The recent challenges in red biotechnology
- for accelerating the development of novel diagnostic tools and pharmaceutics

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Port Island – derived from Mt. Rokko

“The mountain gose to sea” (1960’s-80’s)

Campus zone and Biomedical Industry-cluster are integrated in the Island

Hyogo College of Medicine and Hyogo University of Health Sciences

Kobe Campus; Pharmacy, Nursing & Rehabilitation

Main campus; School of medicine & hospital @Nishinomiya

Sasayama campus hospital

Contents

1. Trends in health care of Japan--- Importance of diagnoses
2. Development of diagnostic tool for infectious diseases using “Red-biotechnology”
3. Combating with Candida albicans by vaccines and drugs in novel mechanism not only by diagnoses
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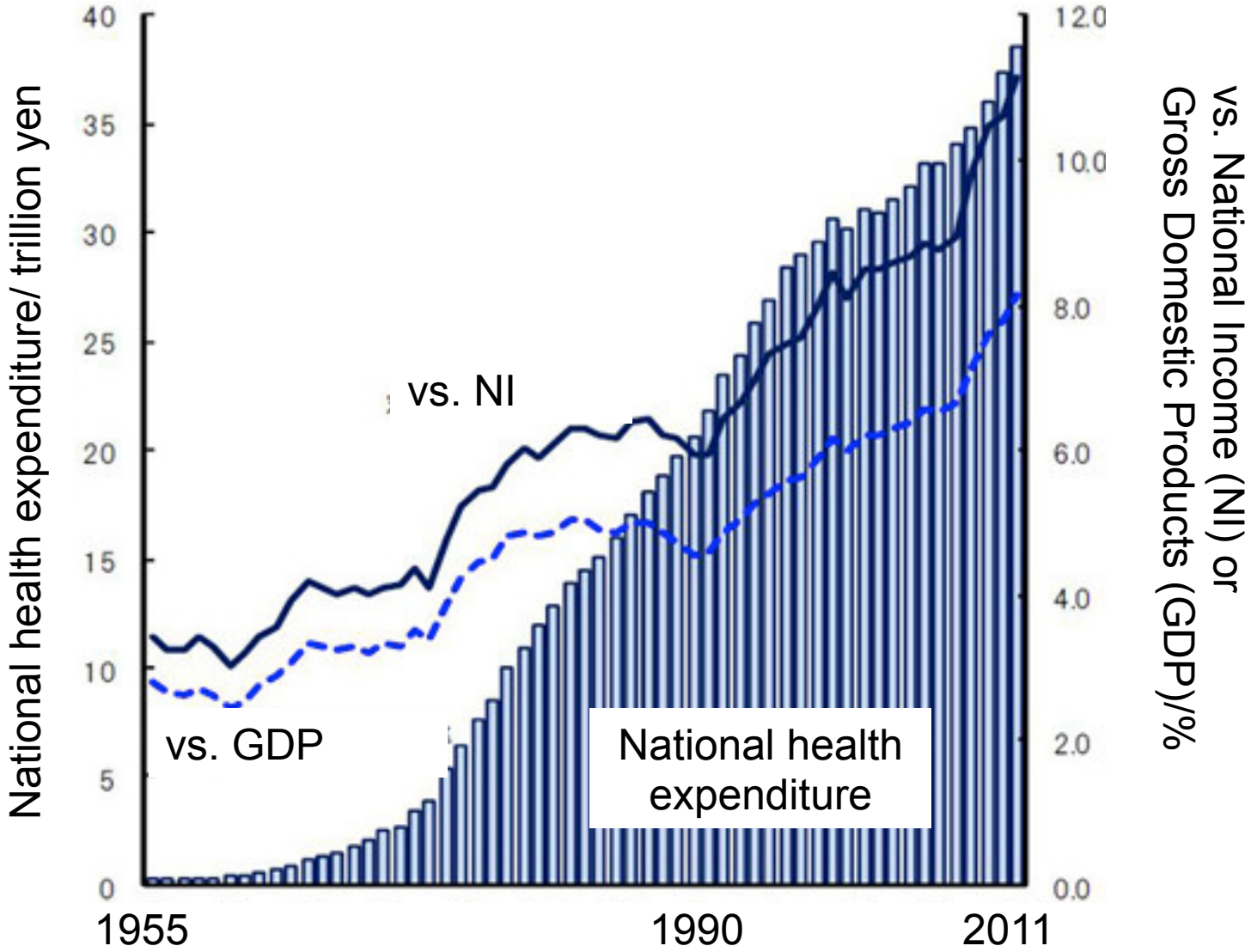
Medical expenditure in Japan



