Mechanistic Insights into *Lactobacillus paracasei* KW3110 and Future Directions

KIRIN R&D DAY 2025
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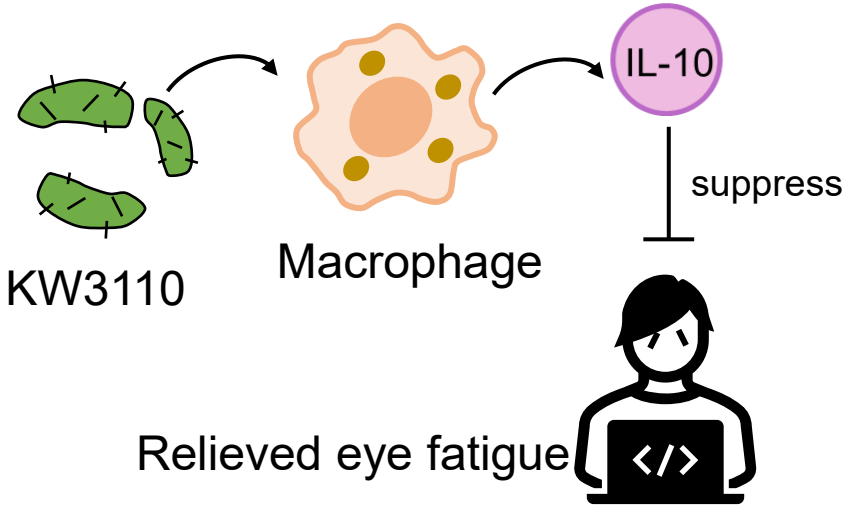
KW3110～A promising ingredient with dual functions～

***Lacticaseibacillus paracasei* KW3110**
A type of lactic acid bacteria discovered by Kirin co., Ltd. and Koiwai Dairy Products Co.,Ltd.

