

**DISCOVERY AND CLINICAL
EFFECTIVENESS OF A COMPOSITION
THAT PROMOTES HAIR GROWTH
(PATENT PENDING)**

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1. Development Background

- Development Background
- Rationale for Selecting Ingredients:
“Lipopolysaccharide (LPS) ” and “pine bark polyphenol”

Development Background

- **Modern Pet disease**
 - Heart disease
 - Cancer
 - atopic dermatitis and alopecia etc
- **The reason of appearance**
 - Stress
 - High calorie of pet food and lack of physical exercises
 - Pet clothes
 - Aging etc

Rationale for Selecting Ingredients

- **Limit of pharmaceuticals**
- **Side effects of medicine**
- **Start caring before occurring a disease**



To focus on the action “Immune function”

Hygiene hypothesis



Many brothers and sisters
Country life with animals



Only one child
Urban life

Most significantly different factor is the exposure amount of endotoxin (LPS) in life.

Hygiene hypothesis: a study of canine atopic dermatitis



Contents lists available at ScienceDirect

The Veterinary Journal

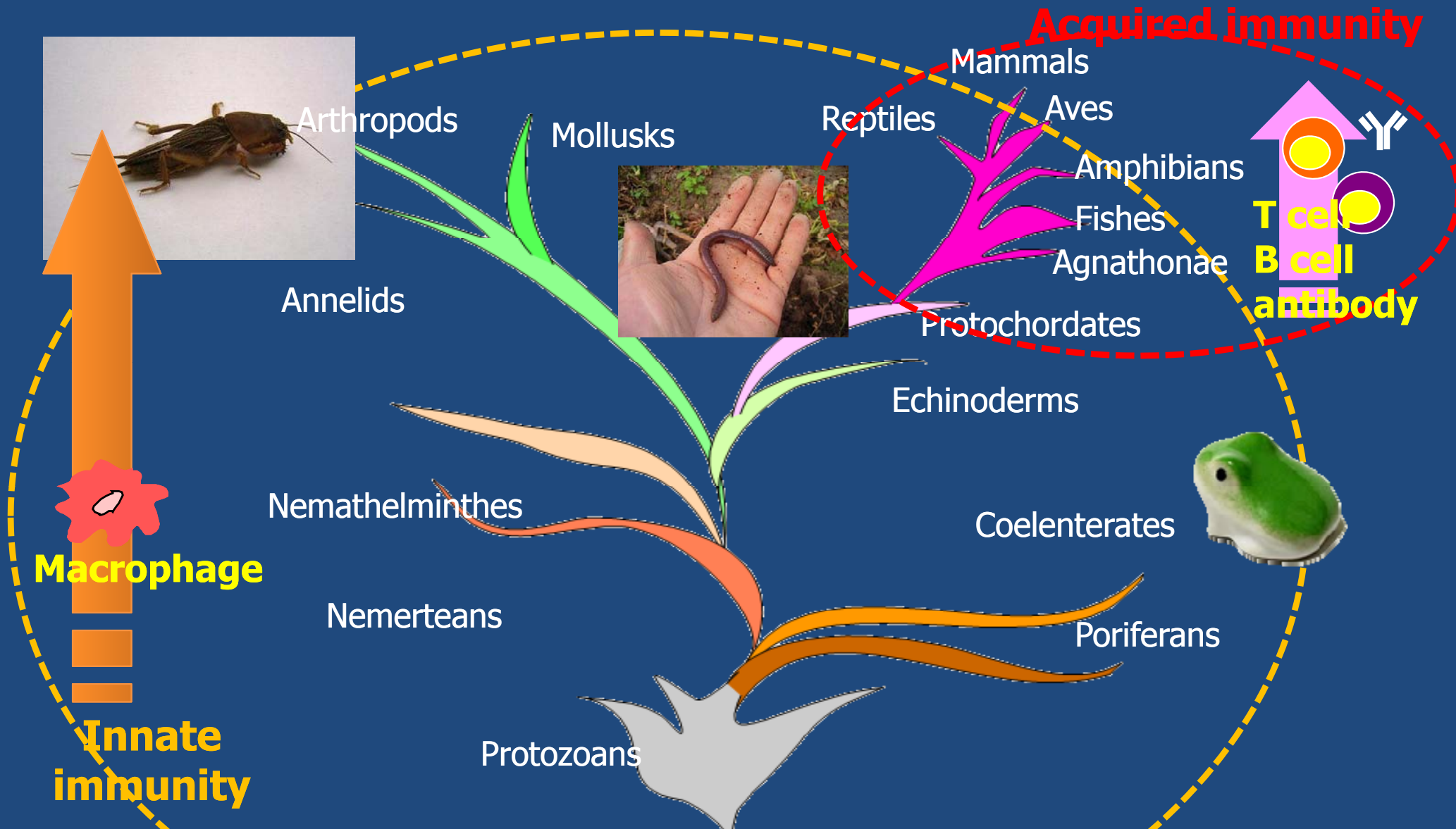
journal homepage: www.elsevier.com/locate/tvj