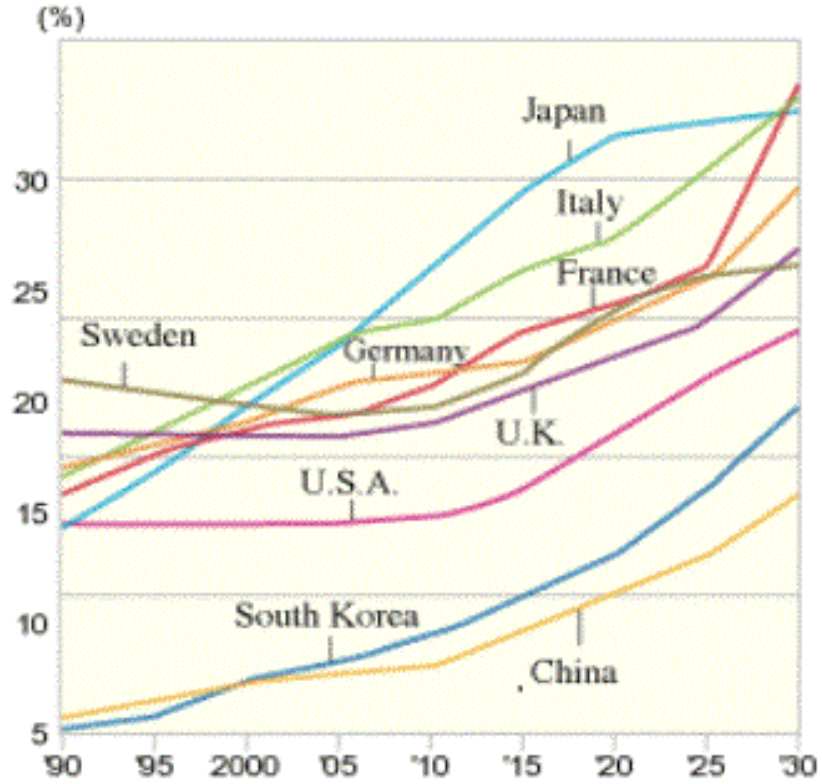
Present solutions to reduce the cost

- Staying periods of patients in hospital is recommended as short as possible
- Promotion on use of generic medicine (license expired and low cost type drug)
- “Treatments” to “Prevention”

→Biotechnologist can contribute in research and development of novel tools !!

