



Preclinical Models of Atopic Dermatitis (AD)

Atopic Dermatitis (AD)

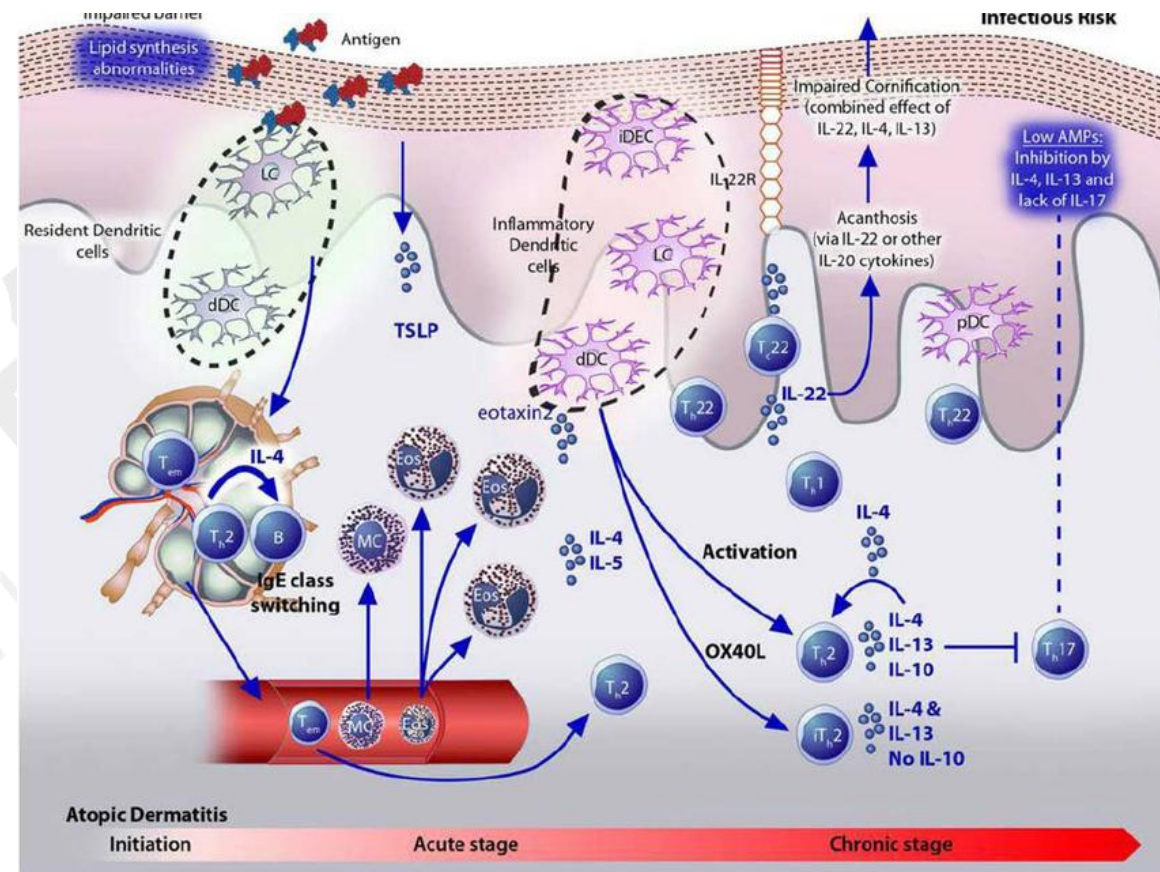
Symptoms and Causes

Atopic dermatitis patients clinically present skin erythematous plaques, eruption, elevated serum IgE and T helper cell type 2(Th2) cytokine levels, such as IL-4 and IL-13. Microscopically, atopic dermatitis patients also show epidermal hyperplasia and accumulation of mast cells and Th2.

In some people, atopic dermatitis is related to a gene variation that affects the skin's ability to provide protection. In other people, atopic dermatitis is caused by too much of the bacteria *Staphylococcus aureus* on the skin.

Models in place:

- DNCB Induced C57BL/6 Model
- DNCB Induced BALB/c Model
- OXA Induced C57BL/6 AD Model
- OXA Induced BALB/c AD Model
- MC903 Induced C57BL/6 AD Model
- MC903 Induced C57BL/6 Chronic AD Model
- MC903 Induced BALB/c AD Model
- FITC Induced BALB/c AD Model
- MC903&OXA induced AD model in C57BL/6
- DNFB+OVA Induced BALB/c AD Model
- IL-33 Induced BALB/c AD Model
- HDM+SEB Induced AD Model in C57BL/6 Mice
- OXA/DNCB Induced AD Model in SD rat
- IL-36 Induced AD Model in C57BL/6 Mice



DOI: [10.1517/14712598.2013.758708](https://doi.org/10.1517/14712598.2013.758708)

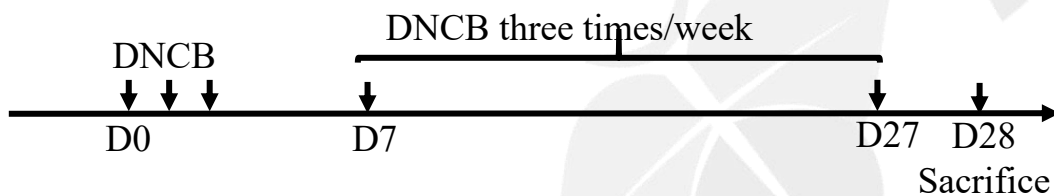
DNCB Induced AD Model

■ Mechanism

Haptens are small molecule irritants that bind to proteins and elicit an immune response and have long been used to study allergic contact dermatitis (ACD). Repeated hapten challenges disrupt the skin barrier, combined with a Th2-biased immune response.

The majority of haptens, such as 2,4-dinitrochlorobenzene (DNCB) and oxazolone (OXA), induce a response shift from Th1 to Th2 is observed following repeated application of hapten, in other words, contact dermatitis to atopic dermatitis-like skin lesion.

■ Haptens Induced Murine AD Mouse Model



Animal	BALB/c, C57BL/6
	C57BL/6 backgrounded transgenic mice
Evaluation	Clinical: Body weight, Ear Thickness
	Cytokine: IL-36, IL-4, IL-17
	Pathology: HE & Toluidine Blue