Inverse association between endotoxin exposure and canine atopic dermatitis

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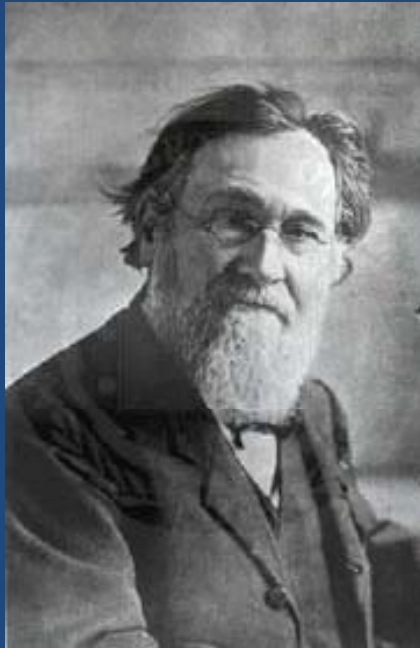


Although 100% of animals have innate immunity, only 5% of animals have acquired immunity.

Note: counted as animal species

Dr. Elie Mechnikov:

Discoverer of lactobacillus, author of “macrophage”



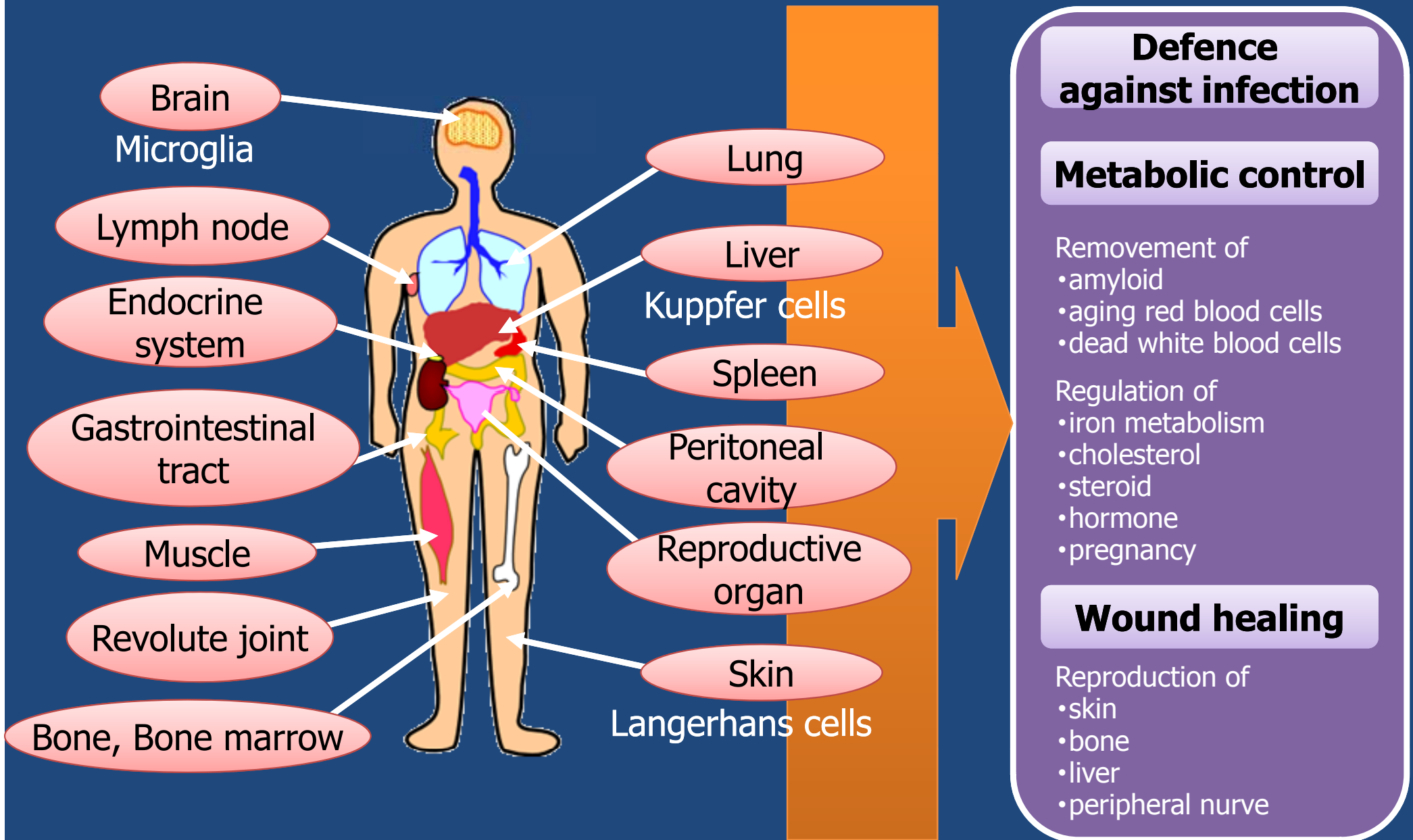
Dr. Elie Mechnikov