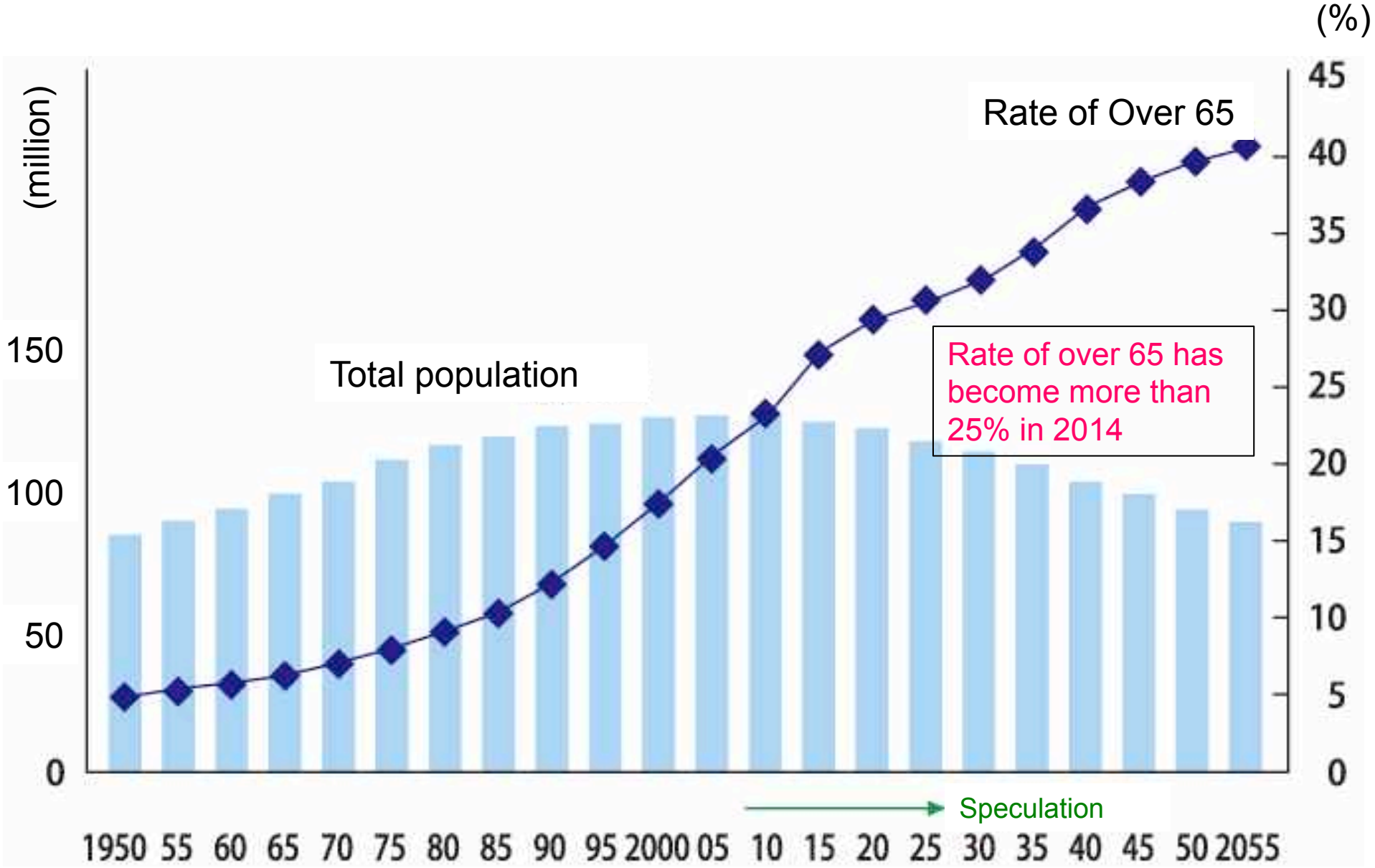
The aging of polulation and healthcare

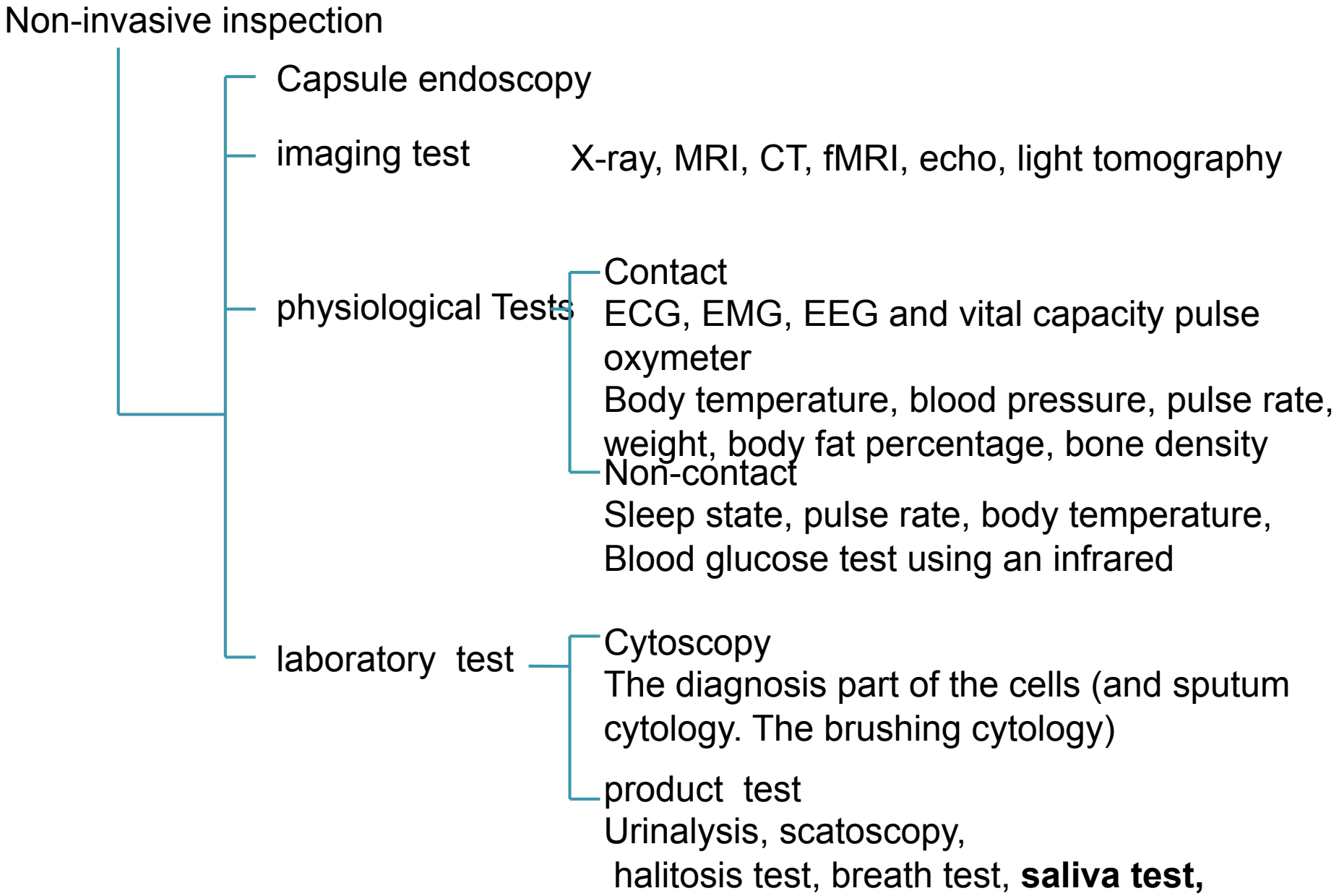
- Percentages of the population above age 65 in the world are steadly increasing.
- The medical expense was 292 billion Euro (2012).
- Payments were categorized as ;insurance 50%, patients 12%, government 38%.



