The 8th Technology Presentation

June 3rd 2011

Sysmex Corporation

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Member of Managing Board and Executive Officer
Head of R&D

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② Detection technology for methylated DNA
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2. Strategy & Progress of R&D

Mitsuru WATANABE
Member of Managing Board and Executive Officer
Head of R&D

2. Strategy & Progress of R&D

（1）Direction & Strategy R&D

（2）Progress status in launching stage

- Innovative technology in Next generation of hematology system –

① Blood testing technology (New approach for improvement of usability)

② New platelet counting technology (Enhanced accuracy by platelet specific staining)

③ High accurate measurement technology of leukocyte

④ Measurement technology for Hematopoietic Cell（HPC）

2. （1） Outline of Technology Strategy

Vision of R&D activity

Sysmex Way

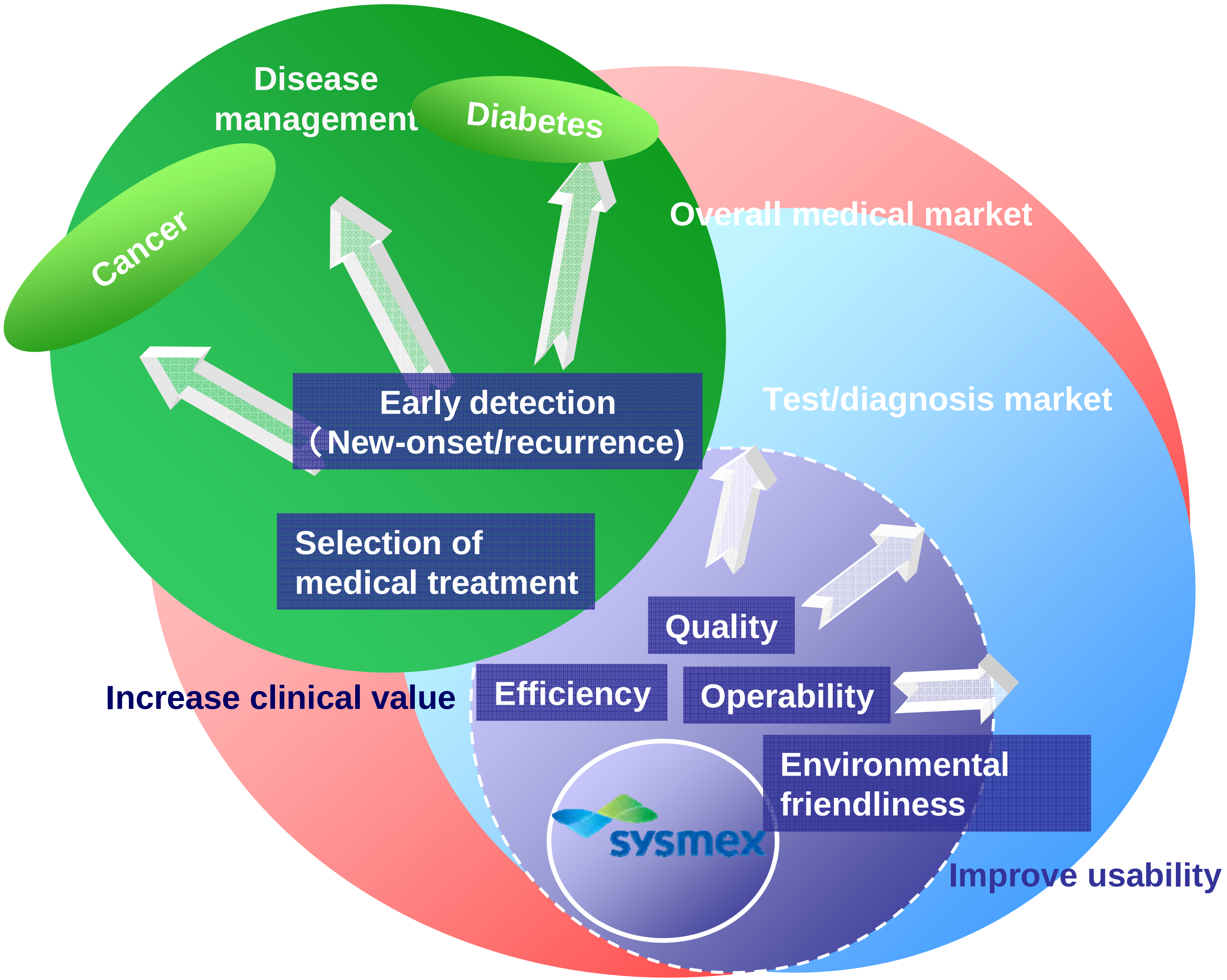
A Unique & Global Healthcare Testing Company

