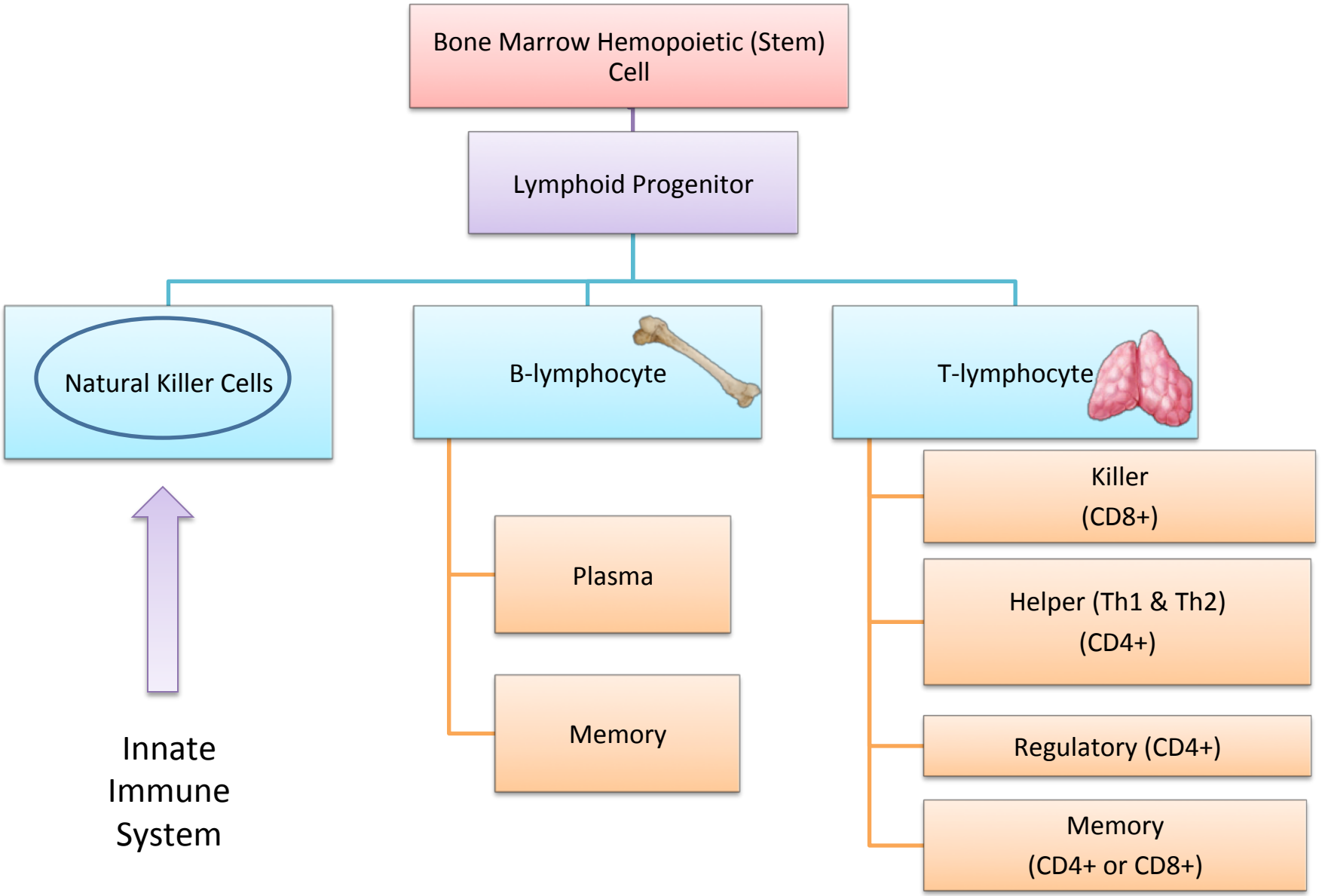
Reversing Immunosenescence

An Overlooked Step in the Fight Against Aging

Michael A. Smith, MD

Director of Education and Spokesperson



Immune and longevity

"The immune system seems to be involved in the chronic oxidative and inflammatory stress conditions of aging. It has been proposed that several age-related changes in immune cell functions, which depend on the redox state of these cells, could be good markers of health, biological age, and longevity."

Alonso-Fernandez P. *The role of the immune system in aging and longevity*. *Curr Aging Sci*. 2011 Jul;4(2):78-100.

Powerful solutions to stay one step ahead of the culprits that compromise your immune response.

Immune Senescence

The age-dependent decrease in immunological competence, which results in inability to respond to new threats and chronic inflammation.

1. Loss of NK cells
2. Loss of naïve cells

Innate Response

3. Build-up of old memory cells
4. Low Helper/Suppressor ratio

Acquired Response

Immune senescence and T-Cells

Naive

Responds to new invaders

Numbers tend to decrease with age

Inability to mount immune response

Vs.