Main source: Ministry of Health and Welfare, Japan

The aging in Japan





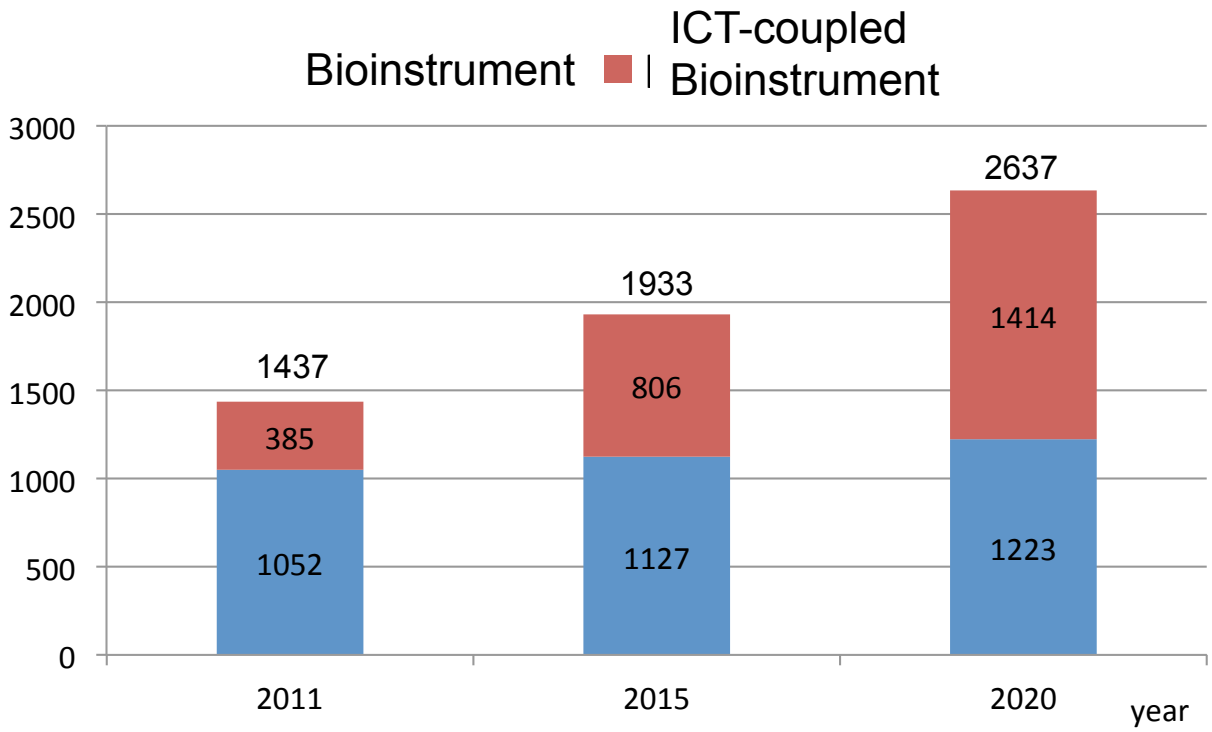
Tsukinoki (ed), “Up-to date non-invasive clinical examination”, CMC Publishing (2015)