DNCB Induced C57BL/6 AD Model

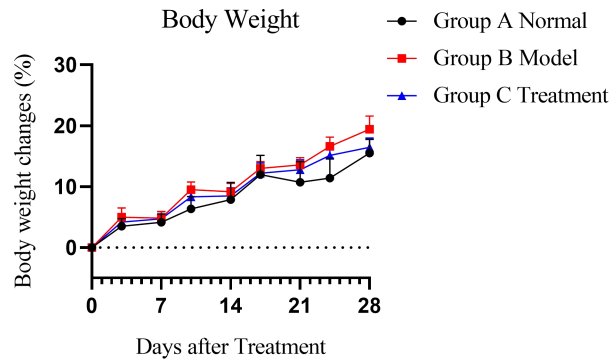


Fig 1 Body Weight

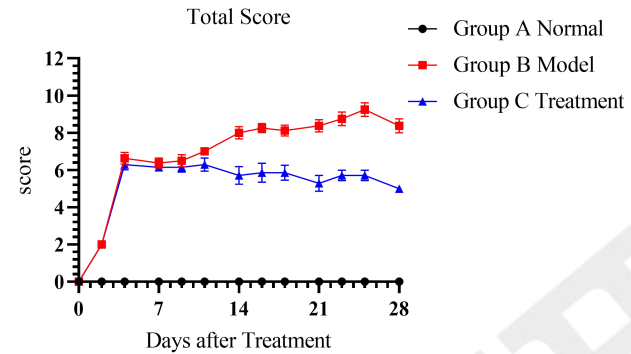


Fig 2 Skin score

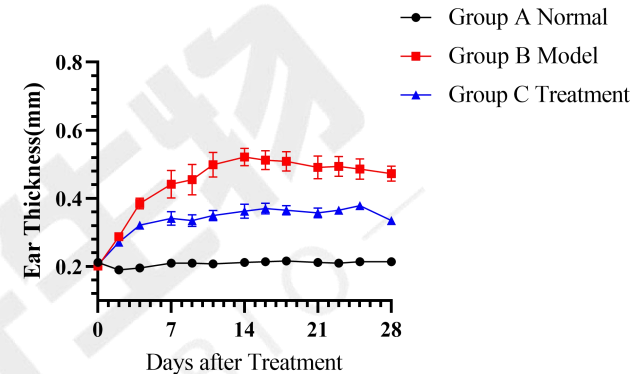


Fig 3 Ear Thickness

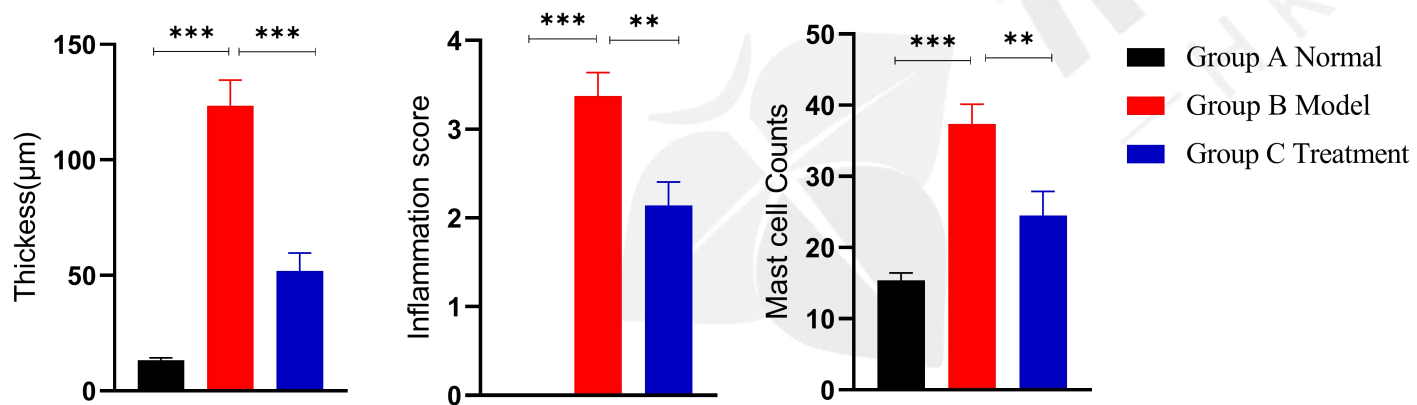


Fig 4 Pathology

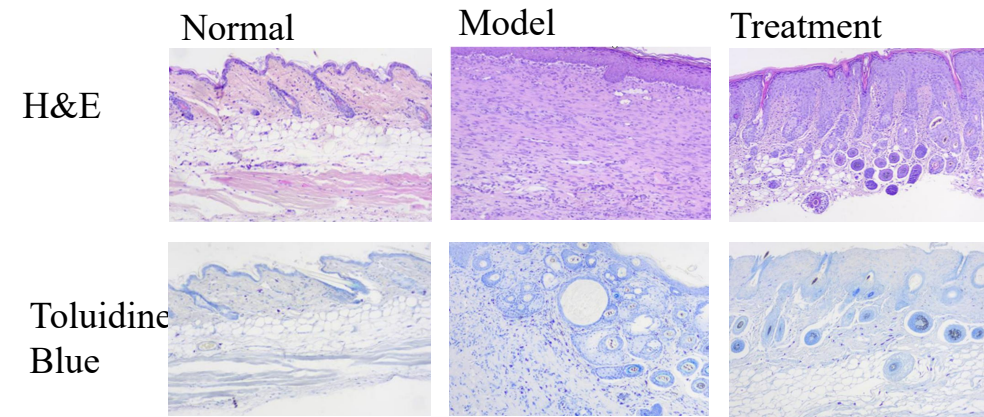


Fig 5 Typical pathological images

DNCB Induced AD Model in BALB/c Mice

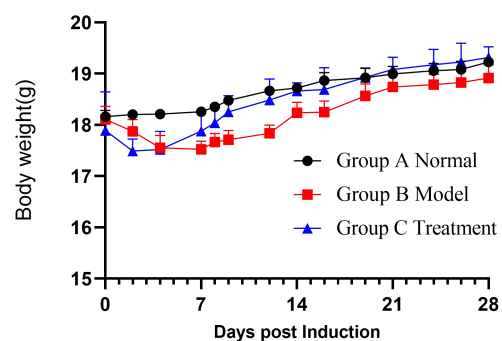


Fig 1 Body Weight

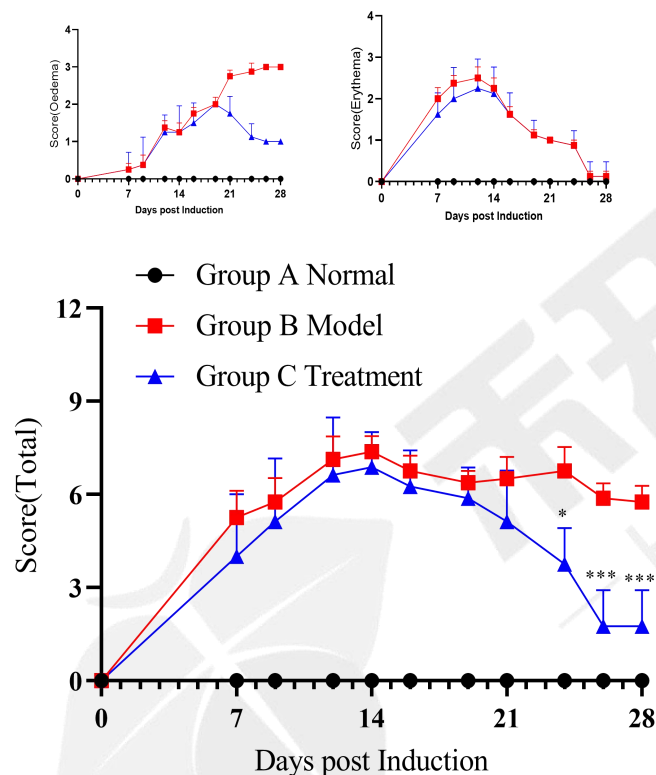


Fig 2 Skin score

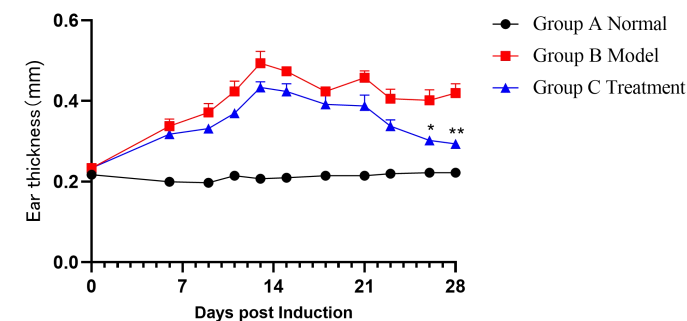
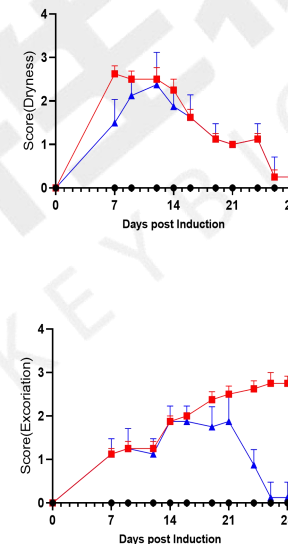


Fig 3 Ear Thickness

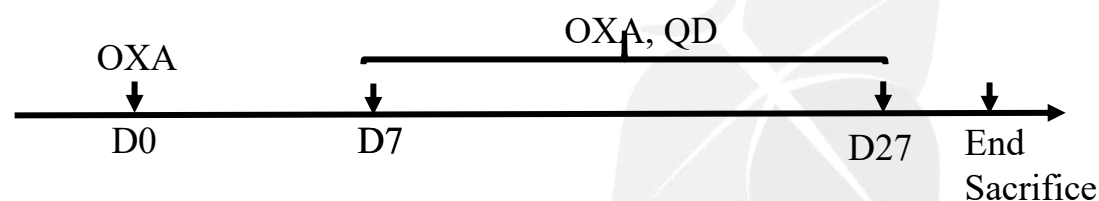
OXA Induced AD Model

■ Mechanism

Haptens are small molecule irritants that bind to proteins and elicit an immune response and have long been used to study allergic contact dermatitis (ACD). Repeated hapten challenges disrupt the skin barrier, combined with a Th2-biased immune response.

The majority of haptens, such as 2,4-dinitrochlorobenzene(DNCB) and oxazolone(OXA), induce a response shift from Th1 to Th2 is observed following repeated application of hapten, in other words, contact dermatitis to atopic dermatitis-like skin lesion.

■ Haptens Induced Murine AD Mouse Model



Animal	BALB/c, C57BL/6 C57BL/6 backgrounded transgenic mice
Evaluation	Clinical: Body weight, Ear Thickness Cytokine: IL-36, IL-4, IL-17 Pathology: HE & Toluidine Blue

OXA Induced C57BL/6 AD Model

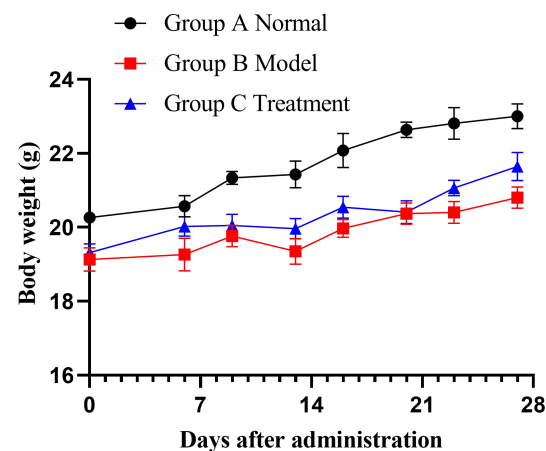


Fig 1 Body Weight

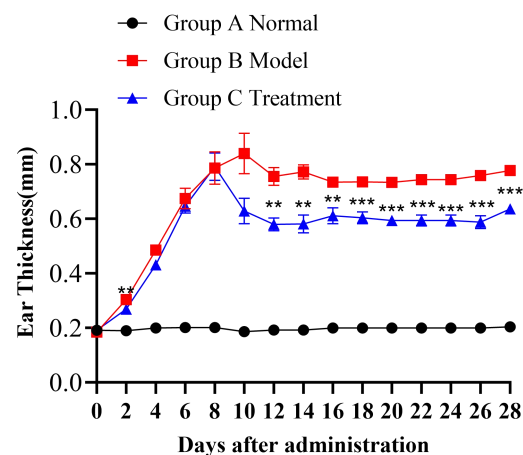


Fig 3 Ear Thickness

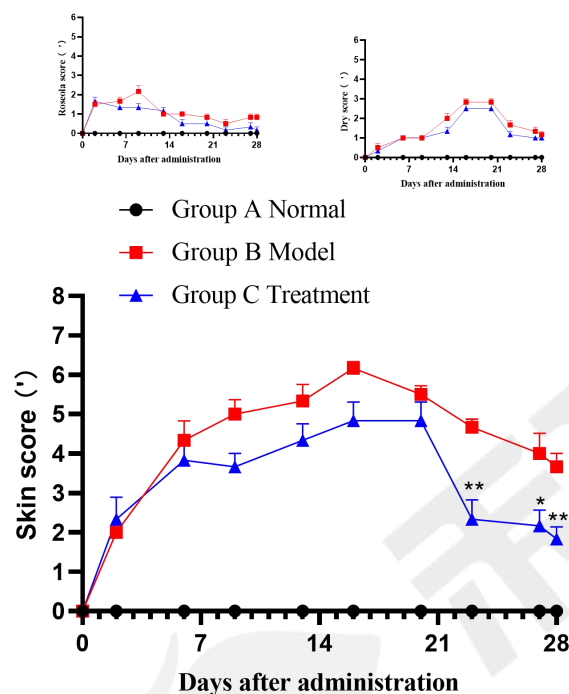


Fig 2 Skin score

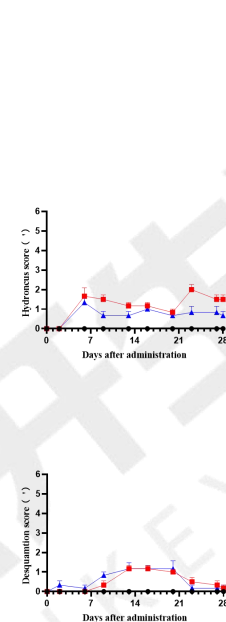
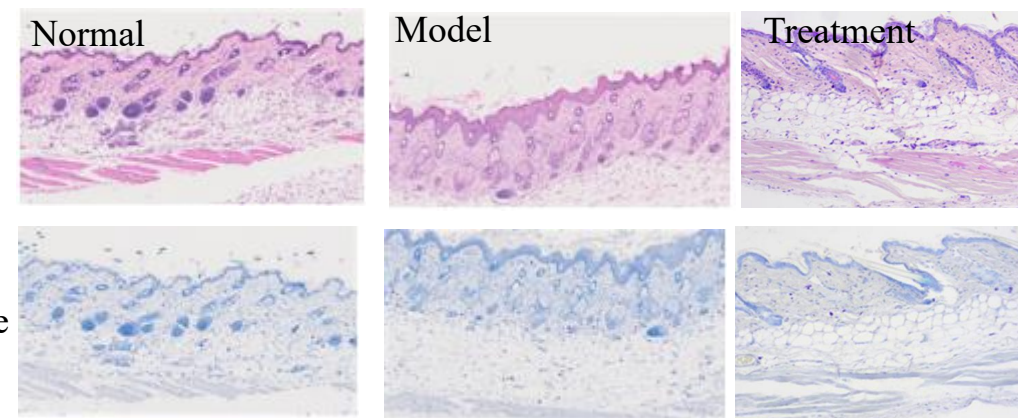