**Extensive phylogenetic work:
proposal of phagocyte theory**



**Macrophages
play an important role
in the body's defenses
(for all multicellular animals)**

Distribution of tissue macrophages and their physiological roles

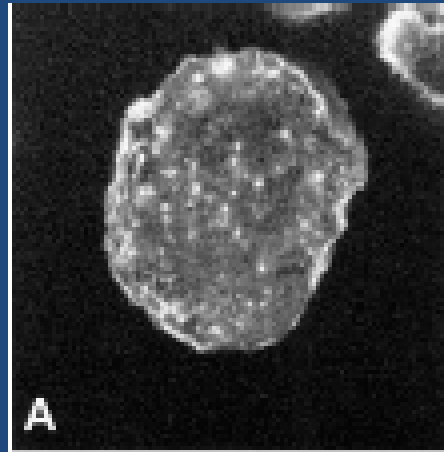


Macrophages are activated in stages

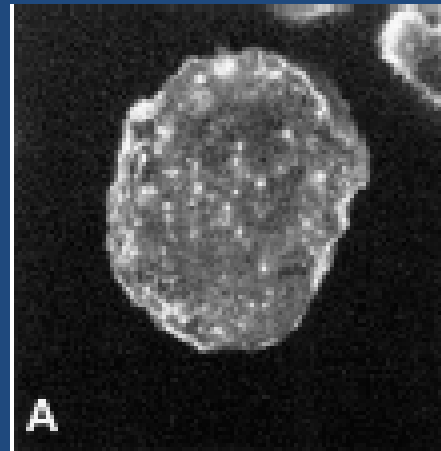
An example:

phagocytic capacity ↑

Preparatory stage for
removal of foreign bodies



Steady-state macrophage
(Resident stage)