Activities and Orientation to diagnoses

- More than 400 companies has gathered at JASIS anually.
- One of trends of diagnostic technology is based on "-omics" (genomics, proteomics, metabolomics) technology + IT

Japan Analytical and Scientific Instruments Show(JASIS)

Future prediction of home ICT（Information and Communication Technology）market by Bioinstrument, technology （100 million yen）



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Estimated market creation effect by the the health and longevity industry#（Billion yen／year）

non invasive inspection methods or diagnoses

Diseases	Market creation effect	Medical expenses inhibitory effect
Diabetes	1017	219
High blood pressure	2322	313
Locomotive syndrome	241	508
Dysphagia, gastrostomy	370	200
Total	3952	1242

∗ Keeping “healthy leads to decrease medical expenses.
∗ Abenomics suggests that one of growth factor is “health care industries”
∗ Early treatments need early diagnoses.

Tsukinoki (ed), “Up-to date non-invasive clinical examination”, CMC Publishing (2015)

Red-biotechnology
(Punainen bioteknologia)

- Green-bio: For agriculture
- White-bio: Alternatives of chemical industry
- Red-bio: For pharmaceutics and medicine

http://www.jba.or.jp/top/bioschool/basic/detail/93.html

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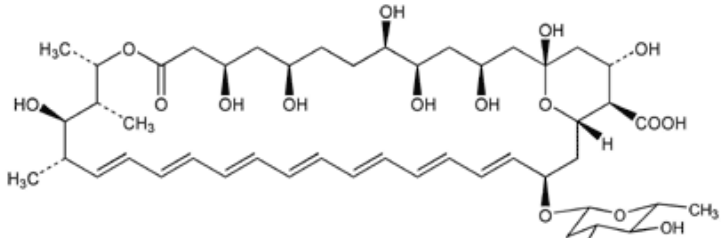
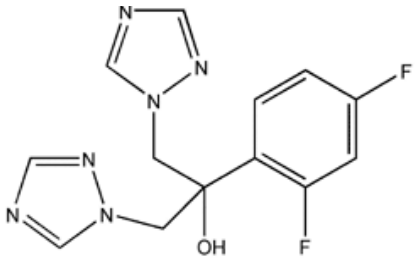
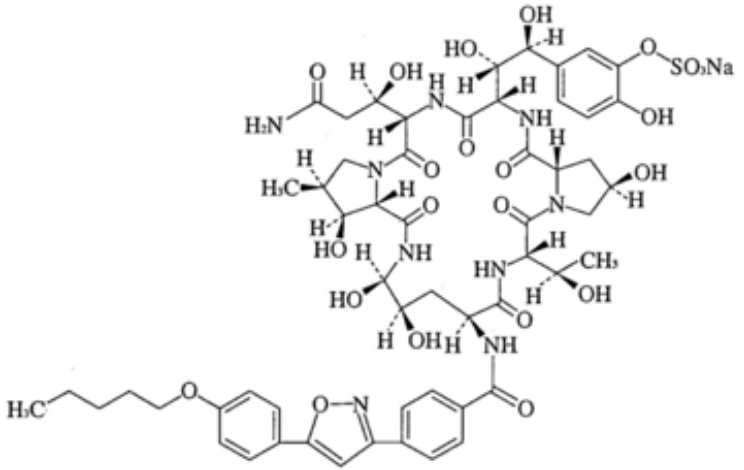
Effective antifungal drugs