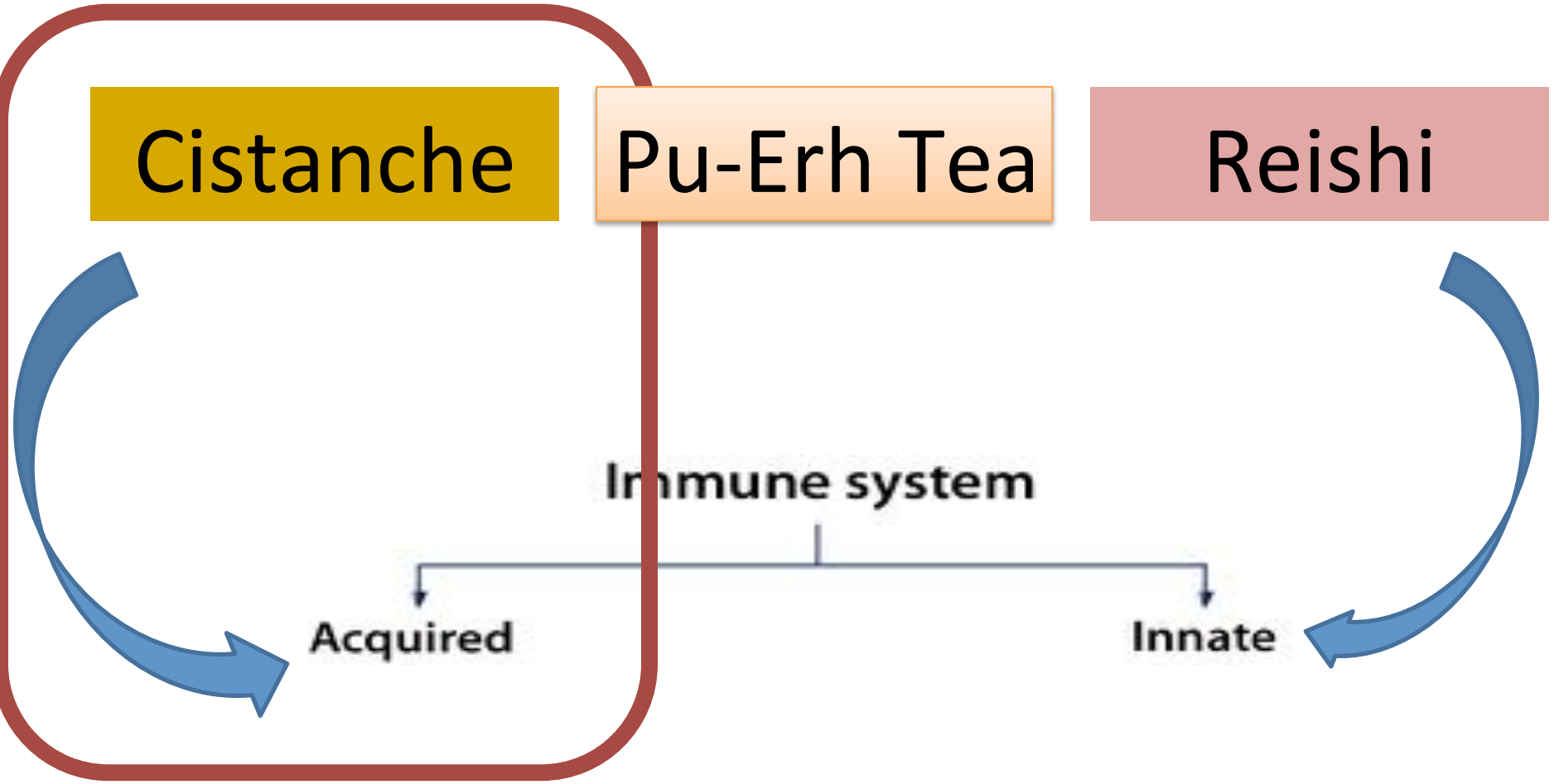
Memory

Responds to invaders already encountered

Cells become numerous, proinflammatory, and ineffective as we age

Chronic inflammation

Immunosenescence



Solution: Cistanche

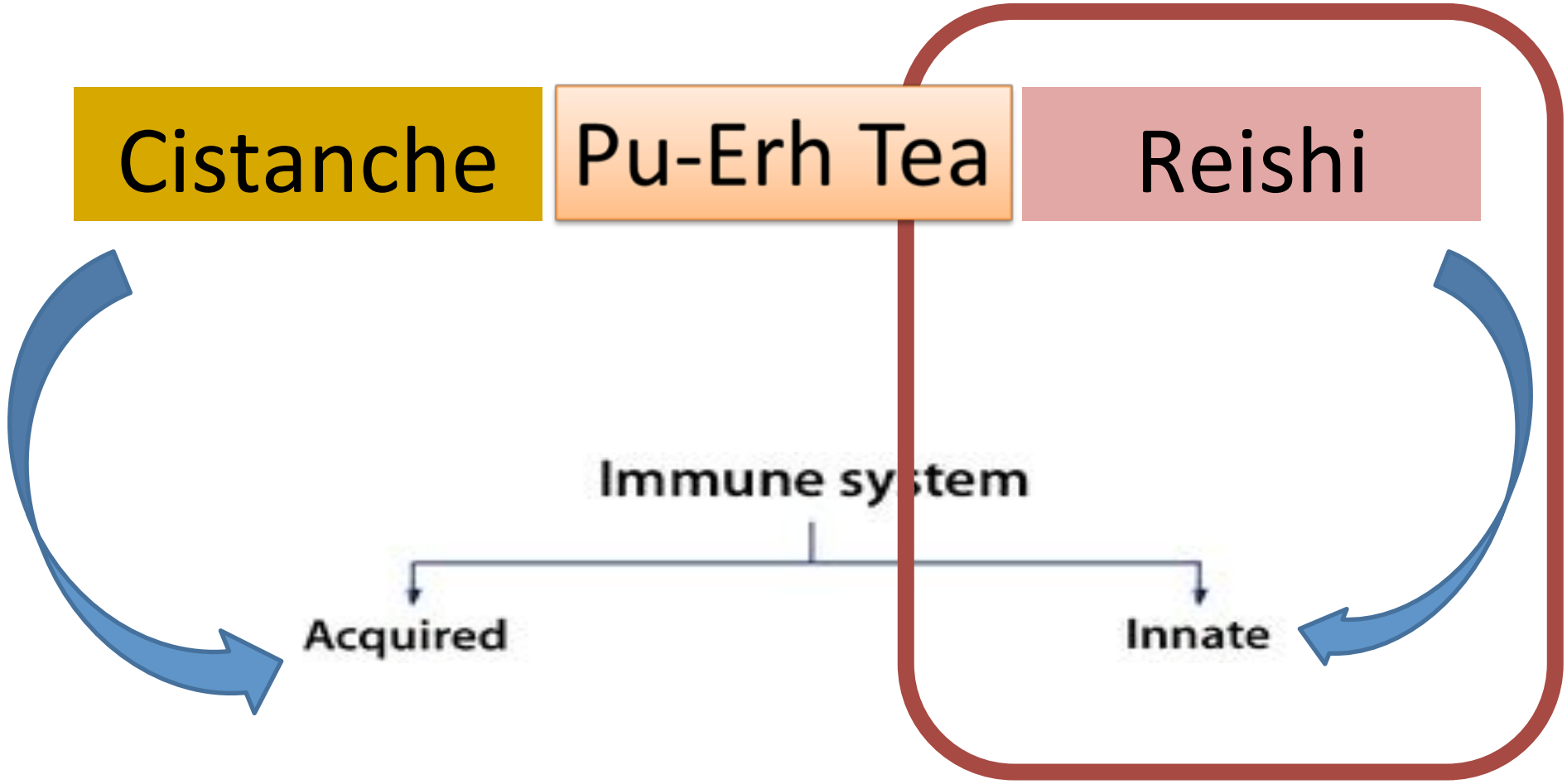
- Cistanche species
  - C. tubulosa
- Traditional Chinese Medicine
- Parasitic species: they lack chlorophyll and get their nutrients and water from other plants.
- A.K.A.: *"Ginseng of the desert*
- *Echinacosides- one of the major constituents of Cistanche.*