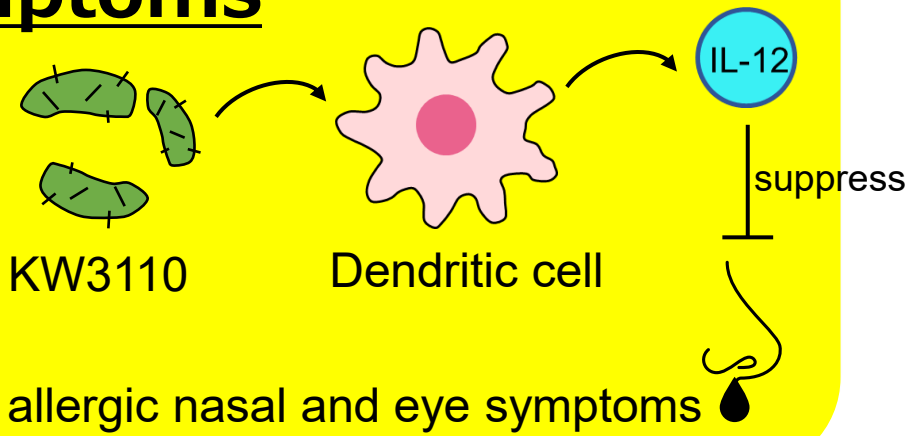
・Relieving eye fatigue

Dietary supplement with functional claim for eye care was launched in 2019



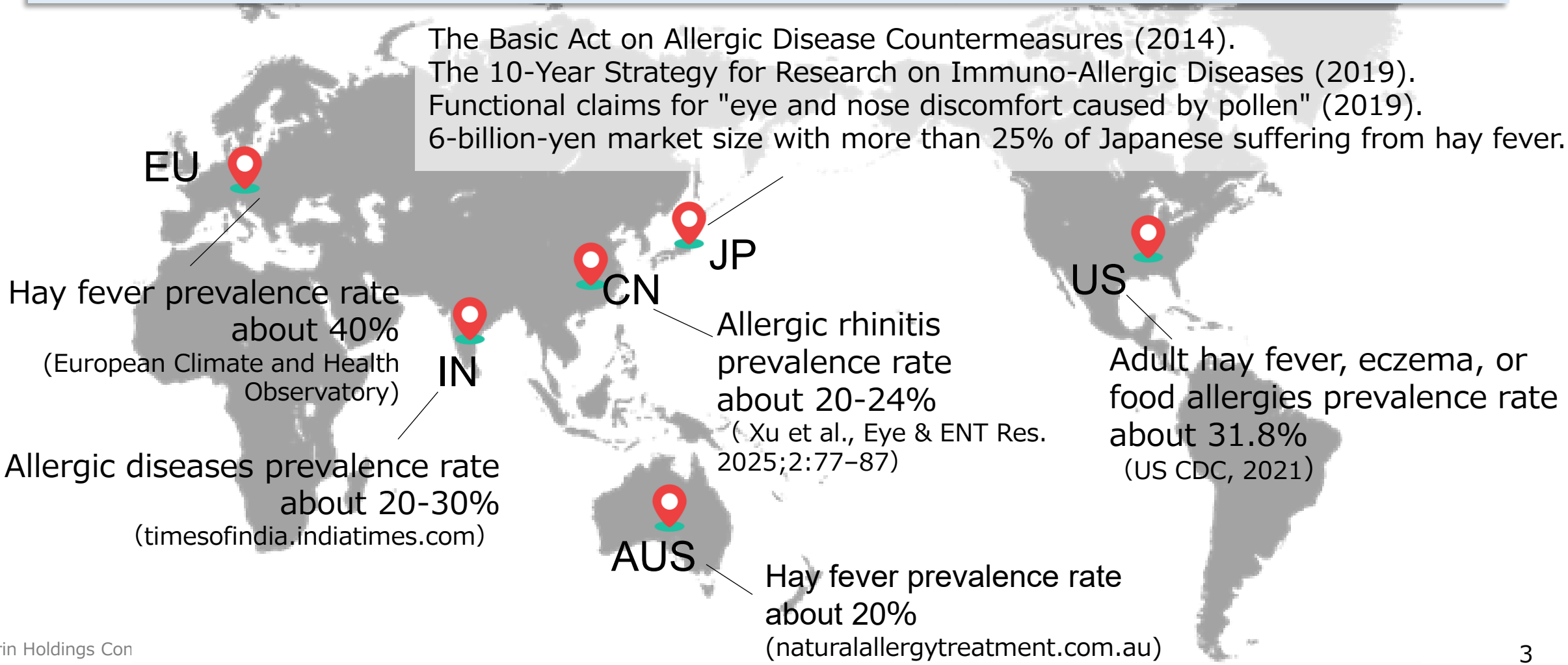
・Mitigating allergic symptoms

Reviewing for potential commercialization



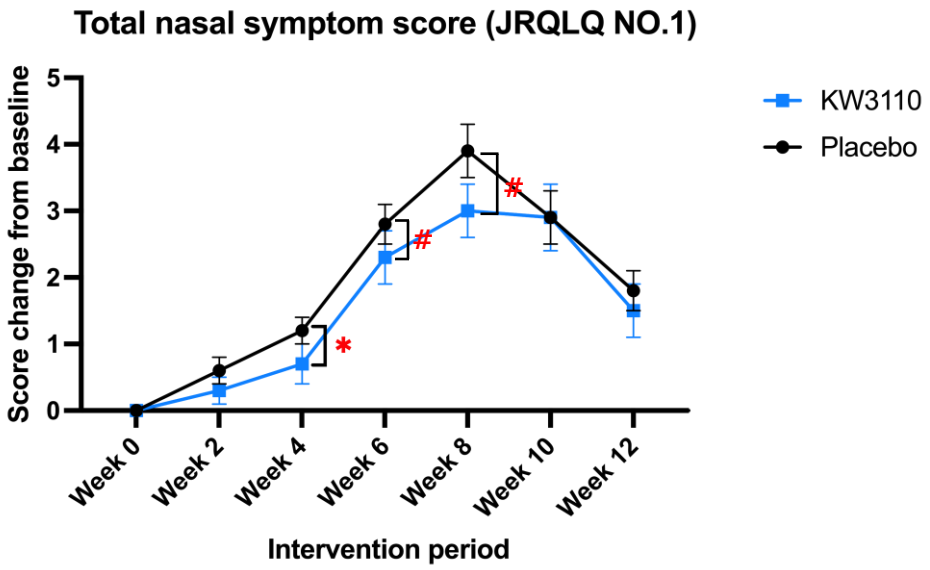
Expanding allergic market

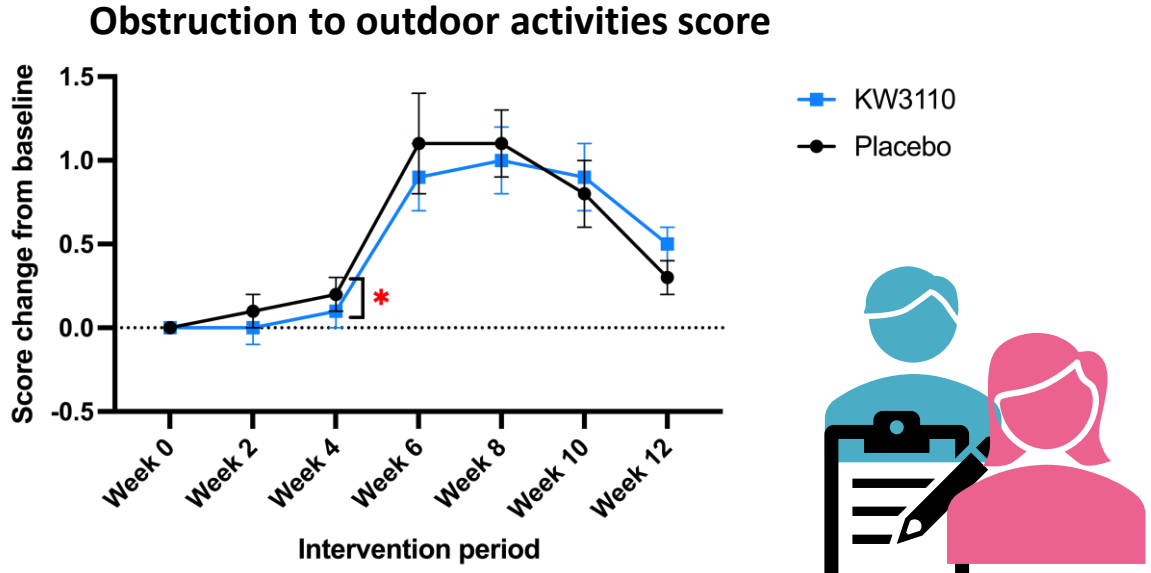
Allergic diseases, including hay fever, exhibit high prevalence globally with notable incidence among young generations in recent years. Epidemiological data forecast further increase in prevalence due to climate change and modifications in lifestyle patterns.



Effectiveness for the nasal and eye symptoms of seasonal allergy (Clinical study)

Effect of heat-killed *Lacticaseibacillus paracasei* KW3110 on mild to moderate seasonal allergic rhinitis symptoms in Japanese adults: a randomized, double-blind, placebo-controlled parallel-group study
Sugihara et al., Front Nutr. 2025 Jun 25; 12:1568329





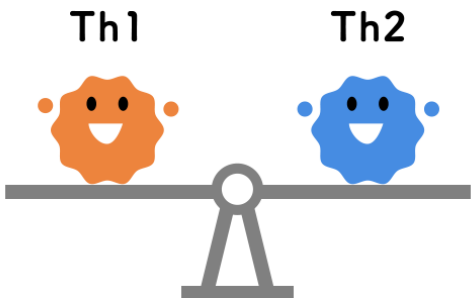
N = 54 (KW3110), 53 (Placebo group), Mean ± SE, #: p＜0.10 *: p＜0.05

RCT study conducted in 2024 demonstrated significant improvements in nasal symptoms and outdoor activities from the primary outcome.