Amphotericin B

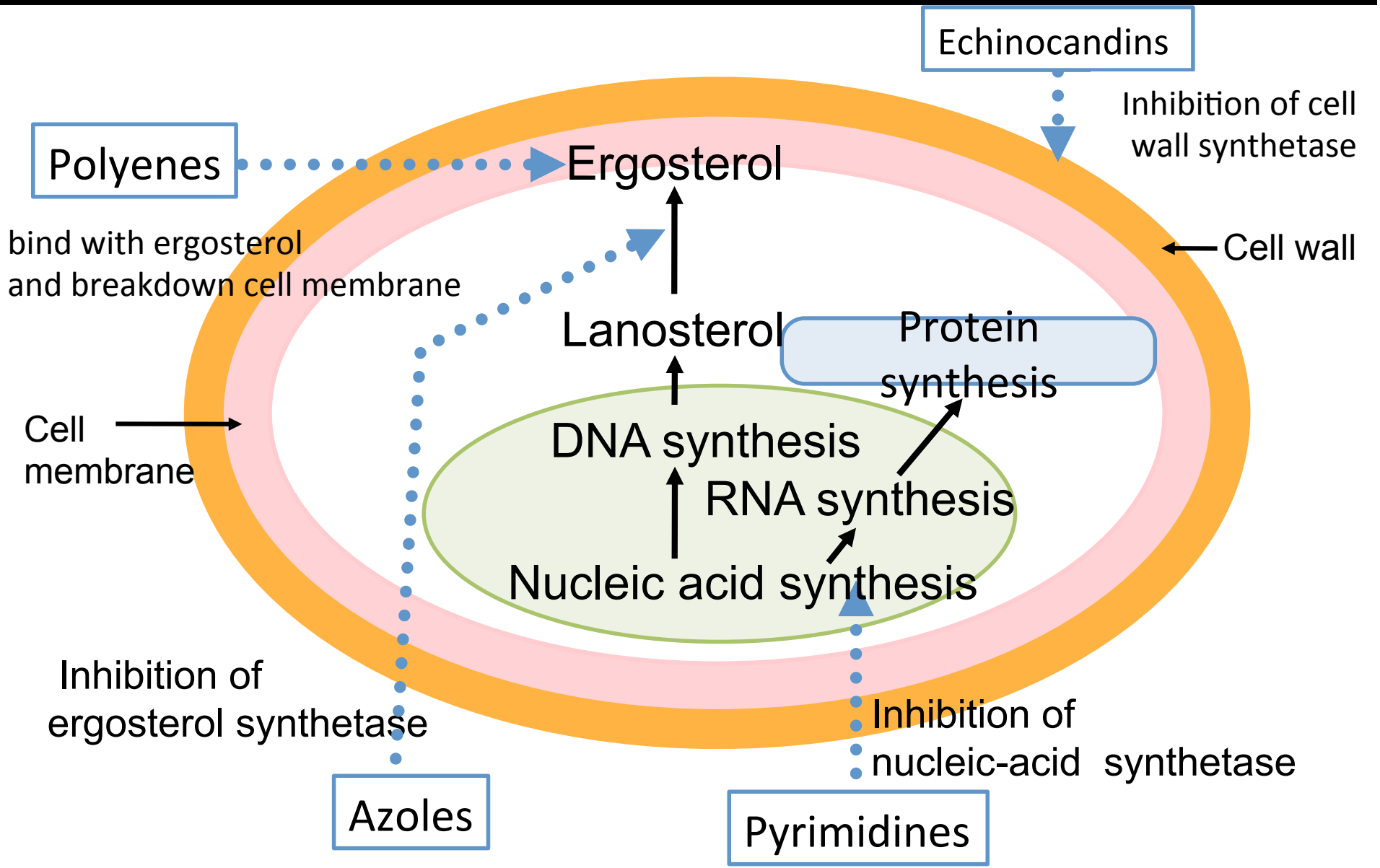


Fluconazole

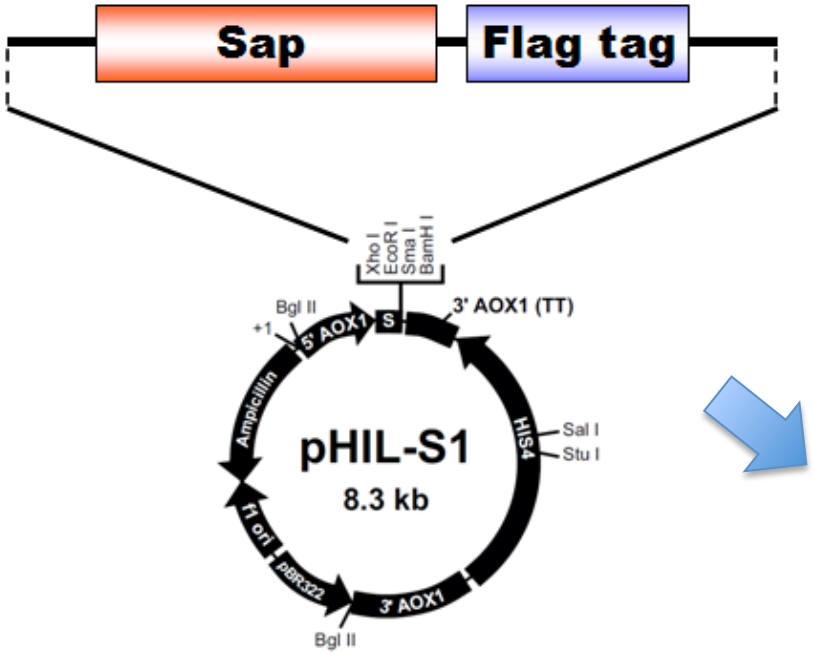


Micafungin

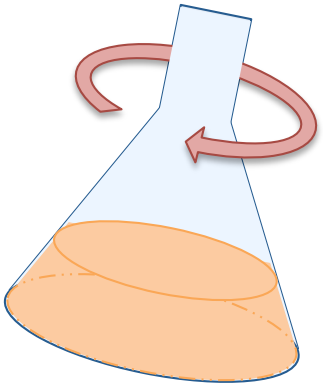
Mechanism of antifungal drugs on *C. albicans*