Fig 4 IL-36a/b levels (Measured using q-PCR)

H&E

Toluidine Blue



OXA Induced BALB/c AD Model

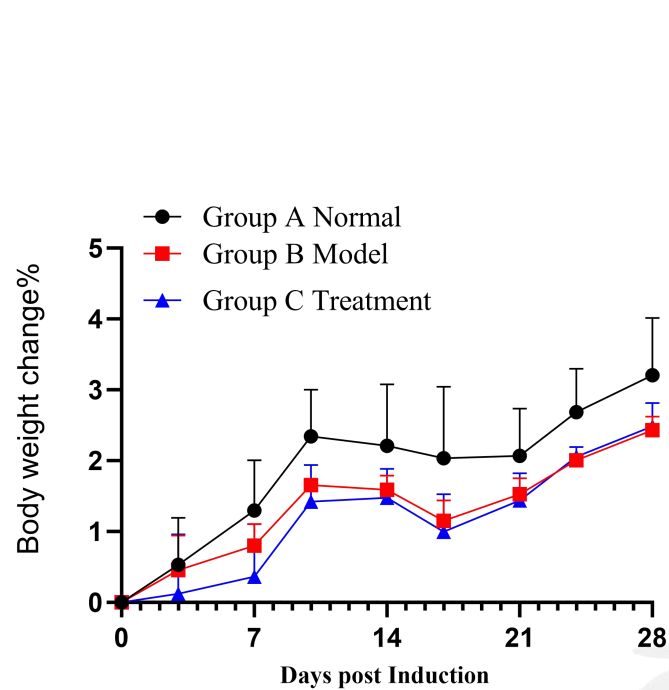


Fig 1 Body Weight

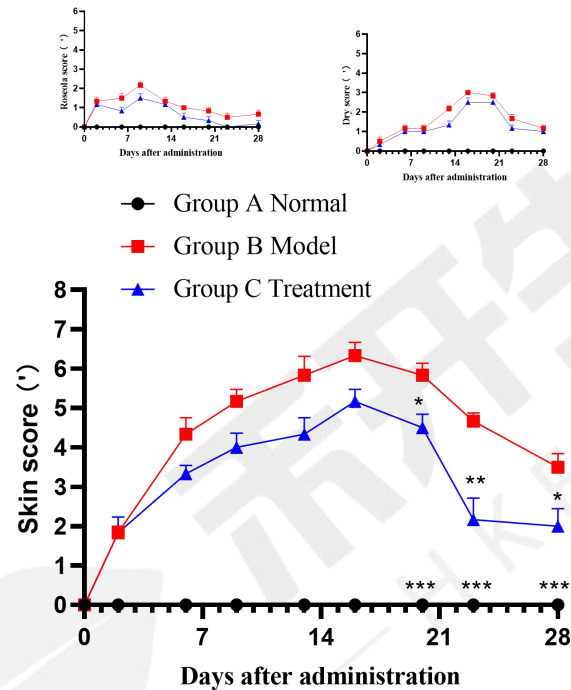


Fig 2 Skin score

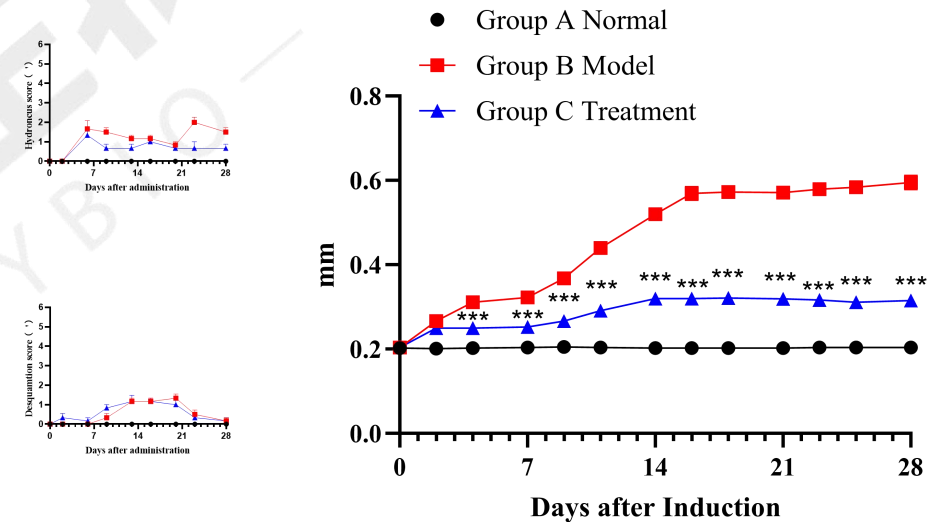


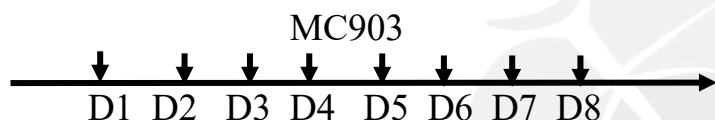
Fig 3 Ear Thickness

MC903 Induced AD Model

■ Mechanism

MC903 (calcipotriol) is an active vitamin D analog without affecting calcium metabolism and has been used for psoriasis patients. It induces irritant skin inflammation in some psoriasis patients as a side effect. In mice MC903 upregulates TSLP and induces atopic disease-like skin inflammation in a TSLP-dependent manner. Collectively, the MC903 model allows us to explore how type 2 skin inflammations are initiated by TSLP and to analyze the roles of various immune cells especially in the early period of inflammations.

■ MC903 Induced Mouse AD Model



Animal	BALB/c, C56BL/6
Evaluation	Clinical: Body weight, Ear Thickness
	Cytokine: IL-17
	Pathology: Ear HE staining