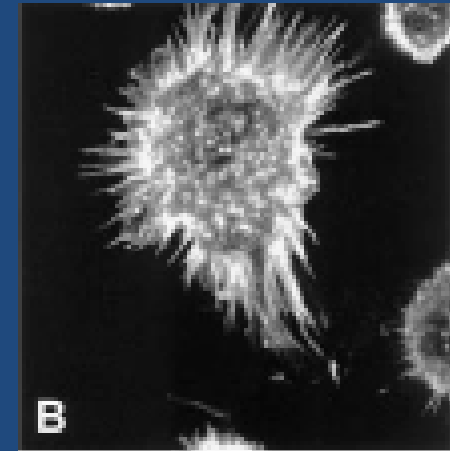


Priming stage

An example:

active oxygen ↑

Inflammatory cytokine ↑



Activated macrophage
(Triggering stage)

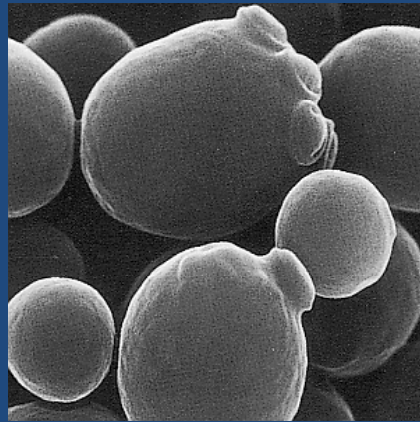


What is LPS?

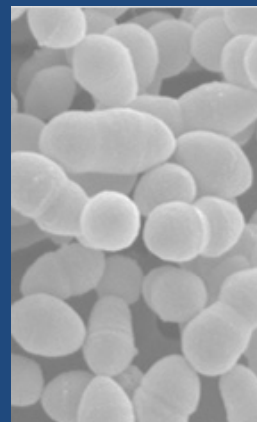
- LPS is a substance contained in bacteria, which greatly enhances **self-healing power**
- LPS is **1,000–10,000 times as effective as β -glucans**, which are already known to be effective ingredients in mushrooms



Fungi



Yeast



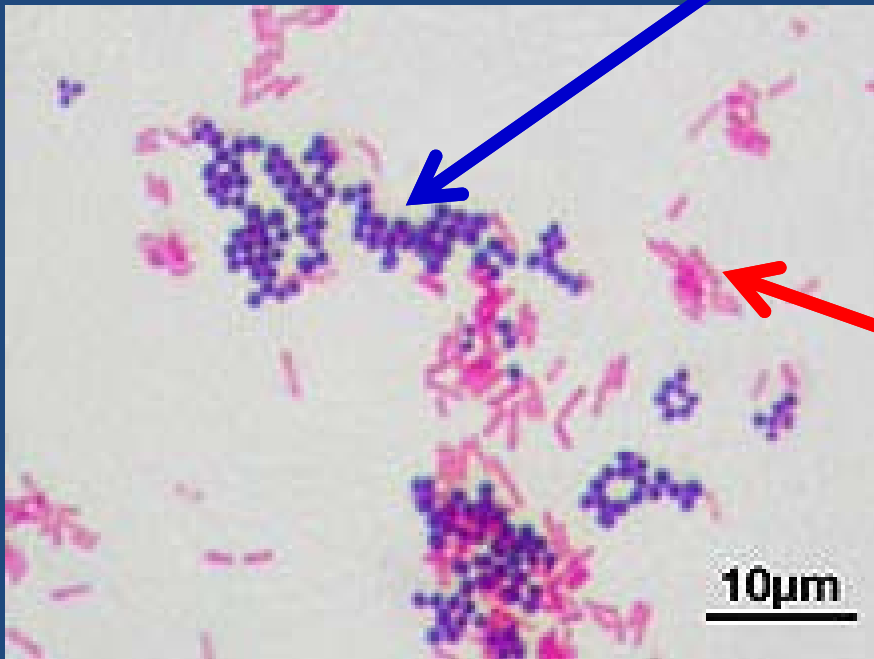
**Lactic
acid**



**Gram-negative
bacteria**

Utilization of micro-organisms

Past (*Lactobacillus*) and future (gram-negative bacteria)