Purification of secretory proteases



P. pastoris



BMMY medium

Purification (ca. 500mg/L)
by FLAG M2 affinity gel

Possibility of a diagnosis of systemic diseases and general condition by saliva Biomarkers

malady / state	Salivary Biomarkers	Literature
AIDS	HIV	C. Liu et al.
hepatitis A	total anti-HaV	L. A. Amado et al.
hepatitis B	anti-HBs	〃
hepatitis C	anti-HCV	〃
Diabetes	glucose	S. Kumar et al.
Stomach ulcer	Helicobacter pyloti	H. Momtaz et al.
Multiple sclerosis	IgG	N. Ramroodi et al.
Breast cancer	HER2	D. De Abreu Pereira et al.
Colorectal cancer	extracellular vesicles	Y. Yoshioka et al.
Oral Cancer	microRNAs	F. Momen-Heravi et al.
Prostate cancer	PSA	N. Shiki et al.
Sexual cycle, pregnancy	sex hormones	C. Matsuki et al.
Stress-related diseases	cortisol	A. Akacali et al.
〃	α-amylase	〃
Smoking	cotinine	J. Stragierowicz et al.
Prohibited drug, narcotics	amphetamine	K. Langel et al.
〃	cocaine	〃
〃	morphine	〃

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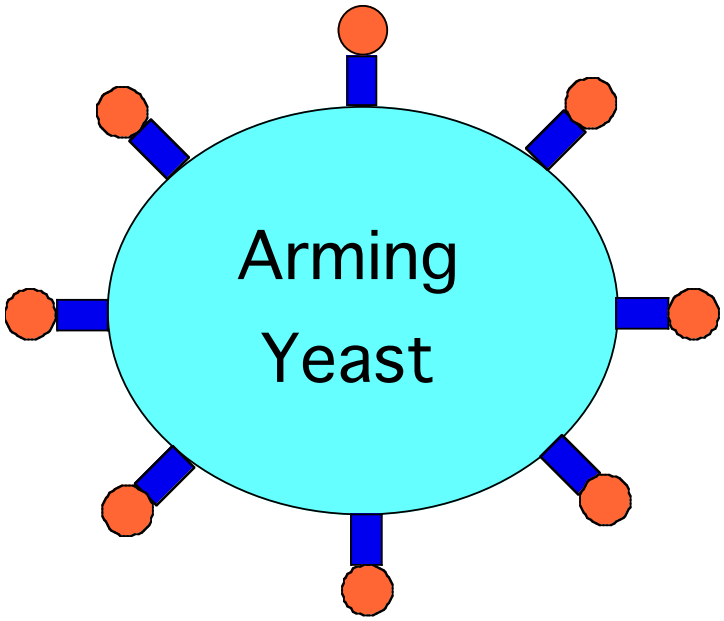
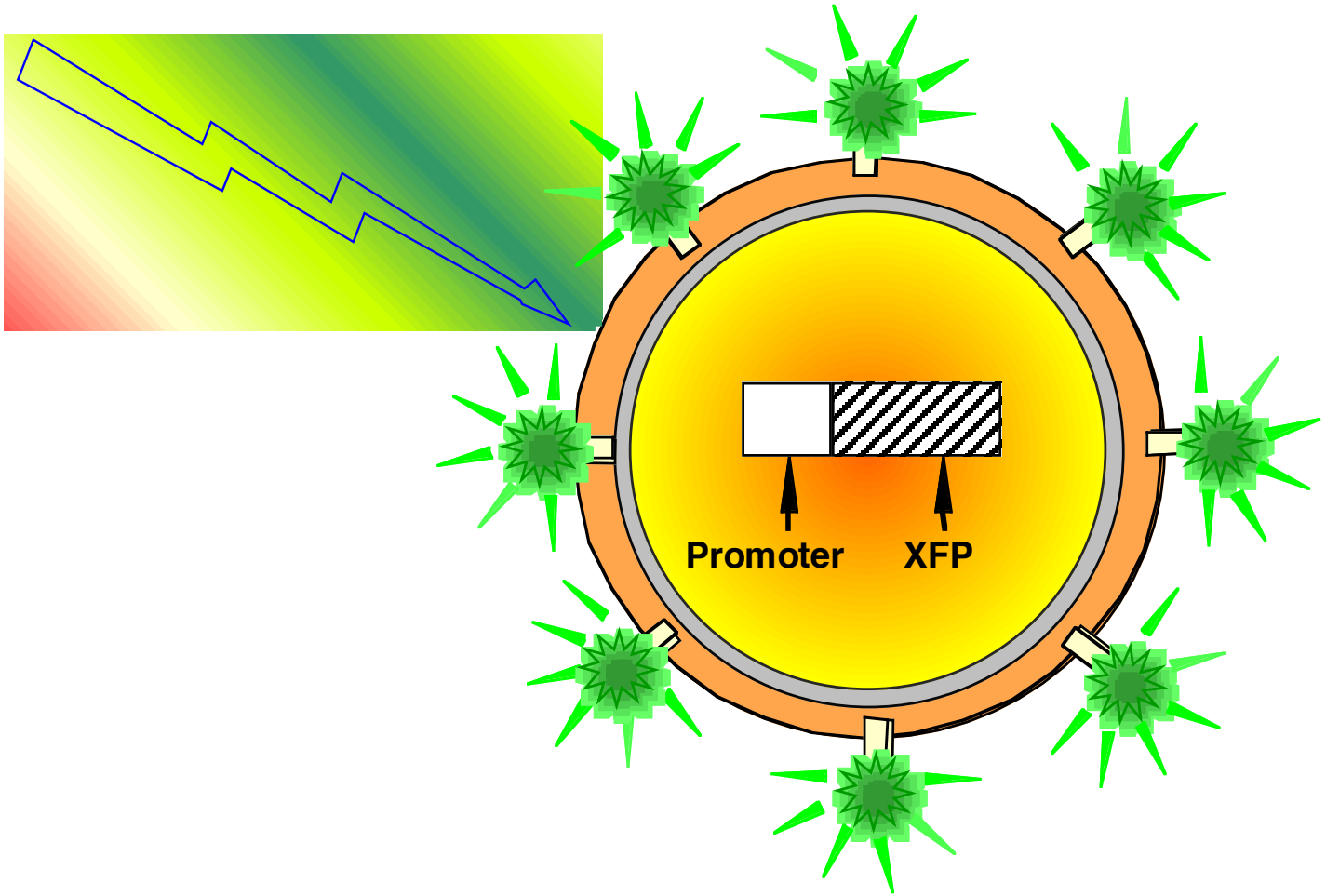
Yeast molecular display