MC903 Induced C57BL/6 AD Model

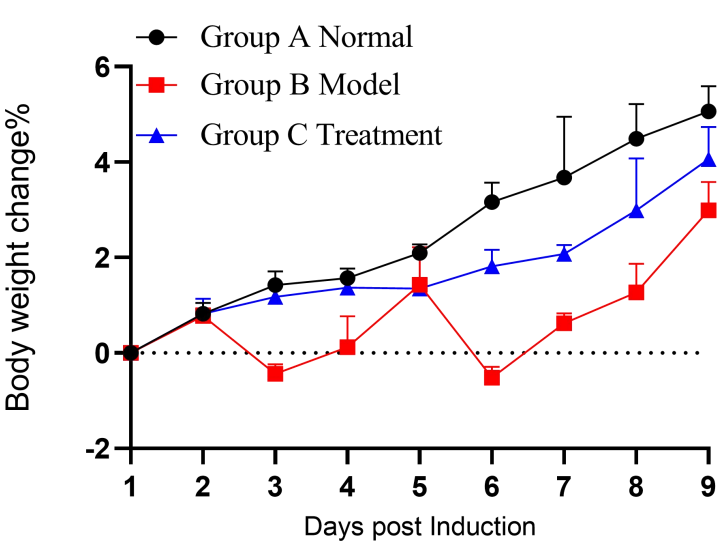


Fig 1 Body Weight

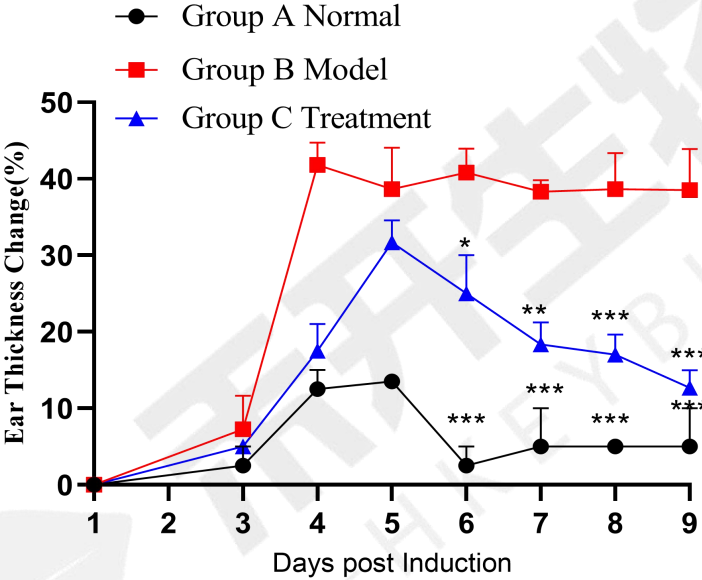


Fig 2 Ear Thickness Change

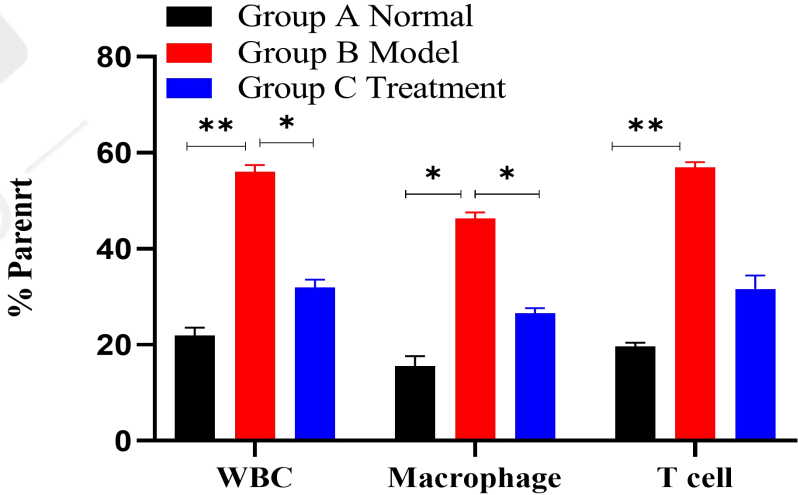


Fig 3 Cells isolated from skin

MC903 Induced C57BL/6 Chronic AD Model

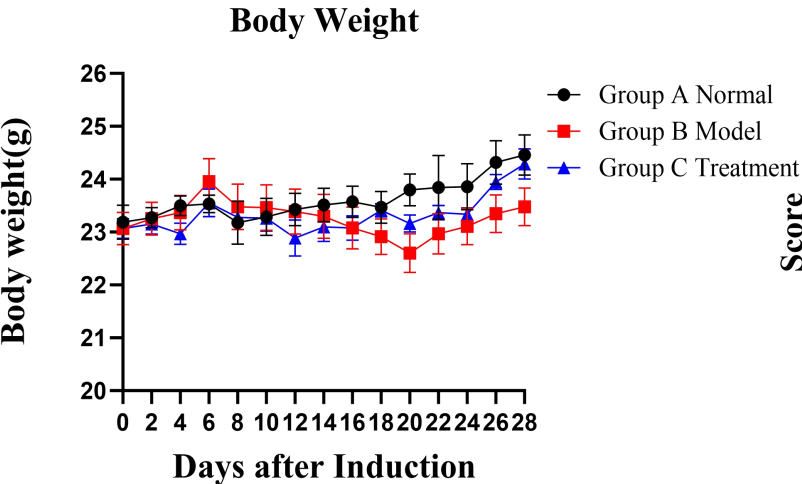


Fig 1 Body Weight

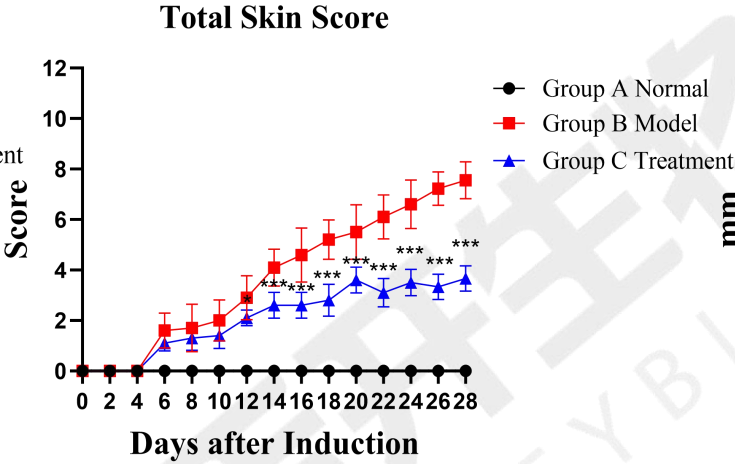


Fig 2 Total Skin Score

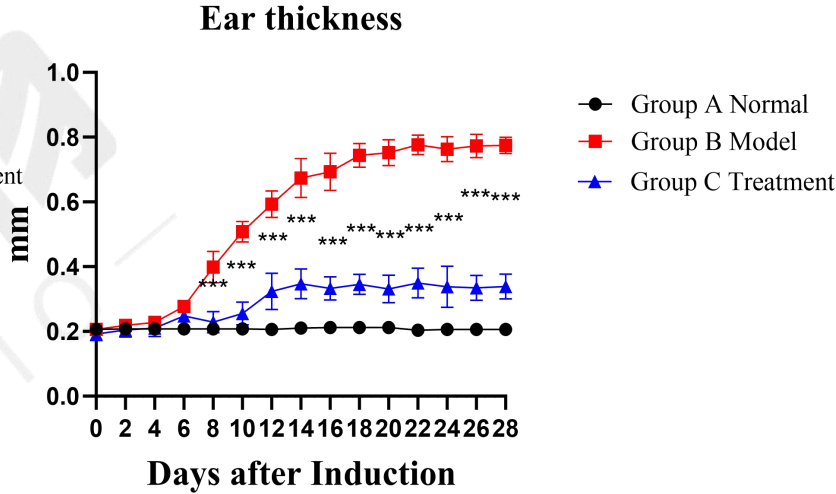


Fig 3 Ear thickness

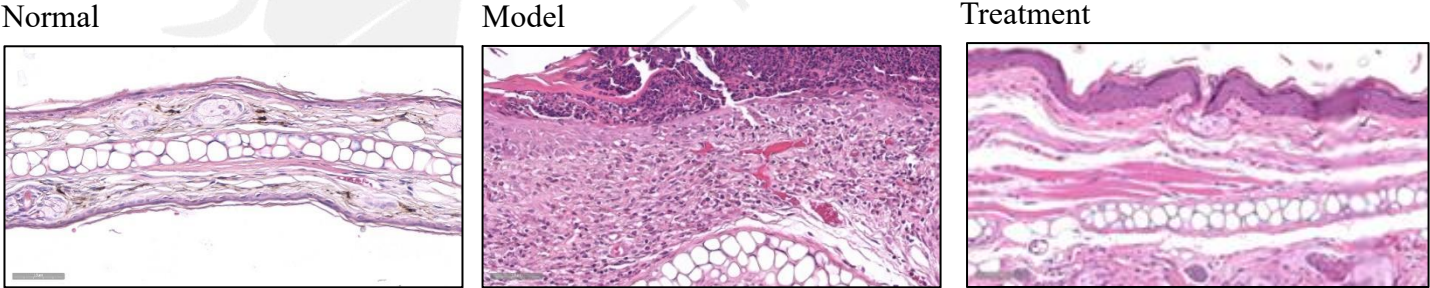


Fig 4 Pathology

MC903 Induced BALB/c AD Model

▼ Dosing

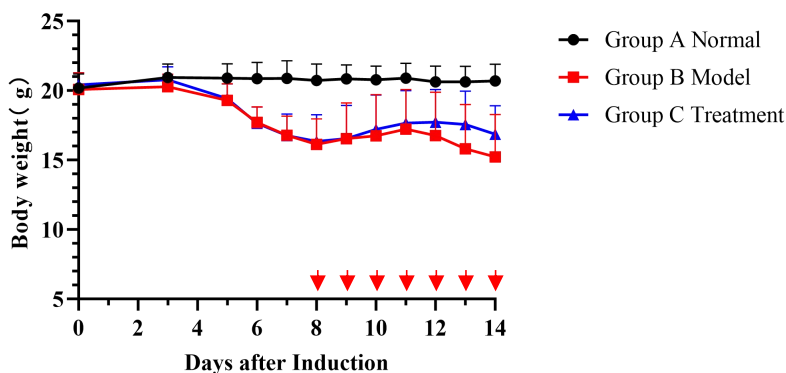


Fig 1 Body Weight

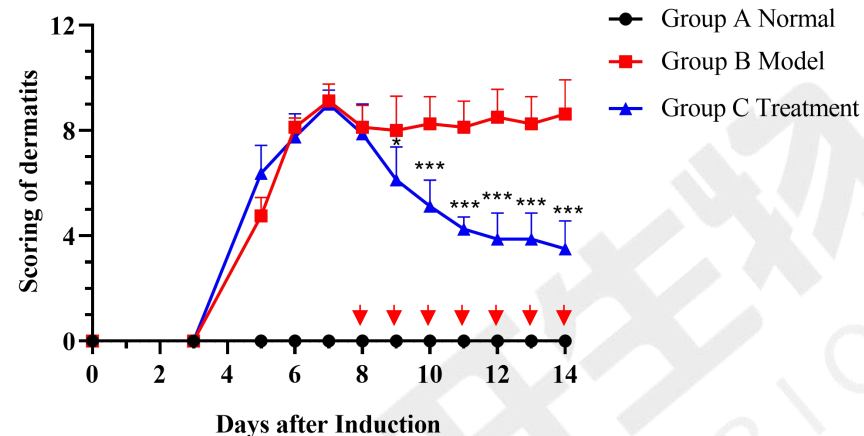


Fig 2 Skin clinical score

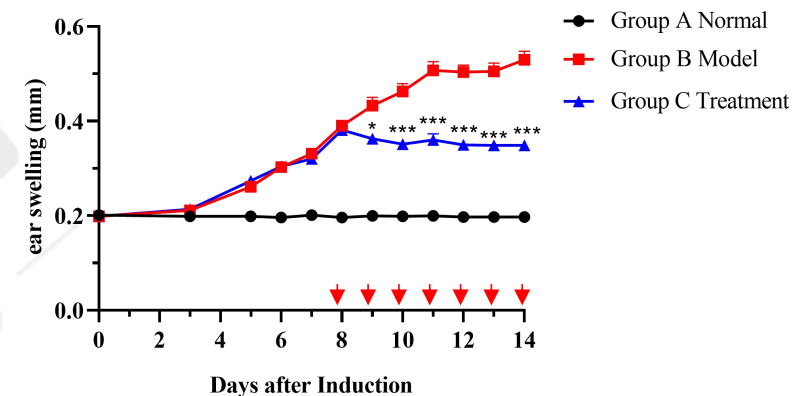


Fig 3 Ear thickness

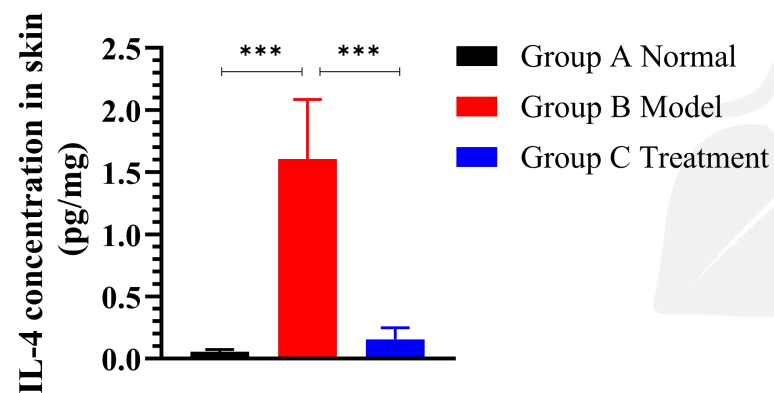


Fig 4 The level of IL-4 in skin

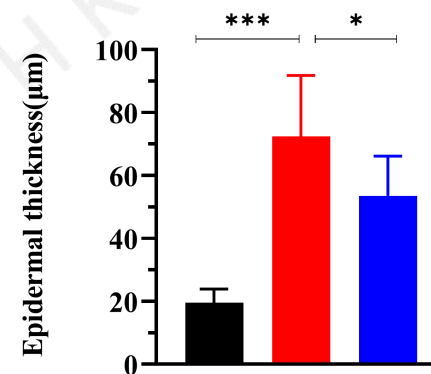
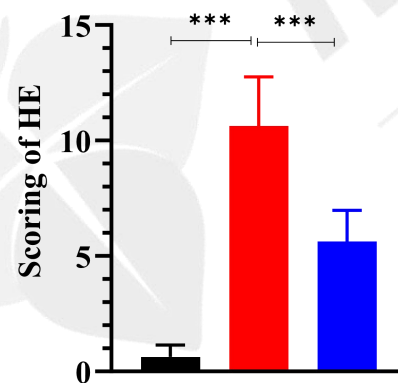
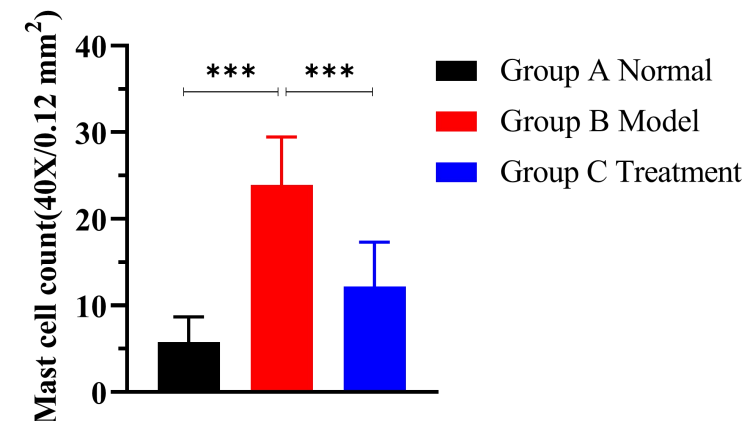


Fig 5 Skin pathology

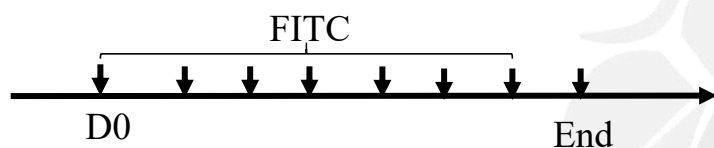


FITC Induced BALB/c AD Model

■ Mechanism

The mice showed normal migration and maturation of skin dendritic cells and induction of hapten-specific T cells in the sensitization phase of FITC-induced AD, and normal induction of local inflammation in the elicitation phase of FITC-induced AD. On the other hand, those mice showed reduced scratching frequency and duration during FITC-induced AD.

■ FITC Induced Mouse AD Model



Animal	BALB/c
	Clinical: Ear Thickness, Ear weight
Evaluation	Cytokine:
	Pathology: Ear HE staining

