reactions are characterized by the release of mediators from activated T cells. The T cells then activate local endothelial cells and recruit macrophages, which results in local inflammation and swelling. There are three major categories of DTH reactions, classified by delivery of the antigen: injected into the skin, absorbed into the skin or absorbed through the gut.

Methods and readouts:

- DTH induced by ip. injection of keyhole limpet hemocyanin (KLH) (standard strain and humanized mouse)
- DTH induced by topical application of oxazolone
- PK/PD blood collections
- Cytokine/chemokine analysis
- Clinical chemistry
- Histopathological evaluation
- Immunohistochemistry
- Flow cytometry in lymph nodes or spleen

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Model: Imiquimod Induced Psoriasis

Psoriasis is a chronic skin condition associated with multiple contributing factors including autoimmune disease. We have characterized a clinically relevant psoriasis model in susceptible mice through the **topical application of 5% imiquimod** (IMQ) cream. Imiquimod (IMQ) is a toll-like receptor agonist that acts as an immune response modifier. Application of IMQ to the skin of mice induces inflammation with features commonly found in human psoriatic skin, including erythema and scaling. The advantage of this model is the fast induction of clinical phenotypes for rapid therapeutic screening and particularly translational into the clinic as it has many of the significant markers of human disease.

This imiquimod-induced psoriasis models human plaque-type psoriasis in which the **IL-23/IL-17 cytokine axis** plays a pivotal role. Study parameters include in-life clinical evaluation of skin, histopathological evaluation of skin sections and cytokine analysis in skin and/or internal immune organs. Our extensive immunology expertise allows our scientists to implement this translational model to mimic human disease and support understanding of the mechanism of action of test drugs.

Methods and readouts:

- imiquimod cream induced psoriasis.
- length: about 2 weeks for dosing and observation, 2-4 weeks for histopathological observation, and another 2-4 weeks for multiplex protein and mRNA analysis.
- clinical chemistry
- scaling & lesion scores and erythema scores measure daily
- histopathological evaluation, PASI scoring & digital images
- histological/IHC assessment of skins
- cytokine/chemokine analysis
- multi-color flow cytometric analysis of lymph nodes or spleen
- PK/PD blood collections