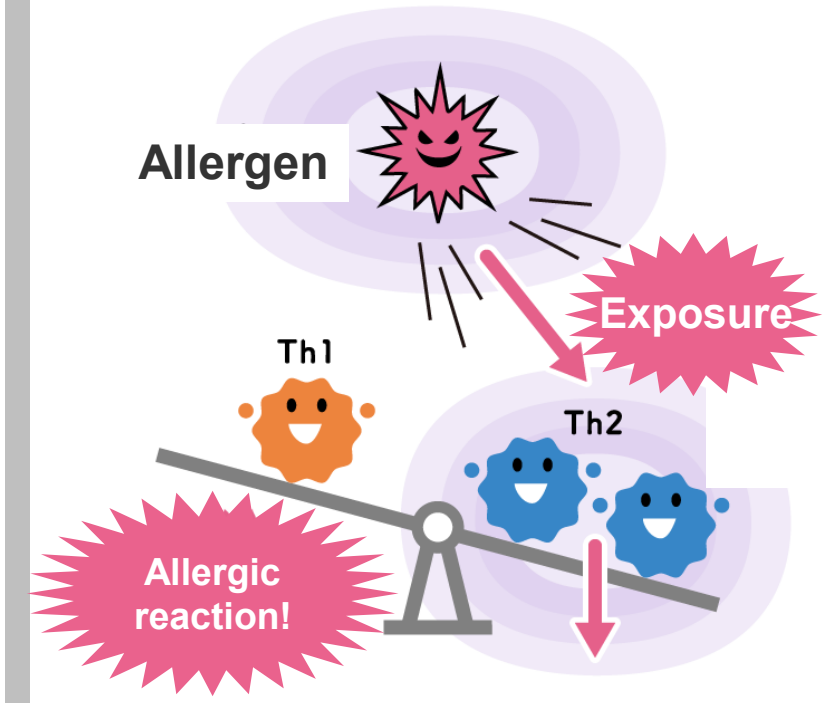
Mechanisms of allergy, actions of KW3110, and unresolved questions

<healthy individual>
Proper immune balance

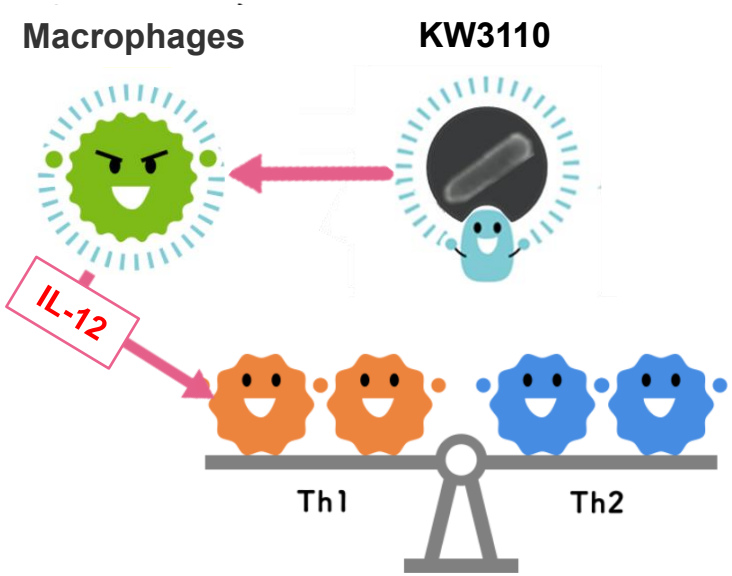
Immune cells involved in allergic reactions