How Cistanche Restores Immunocompetence

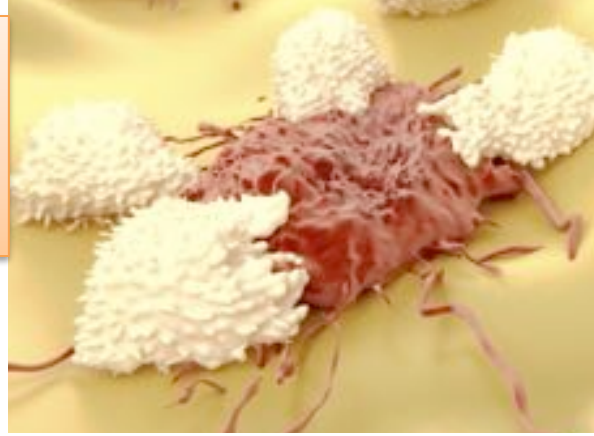
- Stimulates production of new Naïve T-Cells, thus boosting Naïve T-Cell populations.
- Restores normal apoptosis in aging T-Memory Cells, thus restoring appropriate levels of T-Memory cells.
- Recreates the balance between Naïve and Memory T-Cells seen in youthful individuals.

Reduced inflammation and enhanced immune response

Immunscenescence



Reishi Mushroom



- Reishi Mushroom “the mushroom of immortality”
- Used in traditional Chinese medicine for at least 2,000 years
- There are over 5,000 studies documenting the broad-spectrum benefits of the compounds found in the Reishi Mushroom.

Reishi – Innate Immunity

Ganoderma lucidum

Polysaccharides

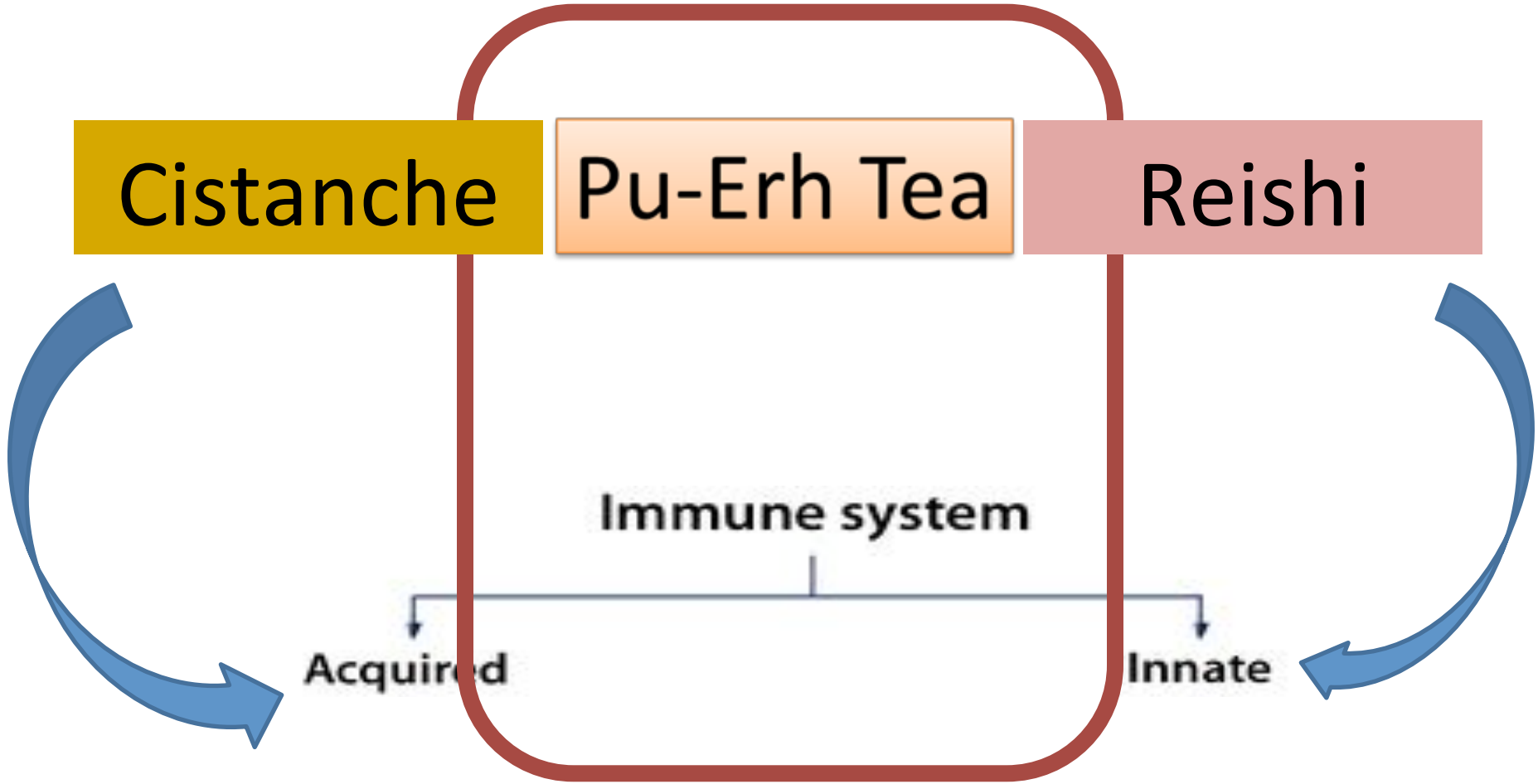
- Trigger the growth and development of bone marrow, where most immune cells are born.
- Assist in the activation of receptors on innate immune cells responsible for recognizing pathogens

Triterpenes

- Enhances NK Cell activity

Am J Chin Med. 2011;39(1):15-27.

