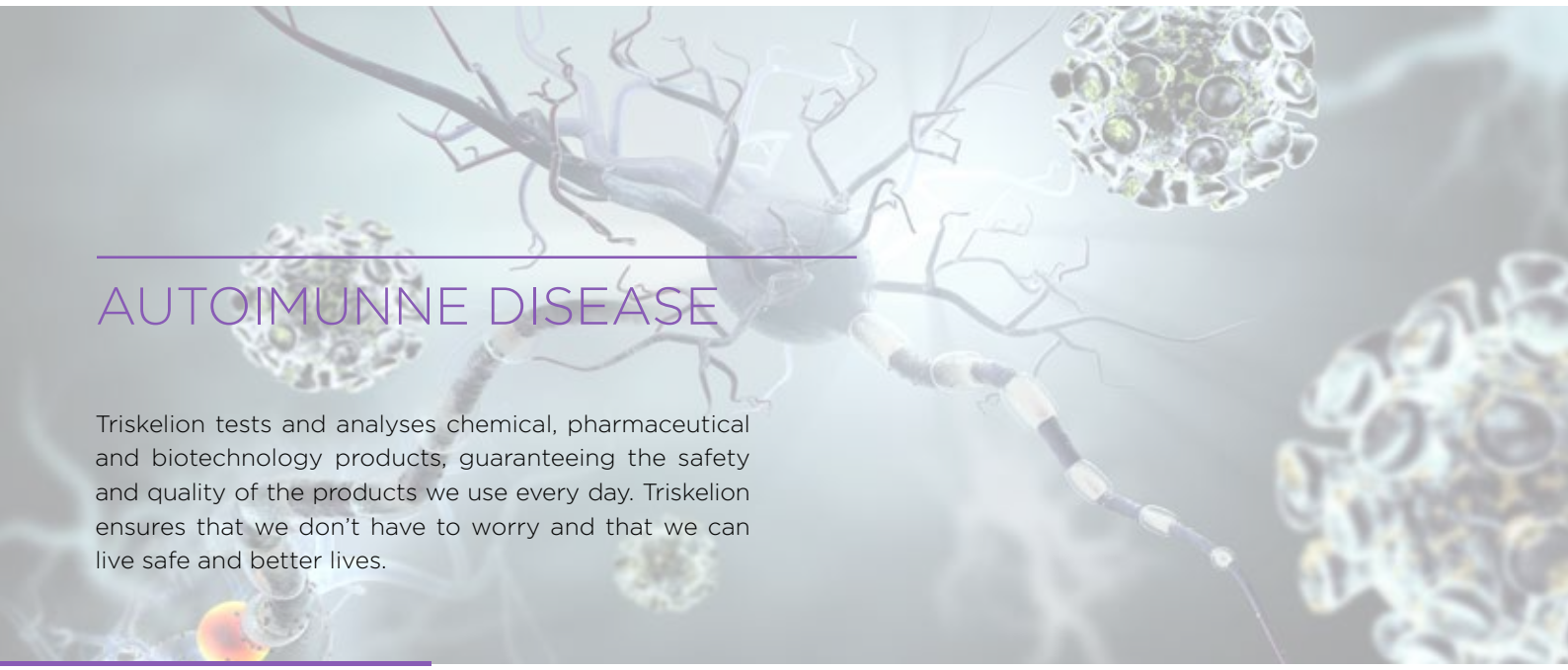
TRISKELION
RESEARCH FOR BETTER LIVING



AUTOIMUNNE DISEASE

Triskelion tests and analyses chemical, pharmaceutical and biotechnology products, guaranteeing the safety and quality of the products we use every day. Triskelion ensures that we don't have to worry and that we can live safe and better lives.

PHARMA

AUTOIMMUNE DISEASES AFFECT A LARGE PART OF THE HUMAN POPULATION, ESPECIALLY IN THE DEVELOPED WORLD. THIS TYPE OF DISEASE IS CHARACTERIZED BY A HYPER-ACTIVE IMMUNE REACTION TO SELF-ANTIGENS. AUTOIMMUNE DISEASES, LIKE MULTIPLE SCLEROSIS AND PSORIASIS, ARE OFTEN CAUSED BY A COMBINATION OF GENETIC AND ENVIRONMENTAL FACTORS. ROBUST AND EFFECTIVE ANIMAL MODELS ARE NEEDED; THESE PLAY AN INDISPENSABLE ROLE IN REVEALING THE UNDERLYING MECHANISM(S) OF AUTOIMMUNITY AND EVALUATING THE EFFICACY OF NOVEL DRUG CANDIDATES.

Triskelion has developed mouse models for Multiple Sclerosis (MS) and Psoriasis to allow efficacy evaluation of novel drug candidates. Depending on your needs and wishes, we have different types of models available that can be performed with or without a GLP claim.