<The allergic>
immune imbalance



<Actions of KW3110>
Improve the balance through macrophages, IL-12

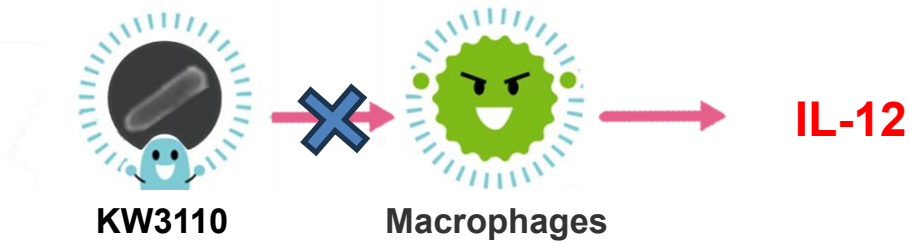


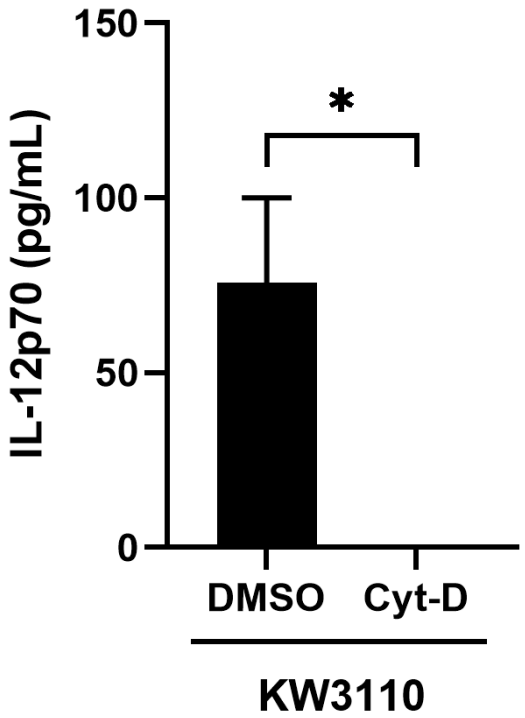
Unknown ponit :
Molecular mechanism of action on macrophages

Understanding of principles through elucidation of molecular mechanisms

Promotion of IL-12 production by KW3110 is clearly important; clarify how KW3110 induces IL-12 production.

Test① : Involvement of Macrophage



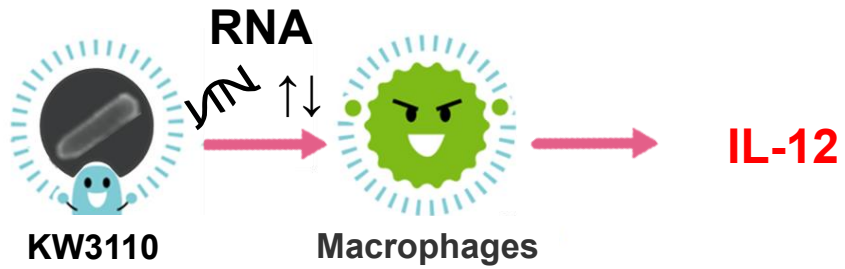


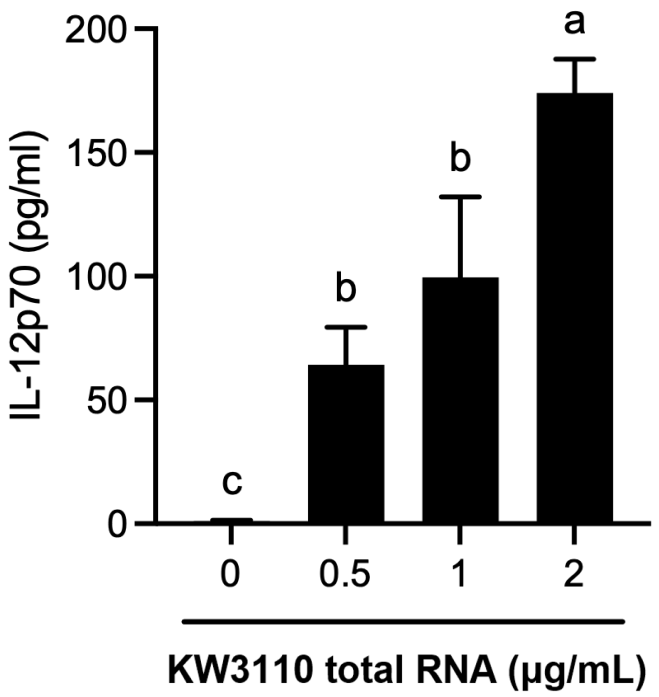
【Result】
Inhibition of phagocytosis abolishes KW3110-induced IL-12 production on macrophages