Immunoscenescence



Pu-Erh Tea

- Traditional fermented tea that was consumed by emperors for longevity
- Native to the Upper Mekong River Region of China's Yunnan Province
- Derived from mature, large leaves of *Camellia sinensis*

Pu-Erh Tea

Ku Cha House of Tea- Boulder, CO

Pu-Erh Tea

- Tea can be broadly classified according to the production method as:
  - Green tea and White tea (unfermented)
  - Oolong tea (partially fermented)
  - Black tea (fully fermented)
  - **Pu-erh tea (post-fermented)**

Pu-Erh Tea

Content (mg g^{-1} tea)	GA Gallic acid
Pu-erh	5.53
Meifoo green tea	0.74
Shanghai green tea	0.37
Hangzhou Lung Ching	1.84
Jasmine	1.13
Fujian Oolong	1.42
Jiangxi Oolong	1.67
Fujian black	2.06

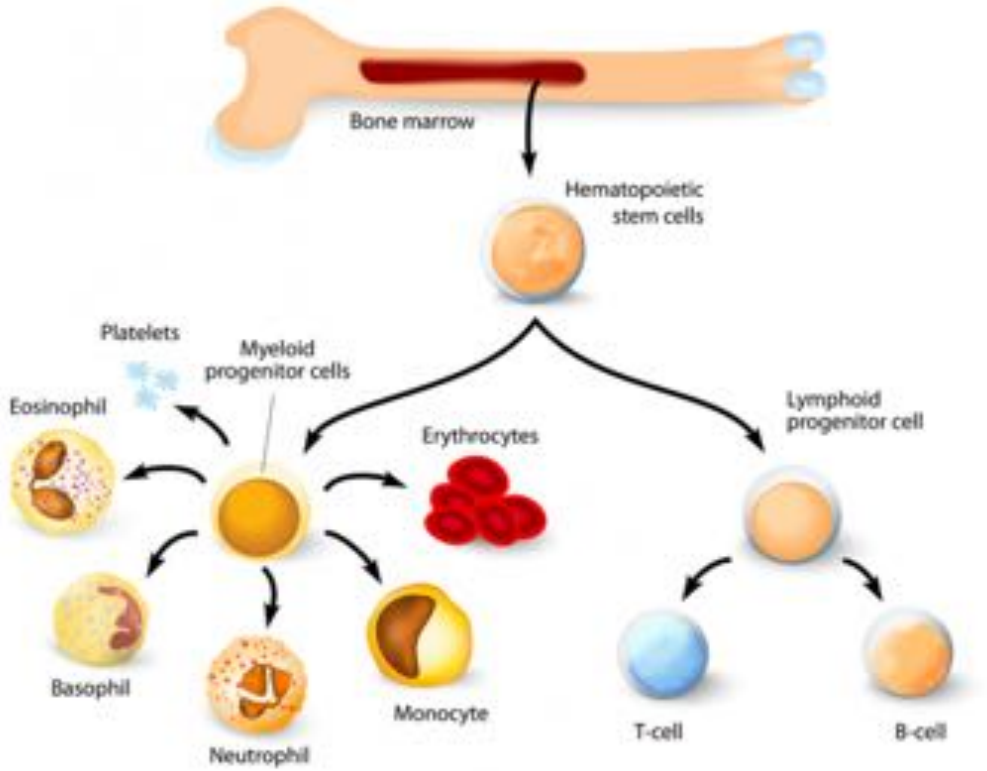
Zuo Y et al. Talanta. 2002;57:307-316

Sample	Polyphenols	Polysaccharide	Theabrownins
Green Tea	56.23±5.17	1.01±0.11	---
Black Tea	42.40±3.35	3.42±0.05	---
Pu-Erh Tea	33.13±3.18	4.81±0.13	7.32-10.50

Zhao H et al. Int J Mol Sci. 2011;12(3):1862-1875.

Proposed Mechanism of Action

Improves bone marrow function, helping to rebuild the peripheral immune cellular components