Created cells by molecular display system are called “Arming yeast”.



Arming budda
千(1,000)手(arm)観音
”Senju-kannon”(in Japanese)

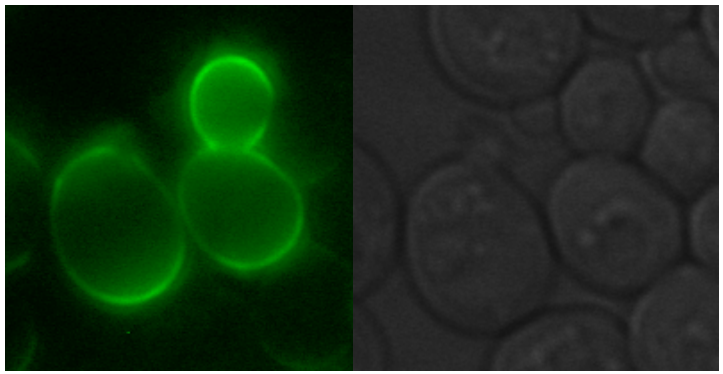
Arming Yeast with Responses to Environmental Changes



Selection of the antigen

- ***Candida* 症に対する候補抗原**

Gene Symbol	Protein Names	Accession	bp	aa	kDa	Description
ENO1	Enolase1	XM_706790	1323	**440**	**47.2**	enzyme of glycolysis and gluconeogenesis; major cell-surface antigen



Display of Eno1p
(*S. cerevisiae*)

For development of novel anfifungal peptide

Summary

- *C. albicans* proteases (Sap 1-10) were characterized.
- The specific peptide was applied to diagnosis of Candidiasis.
- Oral vaccine against candidiasis is also proposed.
- The specific peptide was also applied to combination of antimicrobial peptide.
- We propose comprehensive strategy including diagnostic tools, antifungal drugs and vaccines.

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