FITC Induced BALB/c AD Model

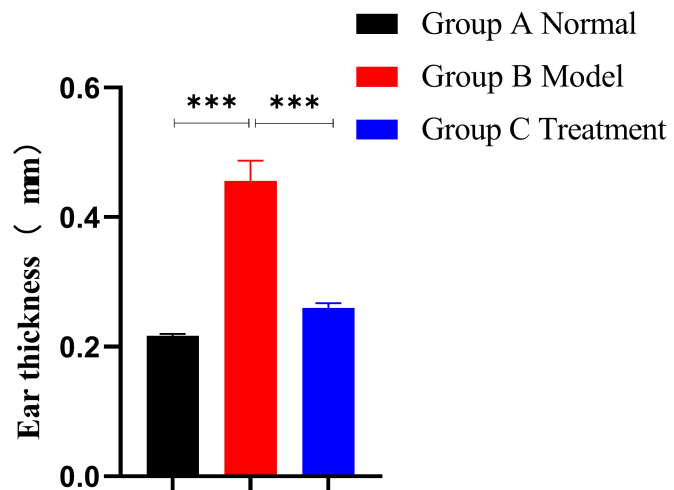


Fig 1 Ear Thickness

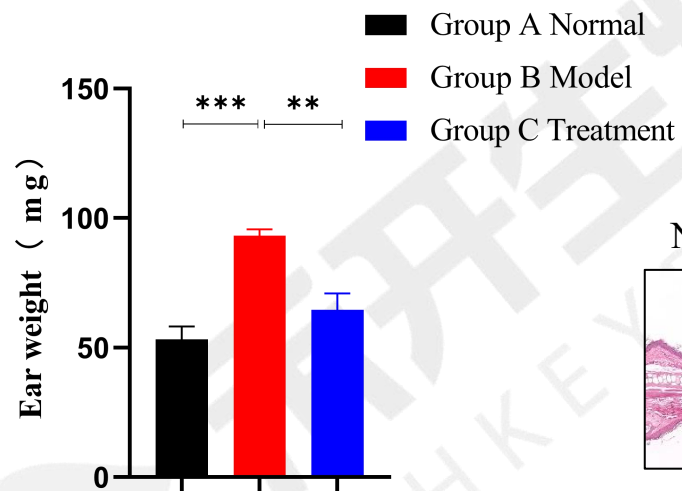


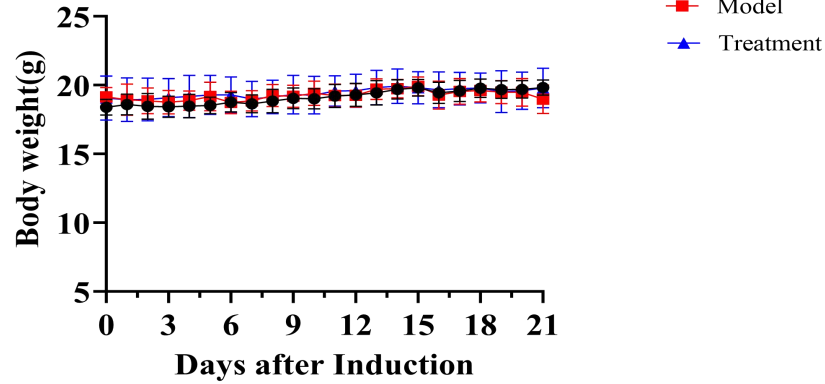
Fig 2 Ear weight



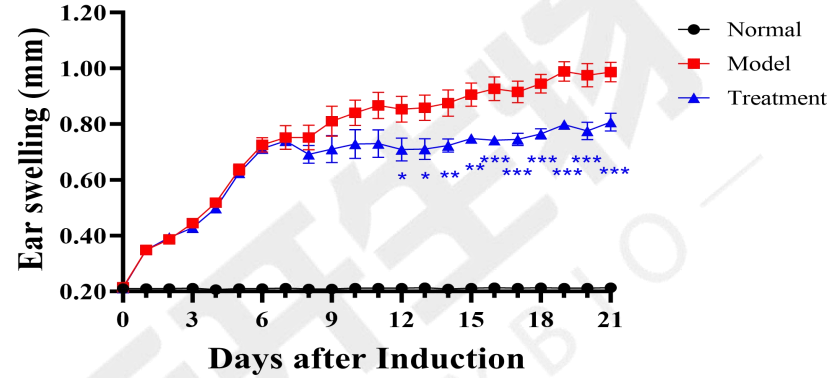
Fig 3 Pathology

MC903&OXA induced AD model in C57BL/6

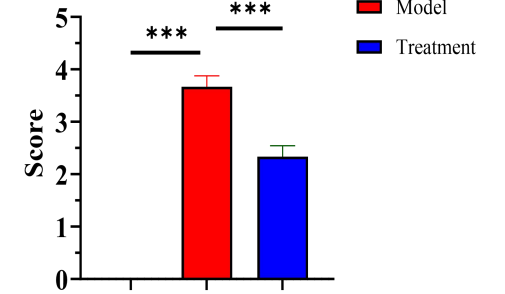
Body Weight



Ear swelling



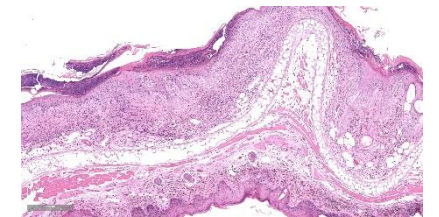
HE



Normal



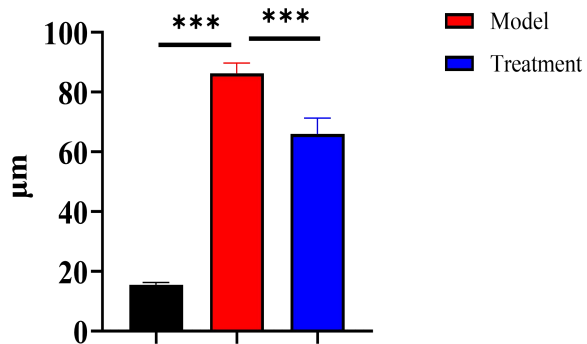
Model



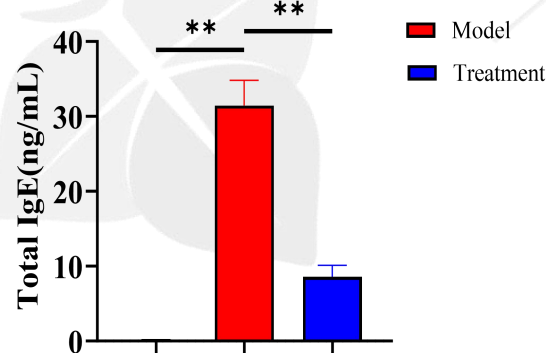
Treatment



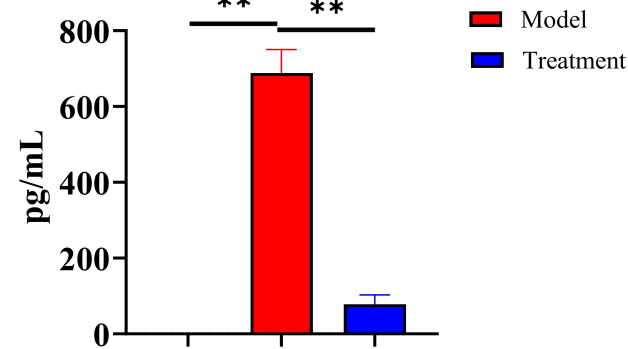
Epidermal thickness



IgE in serum



IL-4 in skin

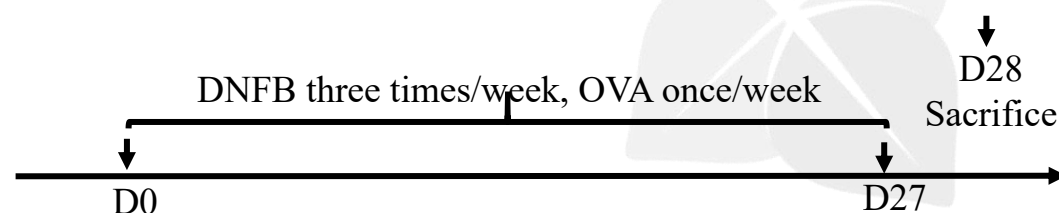


DNFB+OVA Induced AD Model

■ Mechanism

Exposure to dinitrofluorobenzene (DNFB) was found to induce contact dermatitis in mice. When the shaved back skin of mice is exposed to DNFB, cytotoxic T lymphocytes are recruited to the skin and result in keratinocyte apoptosis and further skin barrier dysfunction. Ovalbumin (OVA) is a chicken protein allergen mainly found in egg white that is commonly used to sensitize immune reactions. Prolonged exposure to OVA induces the development of an AD-like dermatitis characterized by OVA-specific IgE and total serum IgE, as well as increased expression of Th2 cytokines and IFN- γ . However, the induction period of AD-like dermatitis using OVA is time-consuming, and the skin lesions are usually mild. Therefore, we designed this study to evaluate the potential of the combined application of DNFB and OVA to build a new AD mouse model that recapitulates the dynamic changes in helper T-cell responses in the progression of acute-to-chronic atopic dermatitis.

■ DNFB+OVA Induced Murine AD Mouse Model



Animal	BALB/c
Evaluation	Clinical: Body weight, score, scratching