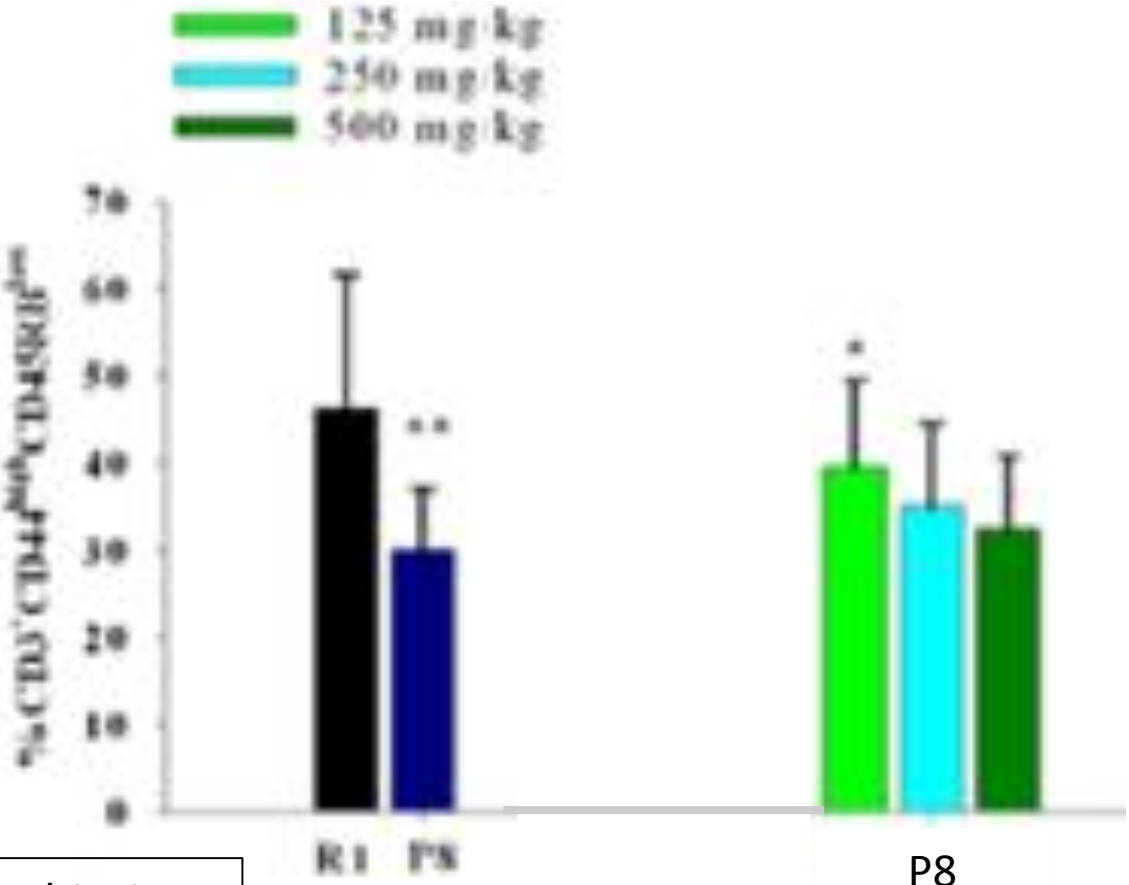


Pu-Erh Tea: Animal Study

- **Subjects**: male SAM-P8 (senescence-accelerated mouse) and SAM-R1 (control) at the age of 8 mo
- **Dose**: 125, 250 or 500mg/kg ripened Pu-Erh extract once daily for 4 weeks to SAM-P8 mice (H.E.D. of 650mg, 1300mg, and 2600mg)

Zhang L et al. Food Chem. 2012;135:2222-8.