Phagocytosis by macrophages is important

※ Cyt-D : Phagocytosis inhibitor

Test② : Identification of the active component in KW3110



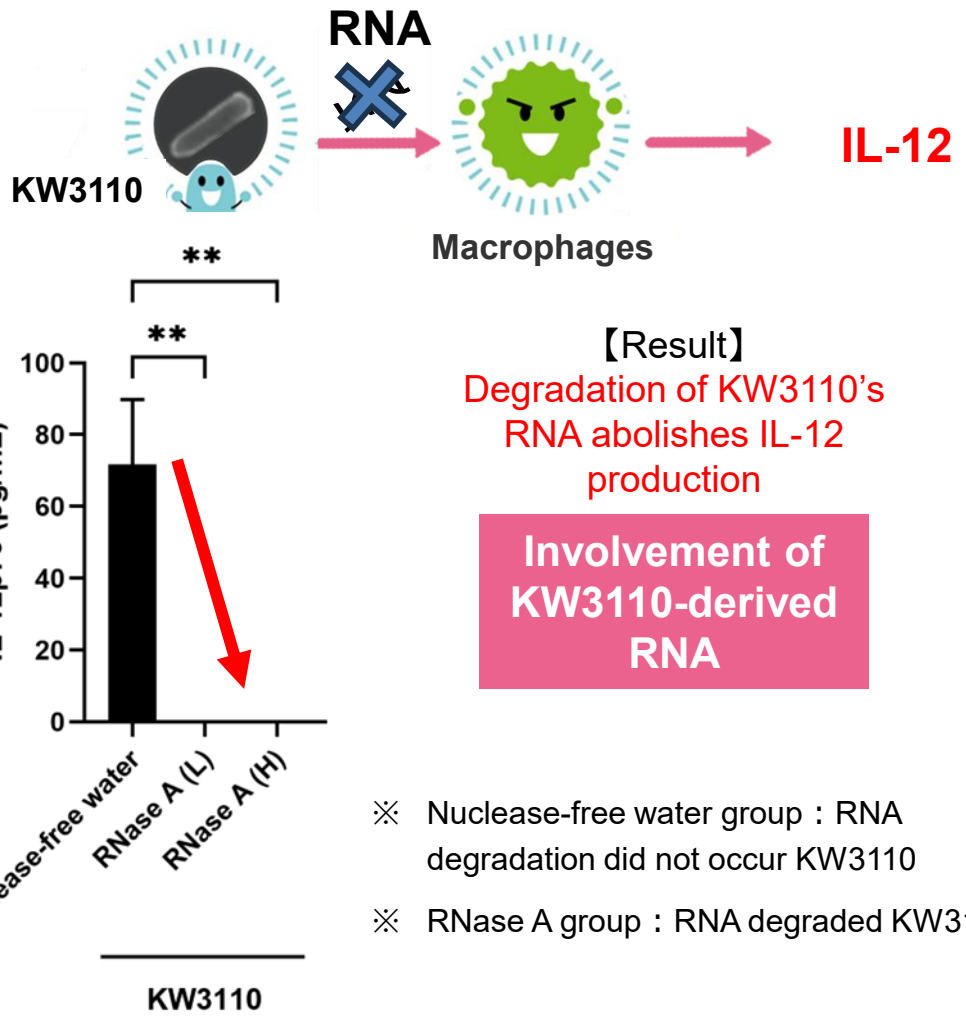


【Result】
Dose-dependent IL-12 production by KW3110-derived RNA

Possible involvement of RNA

Understanding of principles through elucidation of molecular mechanisms

Test③ : Functional role of RNA