- **Gram-positive bacteria (bacteria with good images)**

- *Lactobacillus, bacillus subtilis, etc.*
- Yogurt, pickles, natto, probiotics

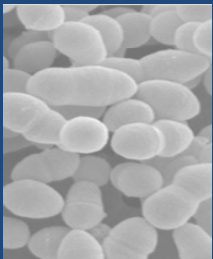
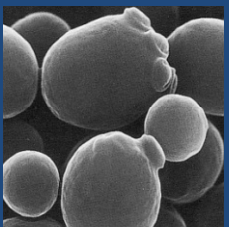
- **Gram-negative bacteria (bacteria with bad images)**

- *E. coli, Pantoea agglomerans, acetic bacteria, Xanthomonas, Zymomonas, etc.*
- Kefir yogurt, nata de coco, vinegar, probiotics

Receptor and intracellular signals of LPS



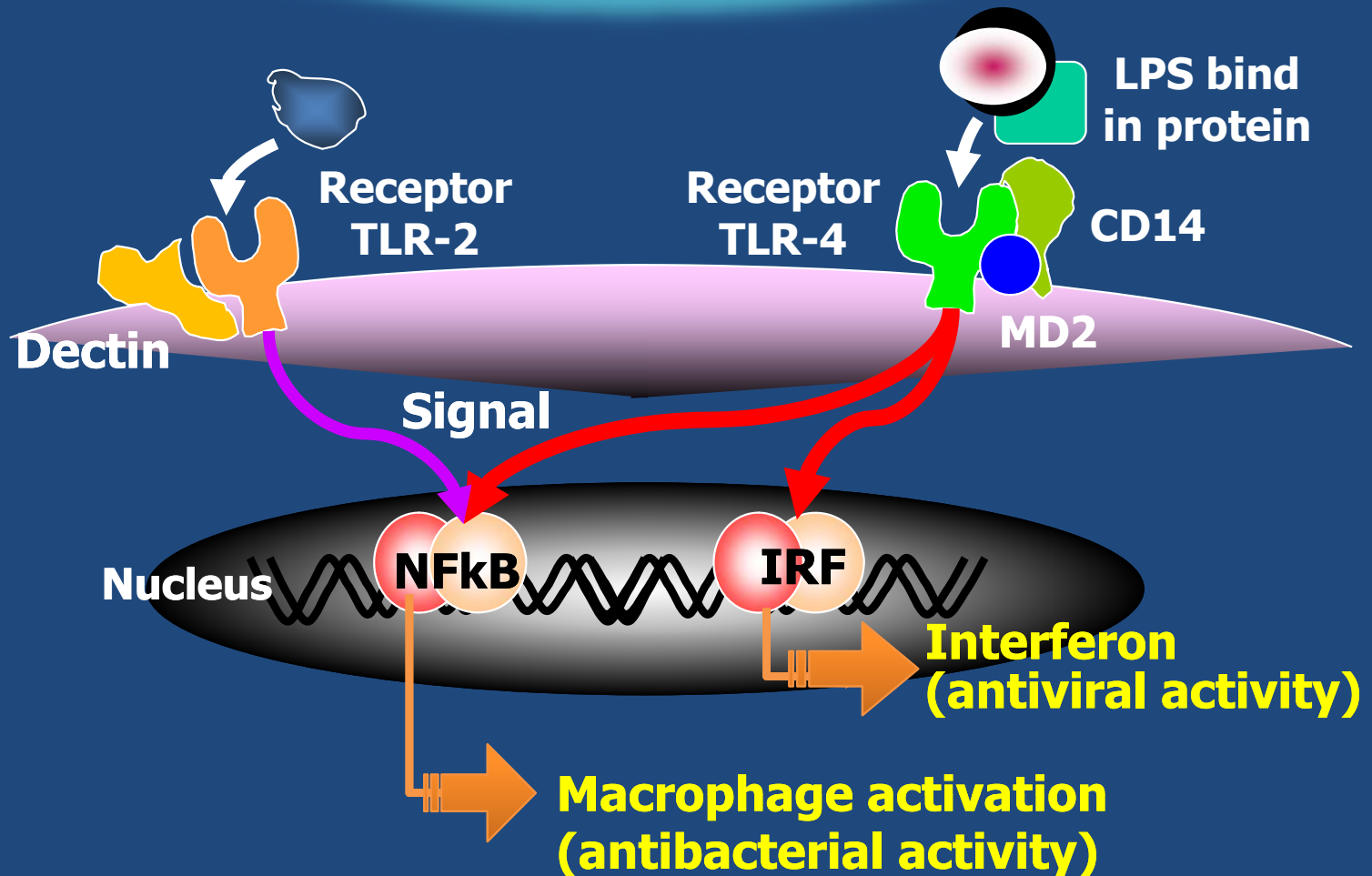
β -1,3 glucan
Peptidoglycan



LPS



The amount for macrophages activation
 β -glucan 1,000–10,000:1 LPS



Screening macrophage activating substances from foods by oral or percutaneous route

1. From foods
2. Waste products

Gluten, starch

Water extract of wheat flour contains Macrophage activating substance

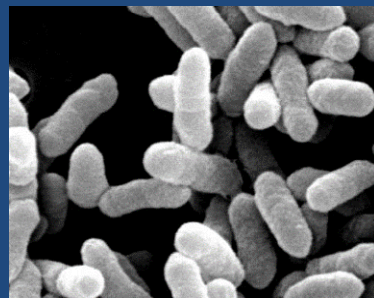
What is the active substance?

Lipopolysaccharide (LPS)

Pantoea agglomerans
A Gram-negative bacteria



Wheat seeds from Canada, USA, Australia, Japan were analyzed concomitant bacteria.