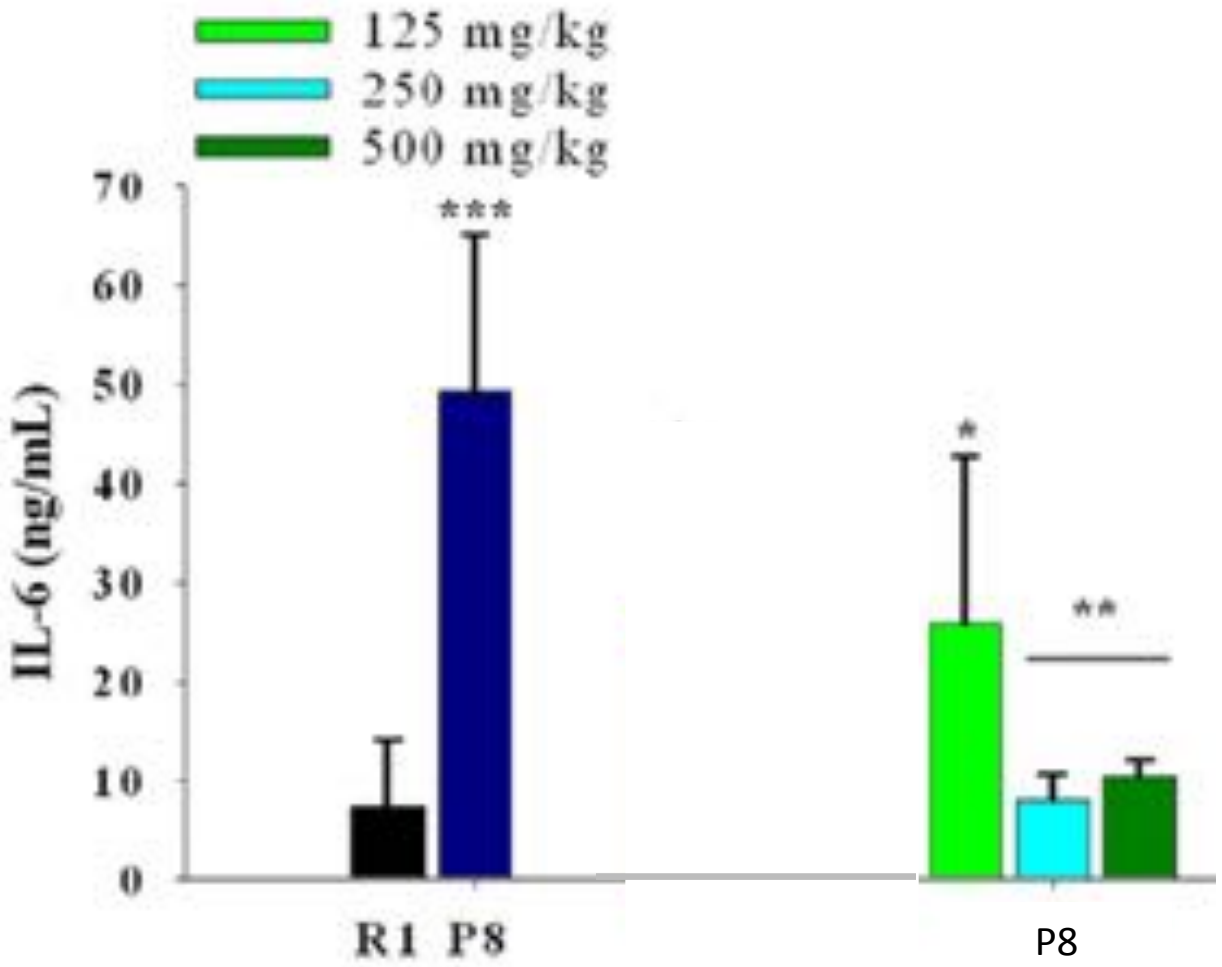
Percentage of naïve T cells



* P<0.05
** P<0.01

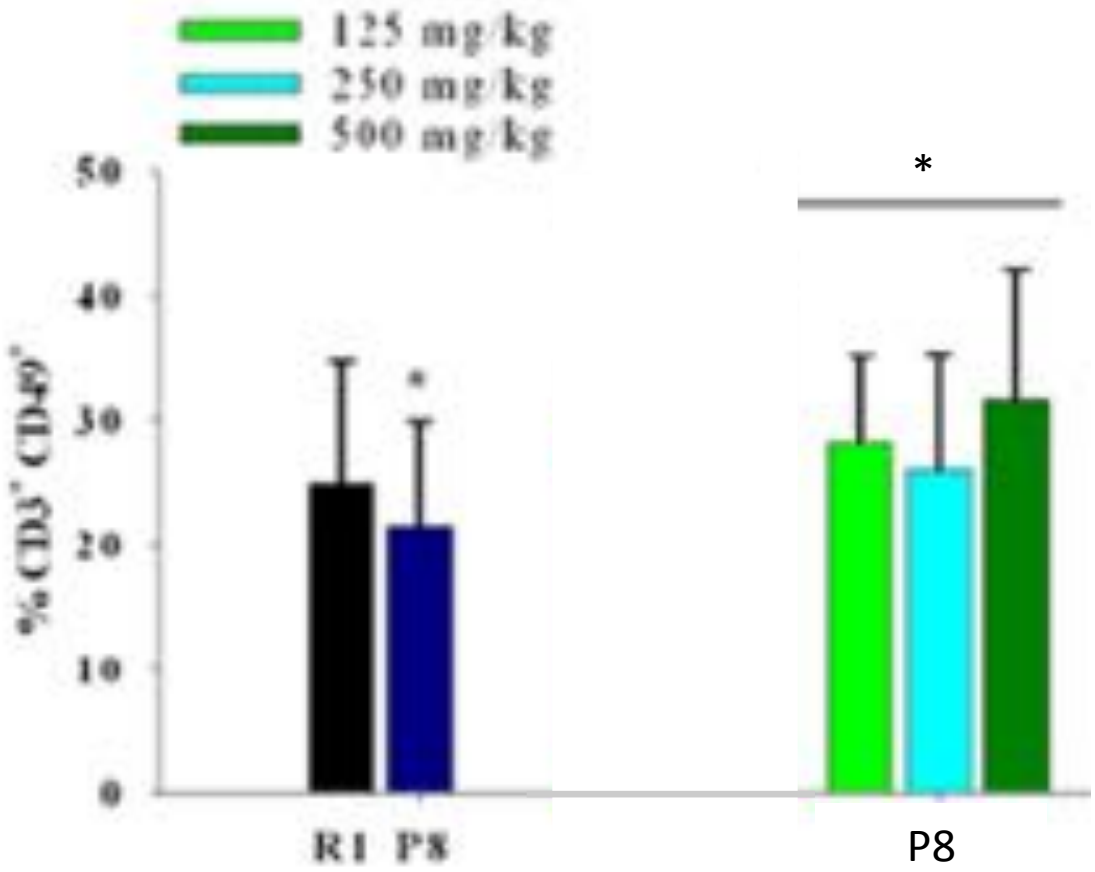
R1: senescence-resistant
P8: senescence-accelerated