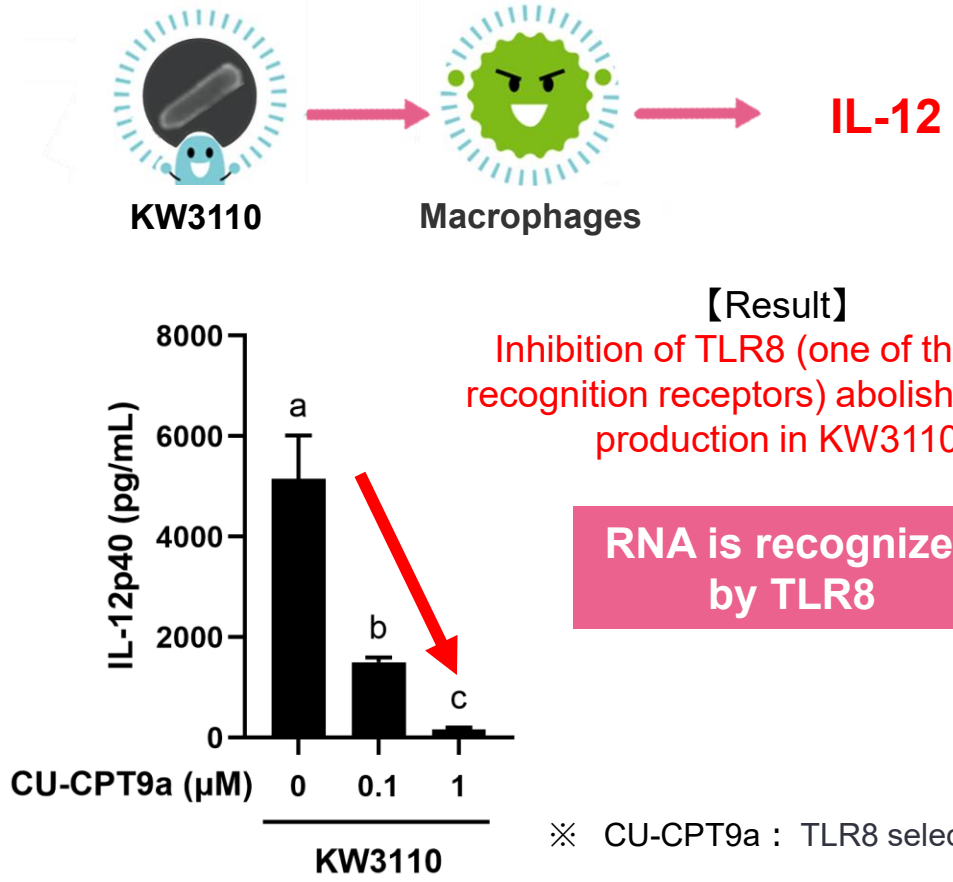
【Result】
Degradation of KW3110's RNA abolishes IL-12 production

Involvement of KW3110-derived RNA

※ Nuclease-free water group：RNA degradation did not occur KW3110

※ RNase A group：RNA degraded KW3110

Test④ : Mechanism of RNA recognition in macrophages



【Result】
Inhibition of TLR8 (one of the RNA recognition receptors) abolishes IL-12 production in KW3110