	Cytokine: Total IgE, OVA sIgE, IL-36, IL-4, IL-17
	Pathology: HE & Toluidine Blue

DNFB+OVA Induced BALB/c AD Model

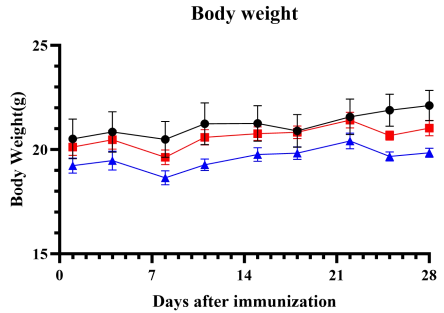


Fig 1 Body Weight

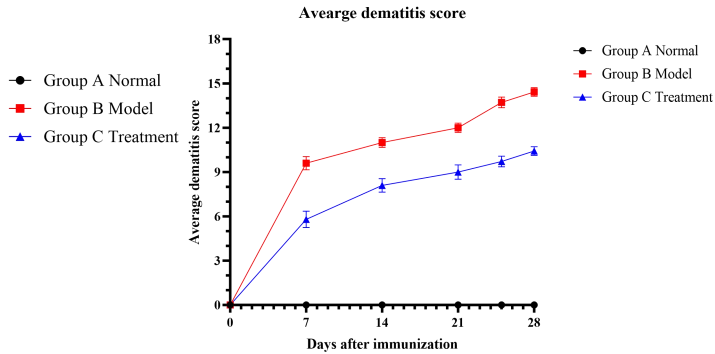


Fig 2 Skin score

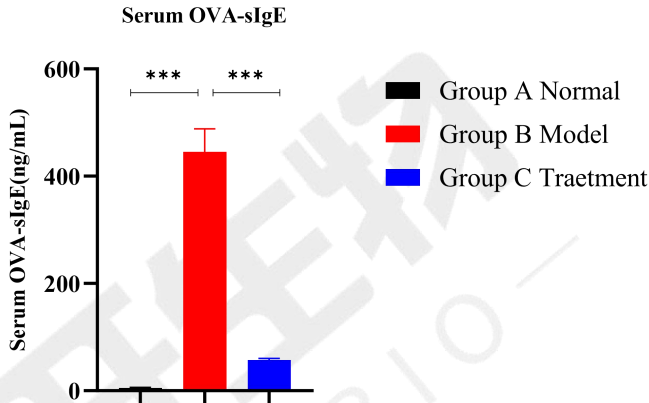


Fig 3 Serum OVA-sIgE

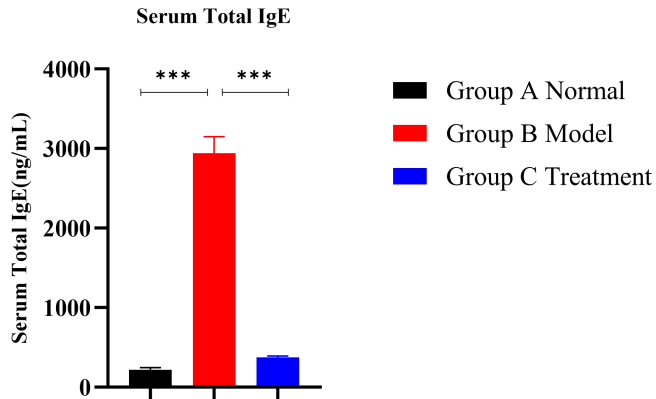


Fig 4 Serum IgE

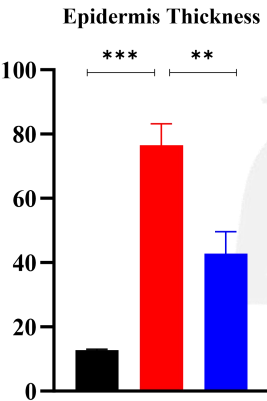
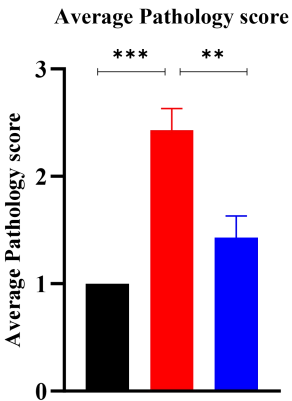


Fig 5 Pathology

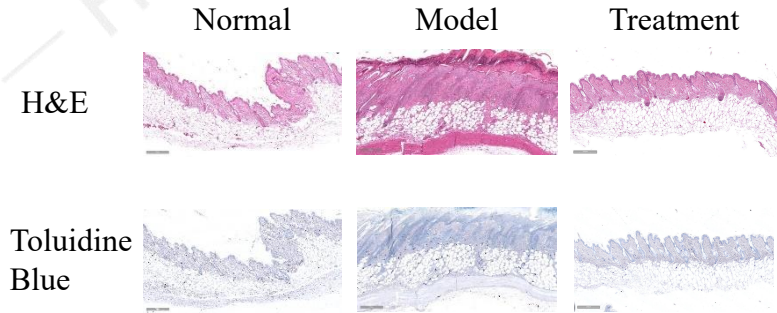
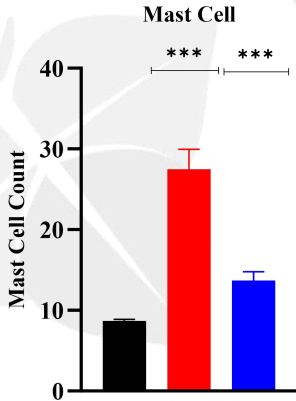


Fig 6 Typical pathological images

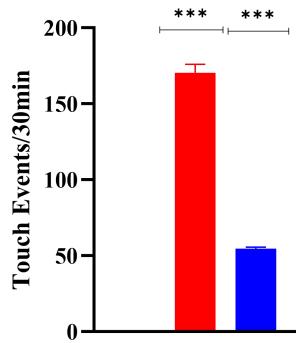


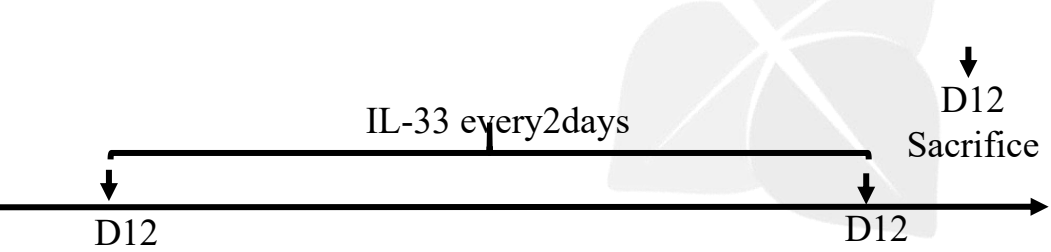
Fig 7 Touch Events

IL-33 Induced AD Model

■ Mechanism

IL-33 is a member of the IL-1 family of cytokines and is a ligand for IL-1R-like-1 or ST2. In contrast with other members of that family, IL-1 and IL-18, which are activated in inflammasomes by caspase 1, IL-33 is produced in an active full-length form and is stored in the nucleus. In response to external insults or various types of cellular damage, IL-33 is released from cells and binds to ST2 on Th2 cells and on various types of innate immune cells including basophils, mast cells, eosinophils, and currently termed group 2 innate lymphoid cells (ILC2s), which induces and activates those cells. The association of AD with a polymorphism of the ST2 gene suggests that immune regulation via the IL-33-ST2 system may be pivotal as a genetic background of AD . Recently, the upregulation of IL-33 in the epidermis and the infiltration of ST2-positive cells in the dermis of the lesional skin of patients with AD have been reported . In contrast, an increase in IL-33 has also been shown in the epidermis of patients with psoriasis, which is mediated mainly by Th1 and Th17 cells.