IL-6 in peripheral blood



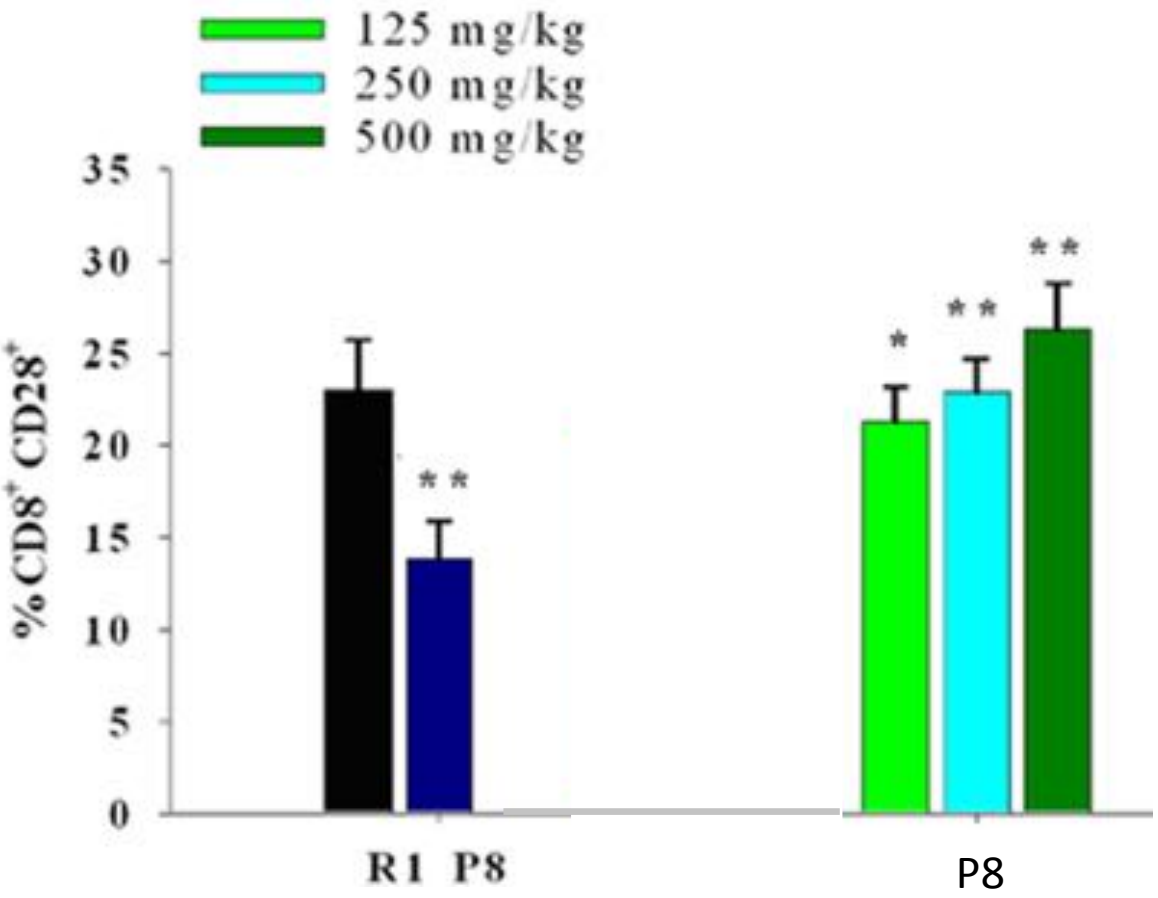
* P<0.05
** P<0.01
*** P<0.001

Percentage of NK cells



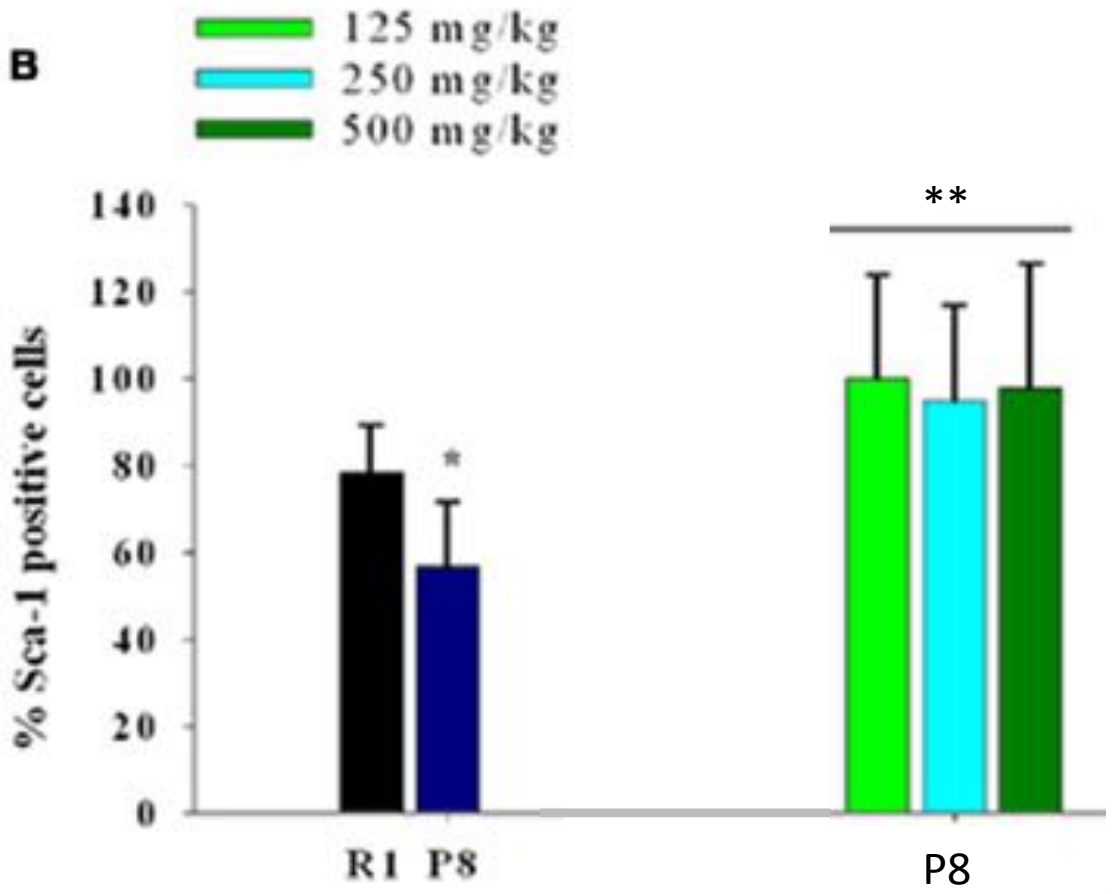
* P<0.05

Subgroup of T Lymphocytes



* P<0.05
** P<0.01

Percentage of Sca-1 positive cells

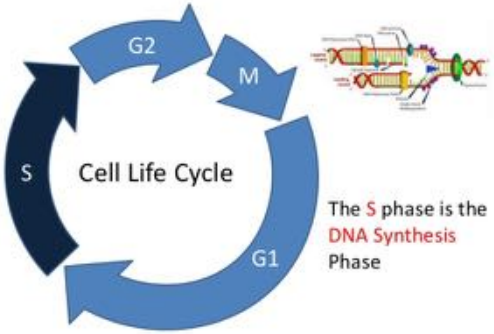


** P<0.01

Sca-1: stem cell antigen

Pu-Erh Tea: Cancer

- In-vitro data in engineered mouse tumor lines
- Inhibits tumor cell growth by down-regulating S phase and causes G1 or G2 arrest at a concentration that does not affect wild type cell



- Down regulates expression of mutant p53 in tumor cells at both mRNA and protein levels

Zhao L et al. Int J Mol Sci. 2011;12:7581-7593.

Pu-Erh Tea: Inflammatory Parameters

- **Subjects**: 90 patients (30-65 yrs) with metabolic syndrome
- **Dosage**: 0.5g BID Pu-Erh Tea extract or placebo, 30 minutes before meals for 3 months

**P<0.01 vs. placebo

Parameter	Placebo		Pu-Erh Tea Extract			
	Baseline	End	Baseline	End	% Change (vs. baseline)	Placebo-Subtracted Δ
HDL (mg/dL)	37.12±10.83	39.06±11.6	34.03±11.99	47.95±18.56**	**+40.9%**	**+35.7%**
CRP (ng/mL)	4.10±0.61	3.86±0.37	4.01±0.82	2.97±0.93**	**-25.9%**	**-20.0%**
TNF-α (pg/mL)	23.24±4.20	23.46±4.63	24.49±5.32	18.97±4.47**	**-22.5%**	**-21.6%**
IL-6 (pg/mL)	34.49±8.02	32.22±8.45	32.66±6.73	25.67±5.62**	**-21.4%**	**-14.8%**
IL-10 (pg/mL)	54.60±9.41	57.02±11.25	52.27±8.80	70.21±13.11**	**+34.3%**	**+29.9%**

Chu SL et al. Chin J Integr Med. 2011;17(7):492-8.