MODELS FOR MULTIPLE SCLEROSIS

Mouse models of experimental autoimmune encephalomyelitis (EAE) are recognized as representative preclinical tools to mimic key aspects of MS. Triskelion has an extensive track record with mouse EAE models, in which paralysis is applied as the primary readout parameter. Additional readouts can be implemented to address specific disease characteristics, such as the level of local inflammation or demyelination in the central nervous system (CNS), or the magnitude of the myelin-specific T cell or B cell response. Such parameters may provide additional insight into the mode of action of drug candidates.

We have experience with two different mouse EAE models:

- Immunization of female SJL mice with myelin peptide PLP139-151, inducing disease that resembles the relapse-remitting disease pattern in MS patients. This model is validated with Dexamethasone and Glatirameracetate.
- Immunization of female C57Bl/6 mice with myelin peptide MOG35-55, inducing disease that resembles progressive disease in MS patients.

TRISKELION
RESEARCH FOR BETTER LIVING

PHARMA

TRISKELION'S CORE MISSION IS TO ACCELERATE YOUR DISCOVERY PIPELINE SO YOU CAN PROGRESS TO THE NEXT PHASE OF CLINICAL TESTING. WE DO THIS BY PROVIDING CLINICALLY RELEVANT AND HIGHLY TRANSLATIONAL MODELS OF HUMAN DISEASES. PROVIDING THIS DISTINCTIVE SERVICE AT A CONSISTENTLY HIGH LEVEL OF QUALITY IS MADE POSSIBLE BY THE UNIQUE BLEND OF PROFESSIONALS IN OUR TEAM. WE PRIDE OURSELVES ON THE QUALITY OF OUR WORK AND COMPLETING PROJECTS SWIFTLY AND COST-EFFECTIVELY.

AUTOIMUNNE DISEASE

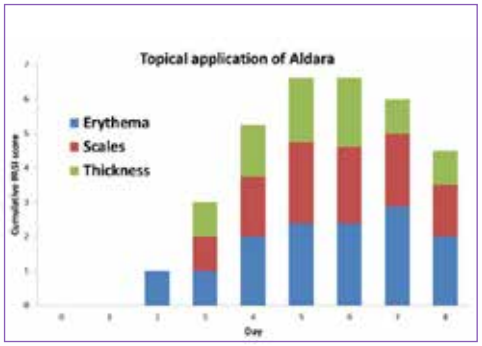


Figure 1. Cumulative Psoriasis Area and Severity Index (PASI) of the back skin following topical treatment twice a day with Imiquimod-containing cream.

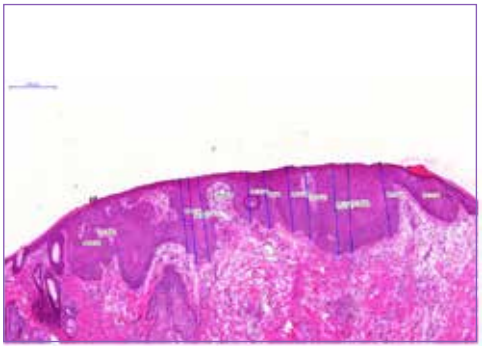


Figure 2: Acanthosis measurement (rete ridge formation and epidermal thickness) in the human skin biopsy obtained in the xenograft mouse model for psoriasis.

MODELS FOR PSORIASIS

Psoriasis is a systemic and chronic skin disease associated with inflammation, papillomatosis and acanthosis. Triskelion offers syngeneic as well as humanized mouse models of psoriasis to evaluate the efficacy and mode of action of your drug candidates. We have experience with two types of models: An imiquimod (IMQ)-induced model in female Balb/c mice and a humanized xenotransplantation model in female Beige Nude XID (BNX) mice.

IMIQUIMOD MODEL

In this model, skin sensitization is induced by applying an Imiquimod-containing cream twice a day on the shaved back of female Balb/c mice. The model has been validated with Clobetasol.

Readouts include:
- PASI score
- Epidermal thickness
- Immunohistochemistry of the skin for presence of e.g. T cells

Advantages of this model:
- Rapid and cost-effective
- Easy to combine with PK analysis

XENOTRANSPLANTATION MODEL

In this model skin biopsies of psoriasis patients are transplanted on the back of BNX-mice. Tissues for transplantation are obtained in collaboration with network partners.

Readouts include:
- Epidermal thickness (acanthosis measurement)
- Keratinocyte hyper differentiation (Cytokeratin-16 staining)

Advantages:
- Highly translational
- Systemic treatment with antibodies against Tumor Necrosis Factor-alpha demonstrate efficacy in the majority, but not all, of the biopsies in this model, similar to the psoriasis patient population in the clinic

TRISKELION B.V. A TNO COMPANY | Utrechtseweg 48, 3704 HE Zeist | P.O.Box 844, 3700 AV Zeist | The Netherlands | P +31 88 866 2800
pharma@triskelion.nl | www.triskelion.nl | USA tmeijers@tnopharma.com | P +1 416 837 7500 | JAPAN japan@triskelion.nl | P +81 3 6234 4195