■ IL-33 Induced Murine AD Mouse Model



Animal	BALB/c
Evaluation	Clinical: Body weight, score, scratching
	Cytokine:
	Pathology: HE

IL-33 Induced BALB/c AD Model

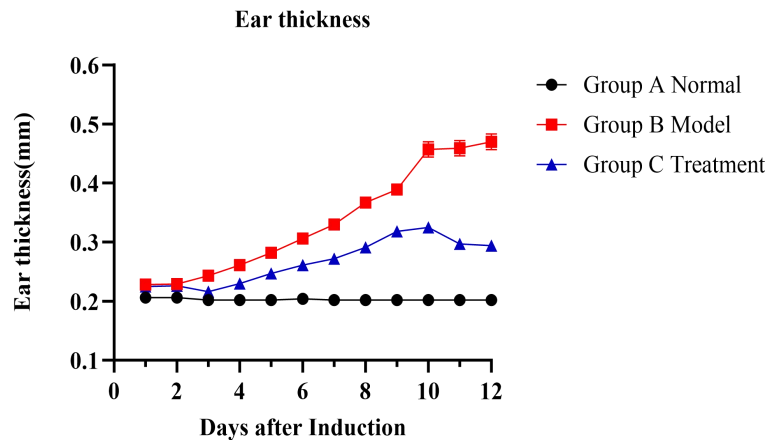


Fig 1 Ear thickness

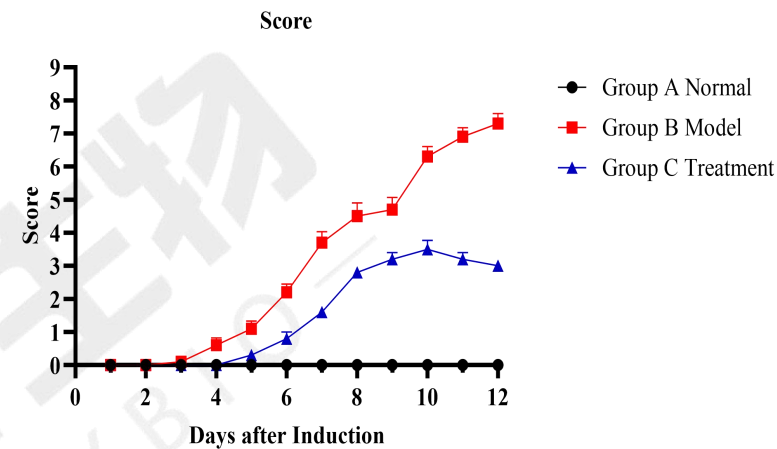


Fig 2 Skin score

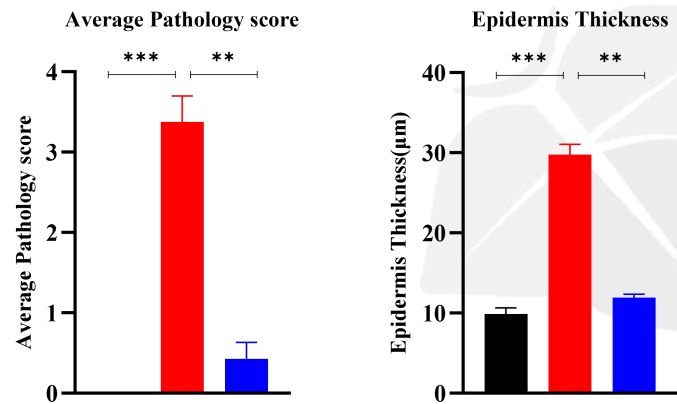


Fig 5 Pathology



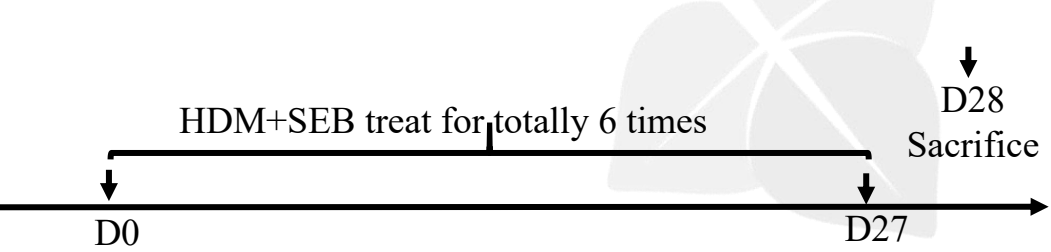
Fig 6 Typical pathological images

HDM+SEB Induced AD Model

■ Mechanism

House dust mite (HDM) allergens are important for the development of AD which are known to contribute to the immunopathogenesis through the induction of IgE binding. The mite allergens have been previously shown to activate toll like receptors, and can also directly activate the inflammasome in epidermal keratinocytes. While early models of immune activation in patients with AD focused on the differential roles for T helper 2 (Th2) and T helper 1 (Th1) in disease initiation and maintenance, Th17 and Th22 also play an important role in the HDM allergens induced AD.

■ HDM+SEB Induced Murine AD Mouse Model



Animal	C57BL/6
Evaluation	Clinical: Body weight, score, scratching
	Cytokine: Total IgE,
	Pathology: HE