Relative mRNA expression

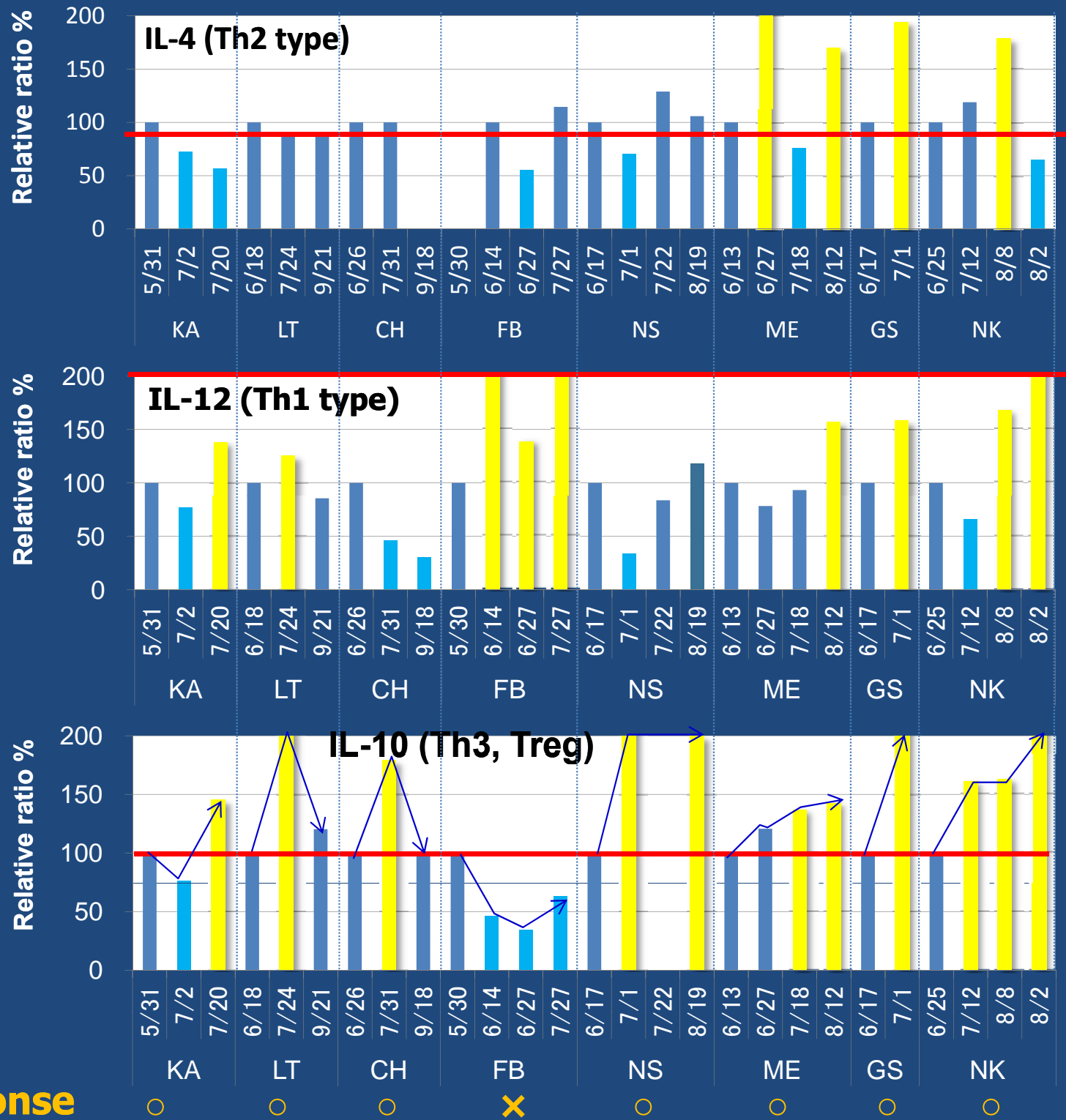
- Less than 80%
- More than 120%



**IL-4 and IL-12:
No correlation
with responses**

**IL-10: increasing
mRNA in
responded dogs**

Response



Pine bark extract



- Extracted from French maritime pines with an average age of 20-25 years from Bordeaux, France.
- Compared with other types of pine, French maritime pine bark is very thick and contains **more than 40 kinds of antioxidants polyphenols.**



Pine Bark Polyphenol Features

- 1. Excellent antioxidant action**
- 2. Improves circulation**
- 3. Stabilizes blood sugar**
- 4. Powerful Anti-inflammatory action**
- 5. Enhances the skin**

2. Clinical Trial Data

Hair-growth promotion effect on bald spots:
Thirteen animals treated with combination of
LPS and pine polyphenol

Details of trials

- **Methods and materials**

- Evaluation of hair-growth effect on alopecia in dogs, cats, rabbits, and hamsters

- **Test materials**

- “LPS tablet” and “Pine polyphenol tablet”

- **Test methods and duration**

- Administration of foods and drugs was not regulated. Combination with other supplements was ruled out. Animals were assigned to receive either an LPS tablet alone, or to receive both LPS and pine polyphenol tablets.
- Test duration was 30 days (in principle).