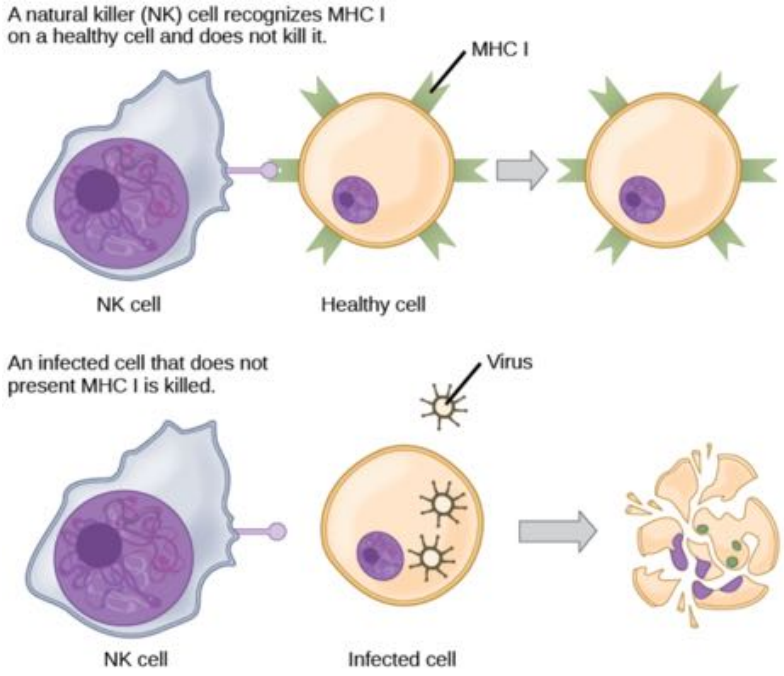
Enzymatically Modified Rice Bran

Boosting NK-Cell Activity

LifeExtension®
Stay Healthy, Live Better

NK Cell Overview

Type of Immune Cell	• Lymphocyte: 10-15% of lymphocyte pool
Target	• Viral infection • Malignant tumors • Only phagocyte in the innate immune system that destroys other human cells.
Mechanism	• Direct cytotoxicity • Secretion of cytokines and chemokines
Maturation	Do not need thymus or intracellular pathogen to mature
Antigen	Do not need exposure to antigen for production or proliferation
Specific Antibody	No memory ability



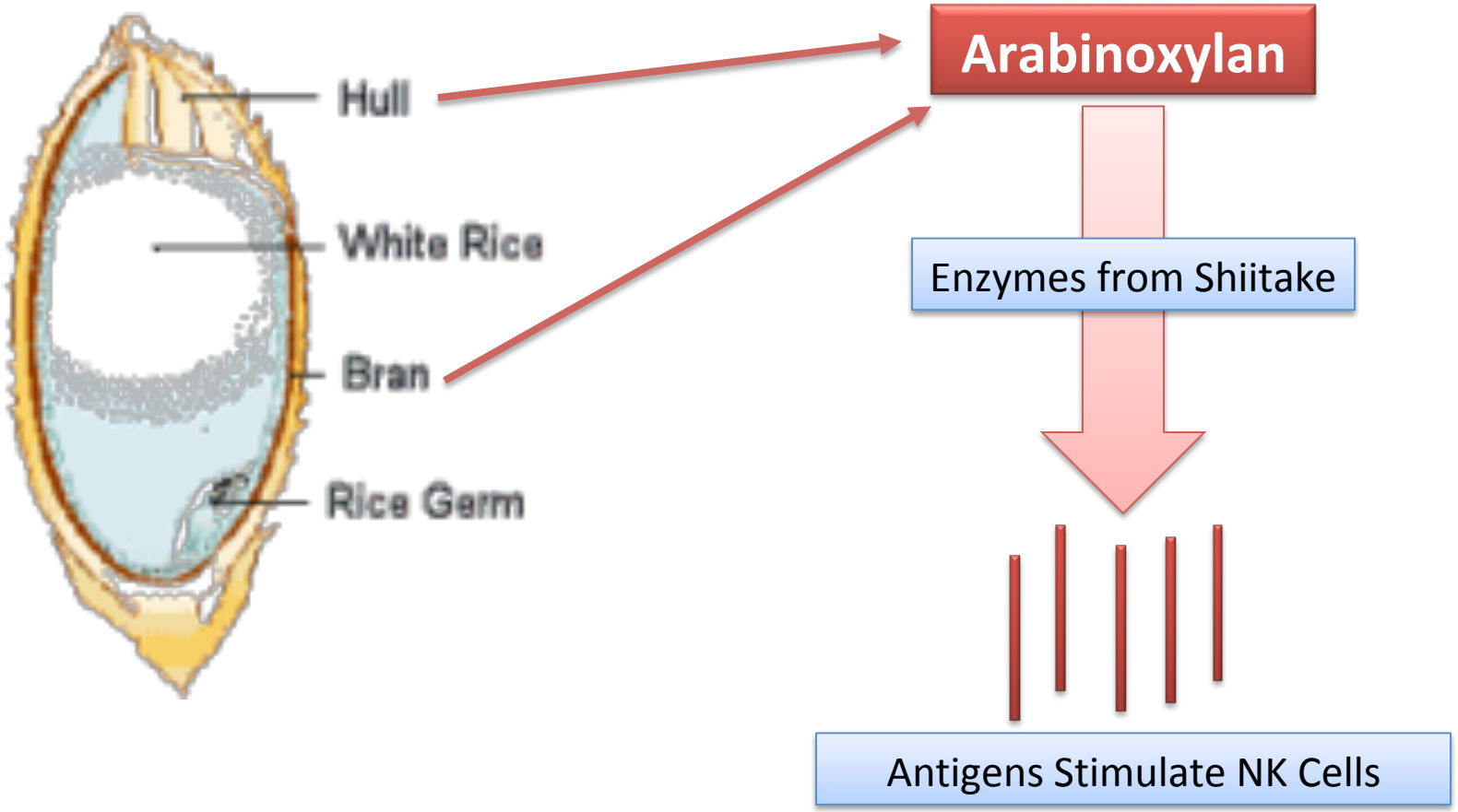
Problem: Decline of NK Cell Function

"The decrease in NK cell function that accompanies physiological ageing is likely to have wider implications for the health of older adults than originally thought."

Proposed Mechanisms

- Decline in the percentage of activating receptors. (alterations in the expression of activators and inhibitory receptors)
- Reduced expression/release of perforin into the immunological synapse that is formed following target cell contact.
- Reduction in production and proliferation.

How is EMRB Produced?



How Does EMRB Benefit Us?

20 Healthy subjects

- 1 to 3 g/day
- 60 days
- 35% increase

Functional Foods in Health Dis. 2012;2(7):265-79

45 subjects w/ low NK cell activity

- 1 g/day for 4 months
- 4x in 2 months
- 7x in 4 months

Abstract 7th Intern. Congress Anti-Aging & BioMed. 1999.

68 patients with liver cancer

- 3-year randomized, control trial
- 1 g/day EMRB or placebo
- 31.6% reoccurrence rate in EMRB group
- 46.7% reoccurrence rate in control group
- EMRB group lived longer:
  - 1 year - 76% EMRB vs. 63% controls
  - 2 years – 35% EMRB vs. 6.7% controls
  - 2.5 years – 11% EMRB vs. 0 controls

Anticancer Res. 2010 Dec;30(12):5145-51

Summary

- Immune function decline is an accelerator of the aging process.
- Reversing immune function decline is possible with targeted nutrition.
- Don’t forget about your immune system!