HDM+SEB Induced AD Model in C57BL/6 Mice

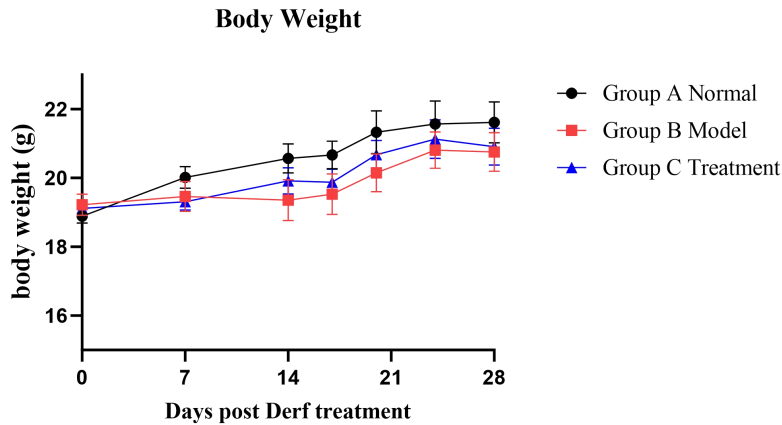


Figure 1 Bodyweight change

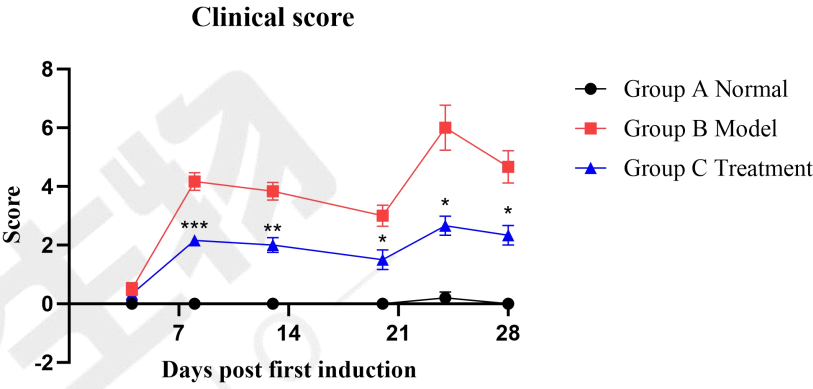


Figure 2 Clinical score

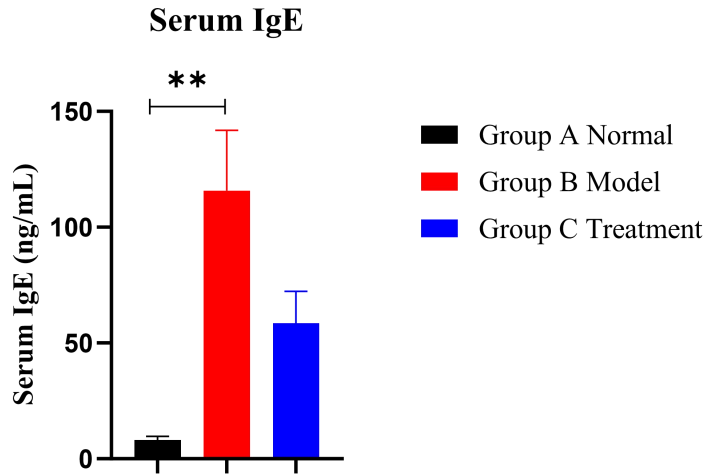


Figure 3 Serum IgE

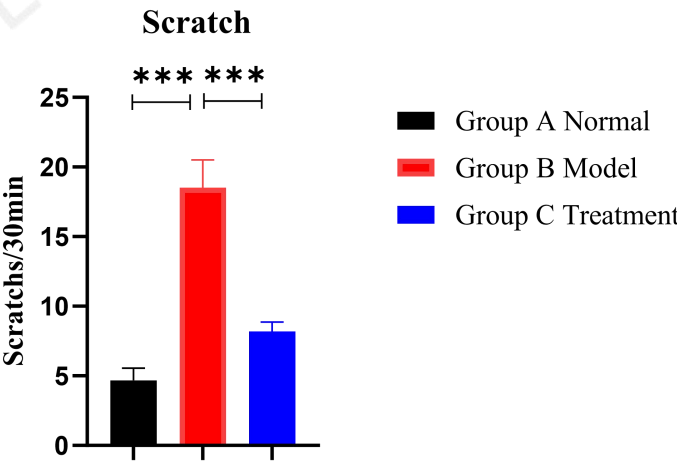


Figure 4 Scratches

IL-36 Induced AD Model in C57BL/6 Mice

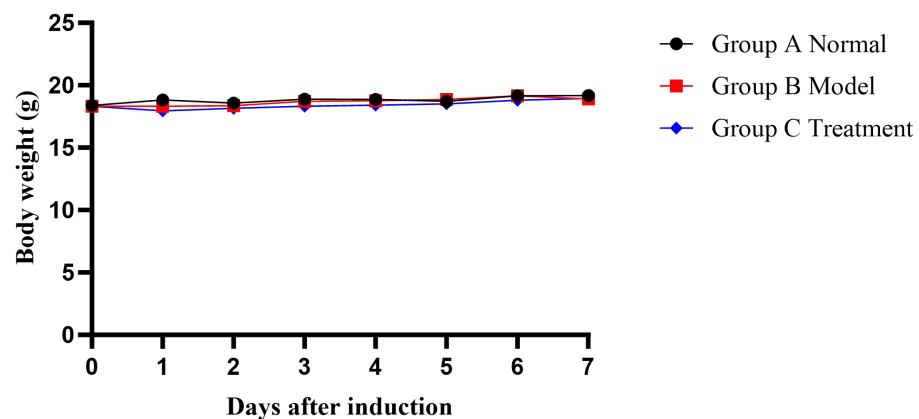


Figure 1 Body weight change

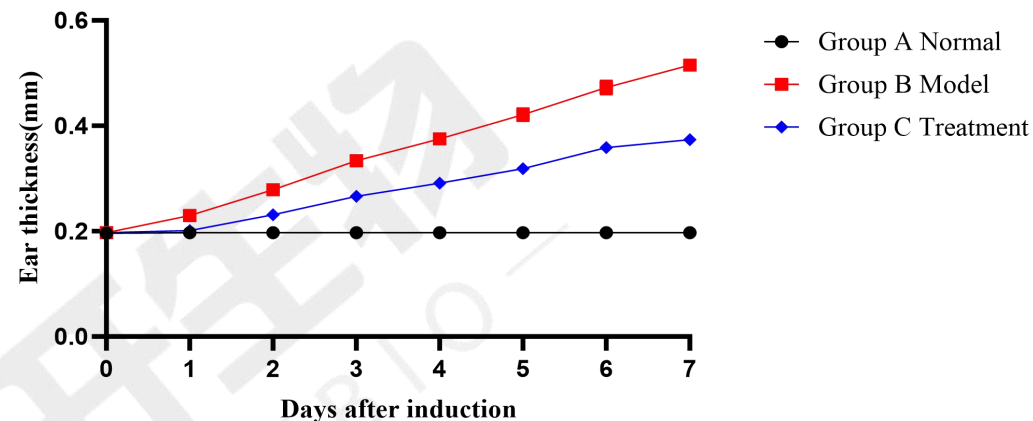


Figure 2 Ear thickness

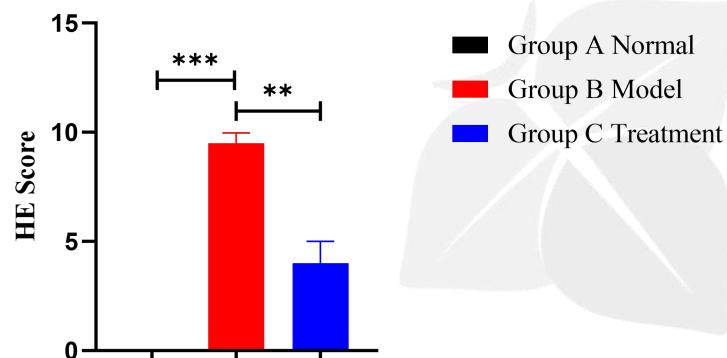


Figure 3 HE Score

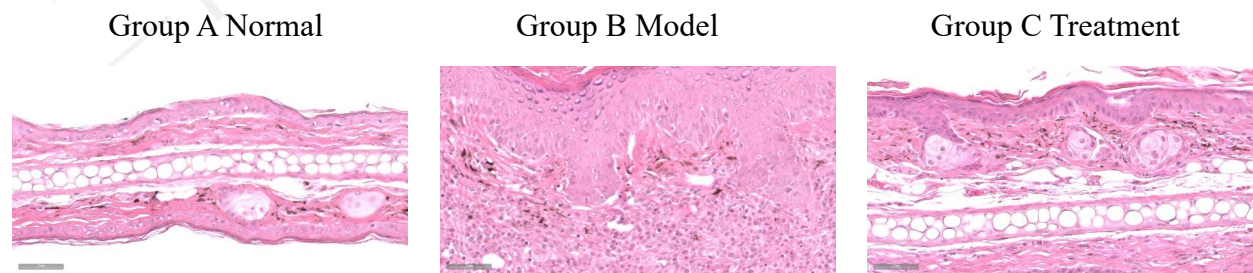
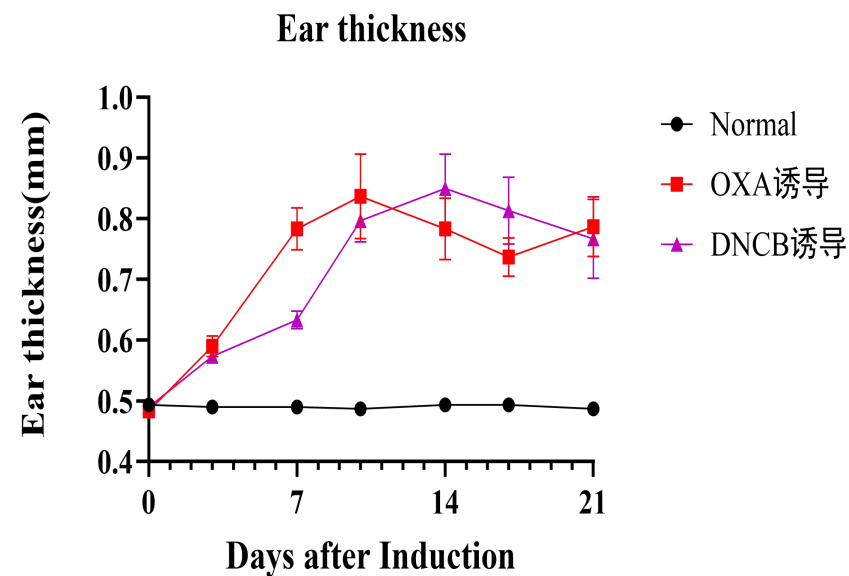
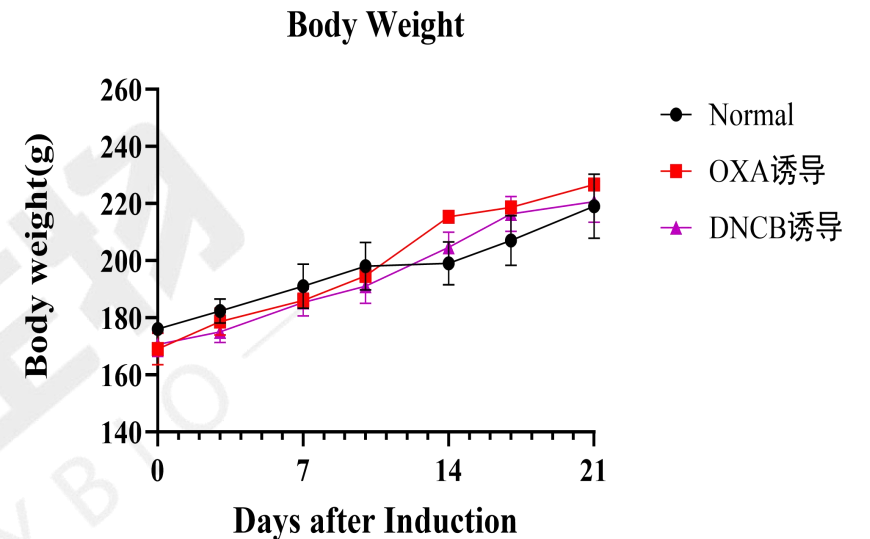
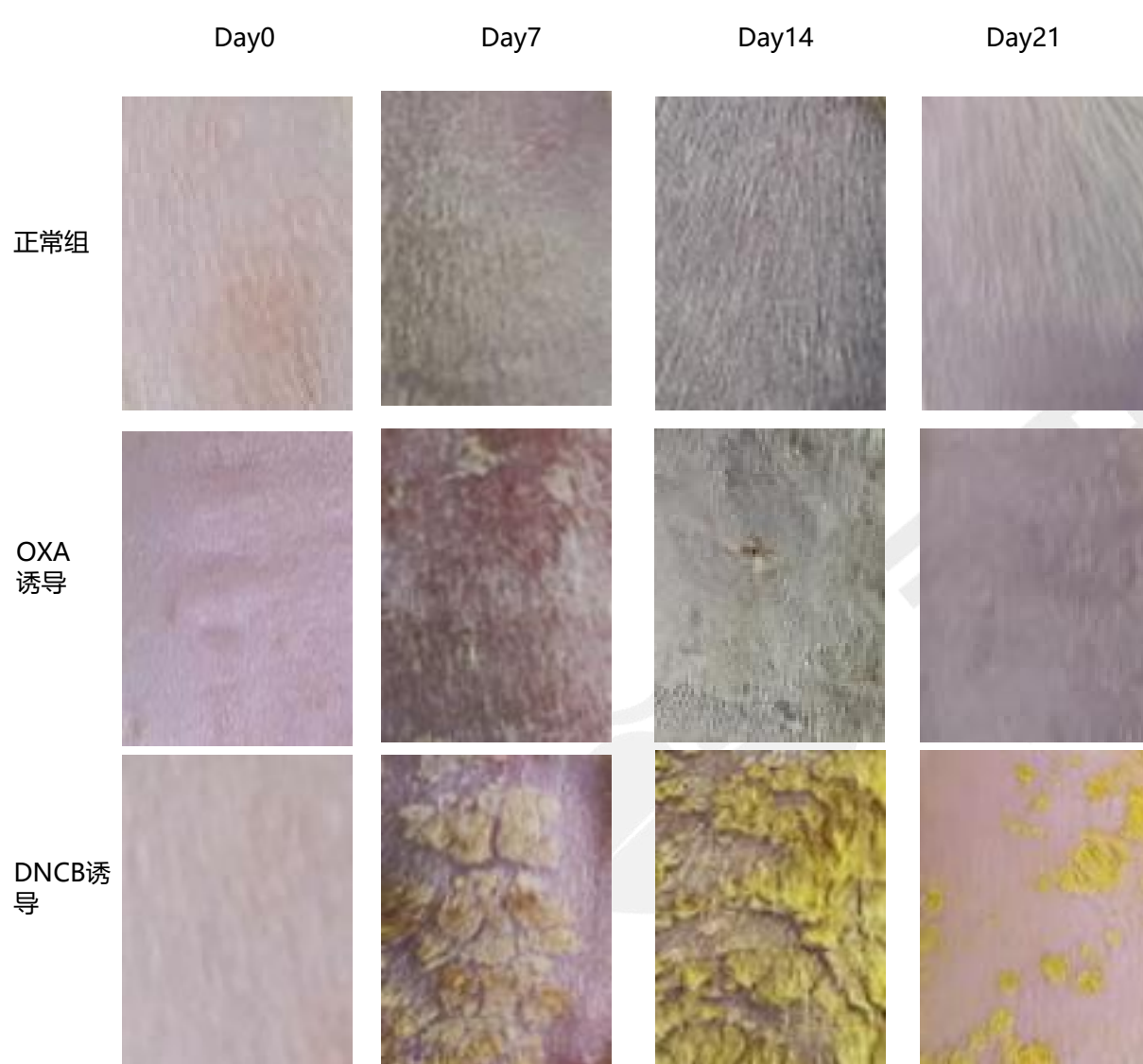


Fig 3 Pathology

OXA/DNCB Induced AD Model in SD rat





禾开生物

— HKEYBIO —

Our Sites

Non-human Private Center: Guangxi
Analysis Center: Suzhou
Rodent Center: Suzhou



WeChat

Hkeybio Tech.

Website: www.hkeybio.com

Email: info@hkeybio.com