- **Test results**

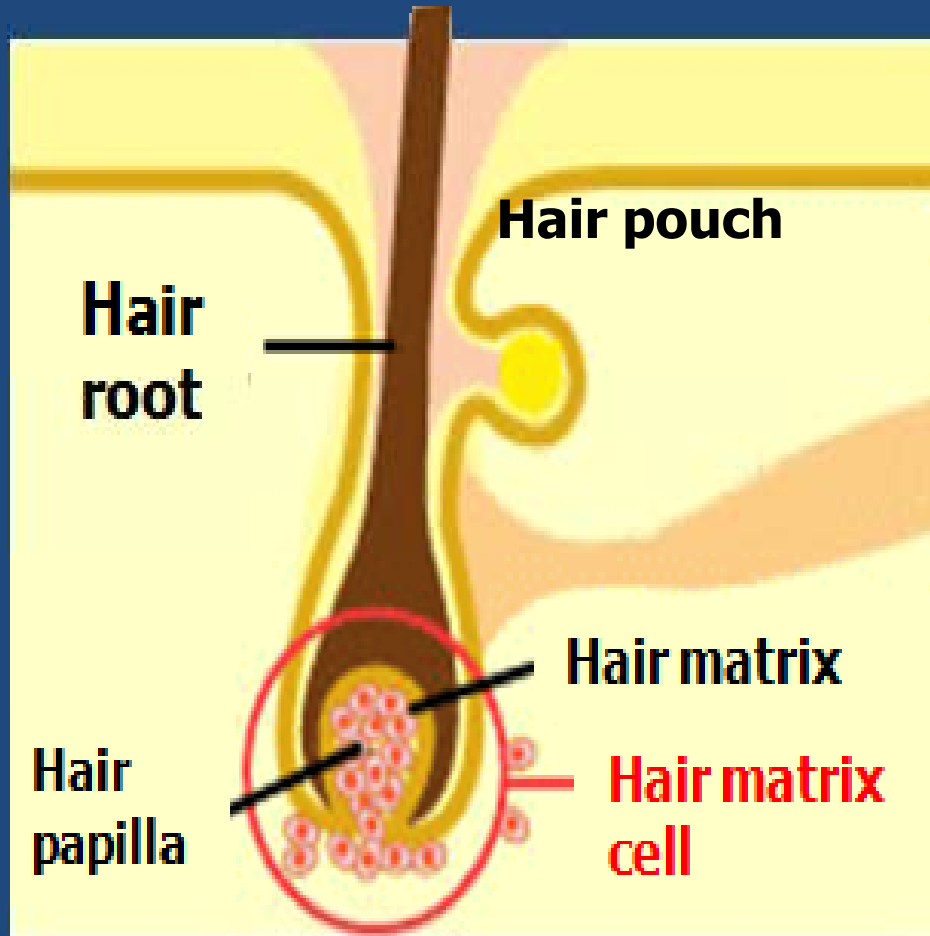
	Hair growth	Number of animals	Rate of hair growth response
LPS alone (n=24)	None	14	58.3%
	Observed	10	41.7%
LPS + Pine polyphenol (n=13)	None	0	0%
	Observed	13	100%

List of 13 animals treated with combination of LPS and pine polyphenol

	Breed	Sex	Age (years)	Body weight (kg)	Concomitant drugs	Dosage		Result
						LPS	Pine pp	
1	M. dachshund	♀	2	3.5	None	2	4	Allergic dermatitis Hair regrew after 12 weeks.
2	M. dachshund	♀	10	4.2	Used	2	4	Atopic dermatitis Hair regrew after 6 weeks.
3	Border collie	♀	7	20	Used	4	4	Dry dermatitis (systemic) A steroid drug was used once.
4	T. Poodle	♀	3	2.5	None	2	2	Allergic dermatitis Deep-colored hair regrew after 7 weeks.
5	T. Poodle	♀	3	3.1	None	2	2	Stress-induced lick dermatitis Hair regrew fully after 3 weeks.
6	T. Poodle	♂	11	3.1	None	2	2	Dermatitis due to subcutaneous infection Hair regrew after 4 weeks.
7	T. Poodle	♂	1	3.9	None	2	2	Stress-induced hair loss Hair regrew after 3 weeks.
8	Cairn terrier	♂	12	8.2	None	3	3	Unexplained hair loss Itching and hair loss were relieved after 4 weeks.
9	Chihuahua	♀	5	3.2	Used	2	2	Allergic dermatitis (Convenia was used for pyoderma)
10	Mix-breed cat	♀	7 (estimated)	2.8	None	1	1	Unexplained hair loss Hair regrew after 4 weeks.
11	Mix-breed cat	♀	12	2.7	None	2	2	Unexplained hair loss Hair regrew after 4 weeks.
12	Hamster	♀	1	Not weighed	None	<1	<1	Unexplained hair loss Hair regrew after 4 weeks.
13	Rabbit	♀	5	2.5	None	1	1	Self-inflicted hair loss Hair regrew after 9 weeks.

3. Putative Mechanisms of Action

Putative mechanisms of action



● LPS

1. Macrophages are turned into priming stage and inhibit induction of catagen-inducing cytokine.
2. Combination of mechanisms generates effect.

● Pine polyphenol

1. Antioxidant effect
2. Blood circulation promoting effect



動物にも

Animals

笑顔は

also

ある

smile.

Thank you for listening.

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