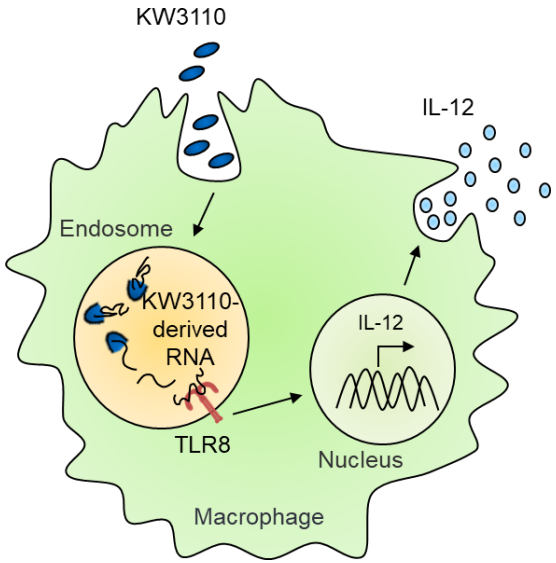
RNA is recognized by TLR8

※ CU-CPT9a： TLR8 selective inhibitor

What we clarified

Possible molecular mechanisms

1. KW3110 is phagocytosed by macrophages.
2. Intracellularly digested and exposed RNA of KW3110 is recognized by TLR8 (one of the RNA recognition receptors).
3. IL-12 is produced.



Lactic acid bacteria	Activity marker	Active component	Recognition receptor (Ligand)
LC-Plasma	IFN-α	DNA	TLR9（DNA）
KW3110	**IL-12**	**RNA**	**TLR8（RNA）**

Understanding principles is the source of competitive advantage

Utilization of elucidated mechanisms for business contribution

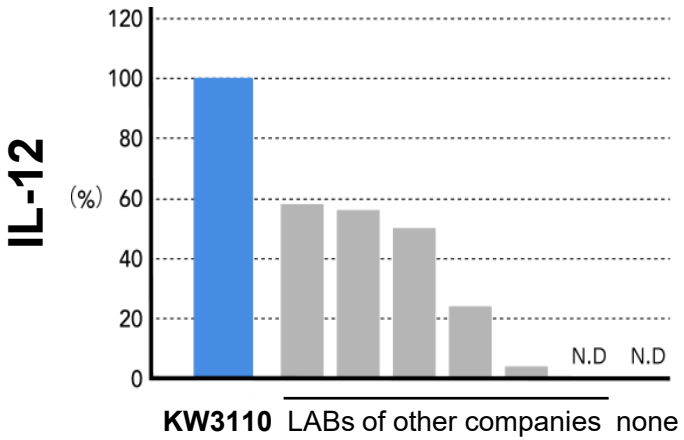
Novel findings are used for technological development to comply with overseas regulations and for academic PR to differentiate the company from domestic and foreign competitors.

Existing findings/evidence

- Allergy alleviation by induction of IL-12 production
- Anti-inflammatory and reduces eye fatigue by promoting IL-10 production

New findings on the mechanism

- Molecular mechanism of action of induction of IL-12 production



- **Accelerate technology development for regulatory compliance**
- **Use for academic PR (differentiation from domestic and international competitors)**

Possibly explain・・・

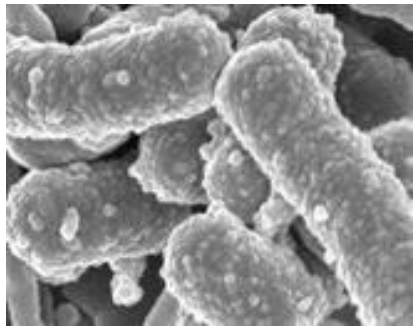
- **why heat-killed KW3110 still have an effect.**
- **why KW3110 has higher IL-12 activity than other LAB.**

※LAB: lactic acid bacteria

International Archives of Allergy and Immunology. 2004;135:205–215 partially modified

Expanding the value of KW3110 through basic research and fundamental principles

Human cell *in vitro* models
Advanced genomic technology
Integrated analysis utilizing DX



Enhancing the value of KW3110 by discovering the active entity of immune modulation

Developing high-quality products and ensuring the conveyed value

Common underlying mechanism

- **Atopic dermatitis**
- **Hay fever**
- **Asthma**
- **…**

- Delivering holistic solutions to customers
- Targeting different life stages
- Reaching beyond various allergic needs