

## Delayed type hypersensitivity (DTH) mouse model for atopic dermatitis

**Species:** mice

**Fields of application:** Inflammation

Dermatitis is a broad term covering a variety of different inflammatory skin diseases. The etiology of widely prevalent atopic dermatitis (up to 15%) is unknown, but a genetically deficient skin epithelial barrier is a major factor. In allergic contact dermatitis (prevalence 7-10%), eliciting factors include local exposure of the skin to environmental agents such as natural rubber, metals (e.g. nickel) and plants, including poison ivy, as well as detergents, drugs, pollen or animal fur. These act as allergens or antigens, inducing immune responses which appear in the form of rashes, bumps and sometimes blisters when severe. Treatment includes allergen avoidance and topical glucocorticoids. Animal models of allergic contact dermatitis and associated responses are useful for testing new therapeutic compounds, but also provide a simple means to study skin inflammation and systemic immune responses.

Delayed Type Hypersensitivity (DTH)

Allergic contact dermatitis is a T-cell-mediated hypersensitivity reaction (Delayed Type Hypersensitivity or DTH Type IV), an immune response which manifests as an inflammatory reaction, due to activation of mononuclear phagocytes. It reaches peak intensity 24 to 48 h after the antigenic challenge. Memory T-cells are generated that persist for many months or years, sustaining the hypersensitivity to the antigen.

**Endpoints/Outcome parameters:** Within IME-TMP, oxazolone is applied to the abdomen (sensitization phase). One week later, the same substance is applied to one ear (challenge phase). Ear thickness and luminol –based bioluminescent imaging (BLI) of myeloperoxidase (MPO) activity are the main outcome parameters.

### **Readout parameters**

The measures at 6h, 24h, 48h and 72h after the challenge with oxazolone include:

Ear thickness with a digital micrometer

Bioluminescent imaging: The IVIS Spectrum (Caliper Life Sciences) is used as optical imaging technology to facilitate non-invasive longitudinal monitoring of disease progression (e.g. inflammation), cell trafficking and gene expression patterns in living animals. Luminol –based Bioluminescence imaging (BLI), a measure of myeloperoxidase (MPO) activity is employed as an *in vivo* marker of inflammation.

We additionally offer fluorescence-activated cell sorting (FACS) / immunohistochemistry (IHC) analysis of tissue and circulating immune cells; analysis of cytokines / chemokines / lipid profile and microglia activation. In addition, in collaboration with the Institute of Clinical Pharmacology (Pharmazentrum Frankfurt/ZAFES, Frankfurt am Main) we offer the use of multi Epitope Ligand Carthography (MELC) which allows staining of the same tissue section with up to 100 fluorescent markers. Other available assays are the Hematoxylin and Eosin (H&E) staining of tissue sections and the vascular (hyper) permeability (Evans Blue) response.

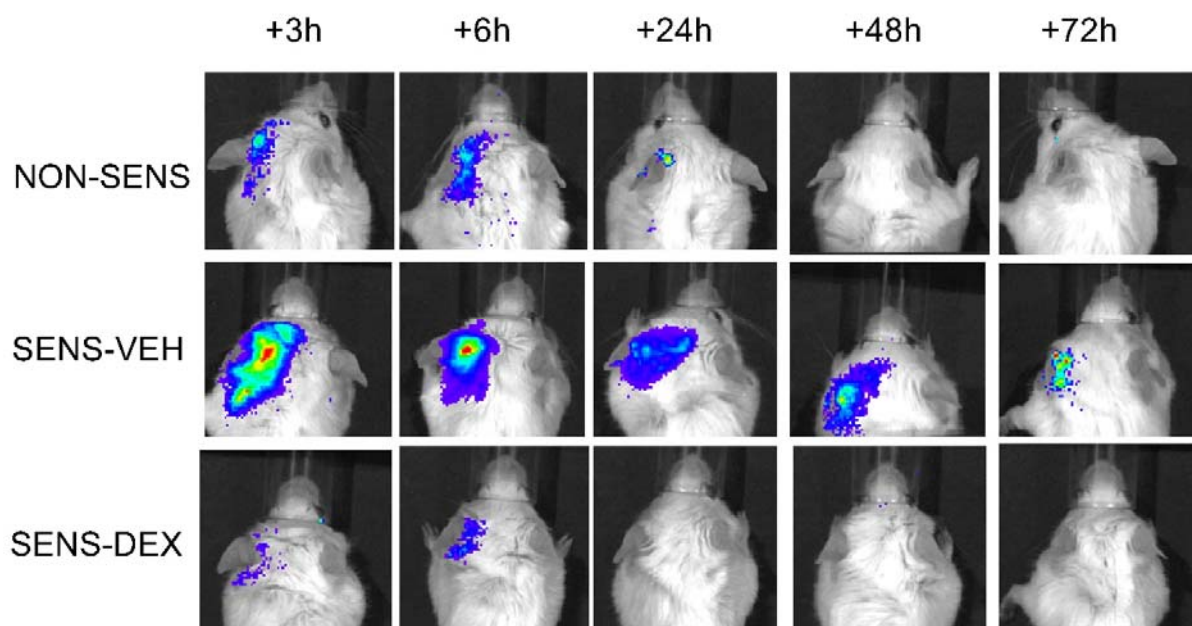
**Quality management and validation:** The model has been validated with the clinical reference compound dexamethasone (DEX).

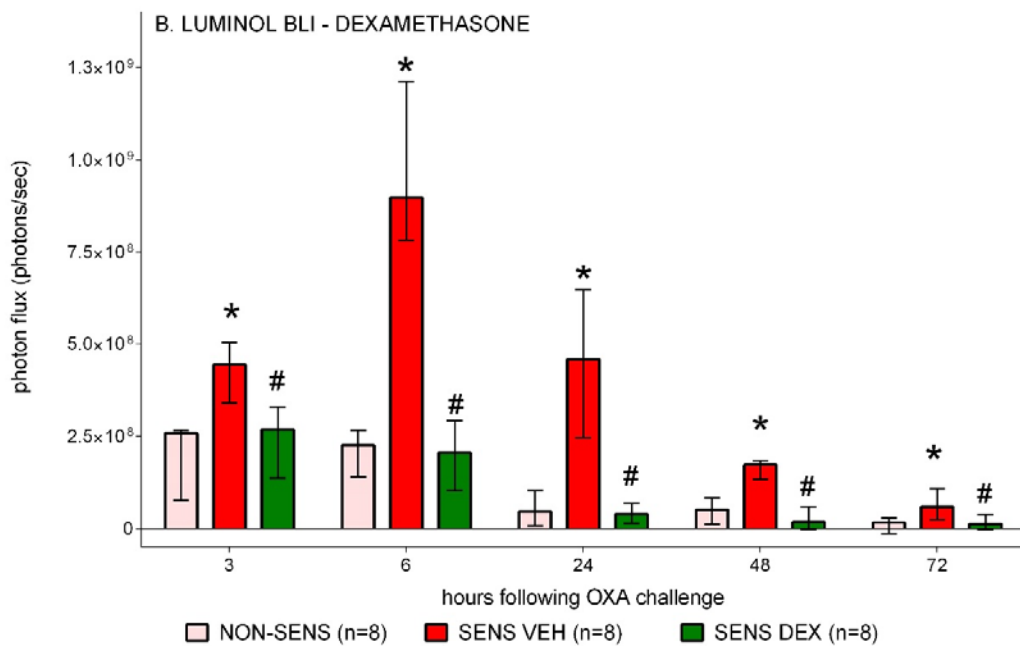
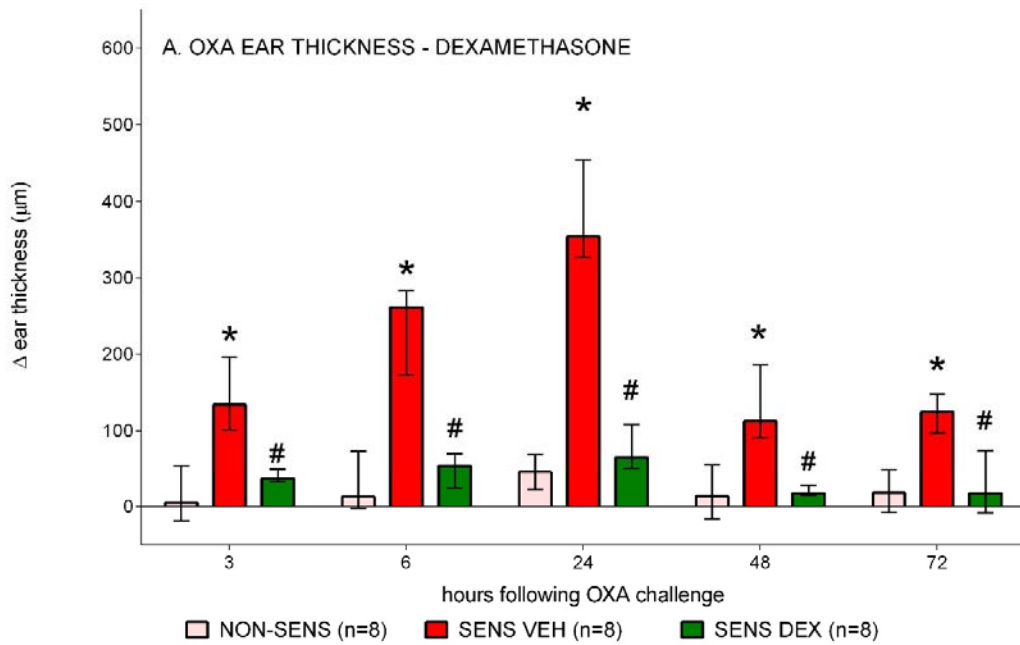
**References:**

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\* vs NON-SENS

# vs SENS VEH

Figure: Effects of Dexamethasone in the DTH animal model for dermatitis and relevant readouts (ear thickness and Luminol –based bioluminescence imaging) at Fraunhofer-TMP

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