Providing highly valuable diagnostics testing
to optimize and standardize medical care

- Improvement of QOL / extension of healthy life expectancy
- Increasing of Medical economy value

Shaping the advancement of health care

Direction of R&D activity



Disease management

Diabetes

Cancer

Overall medical market

Early detection (New-onset/recurrence)

Test/diagnosis market

Selection of medical treatment

Quality

Efficiency

Operability

Increase clinical value

Environmental friendliness

Improve usability

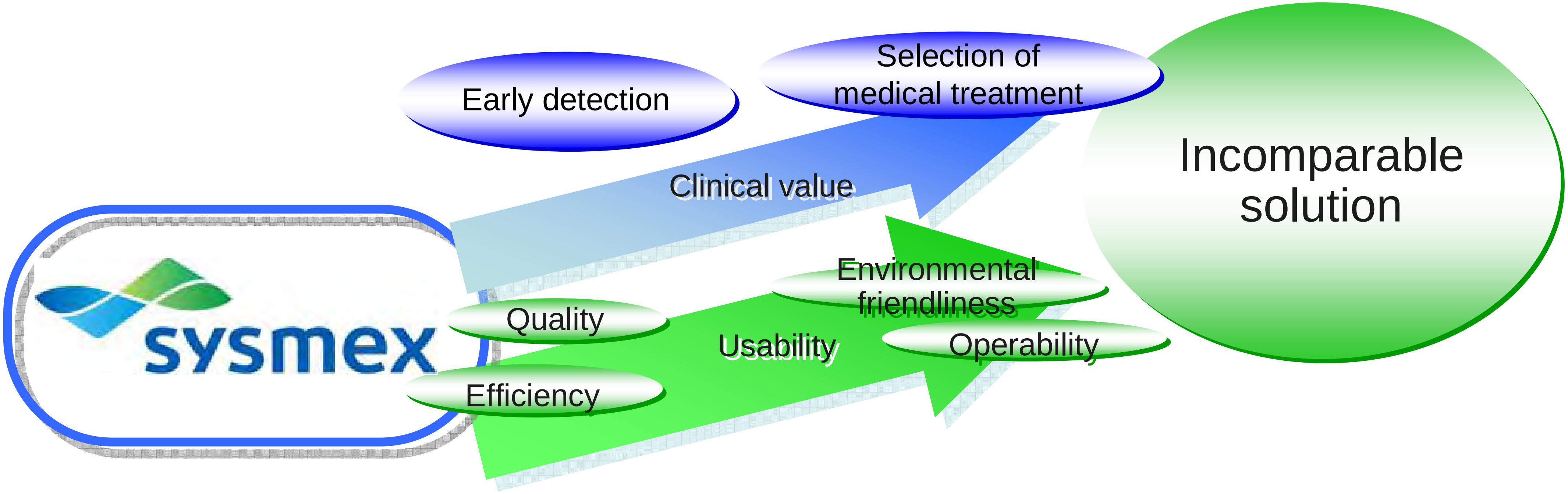
Subject of future investigation as front-runner

Major electronics company entering into healthcare business

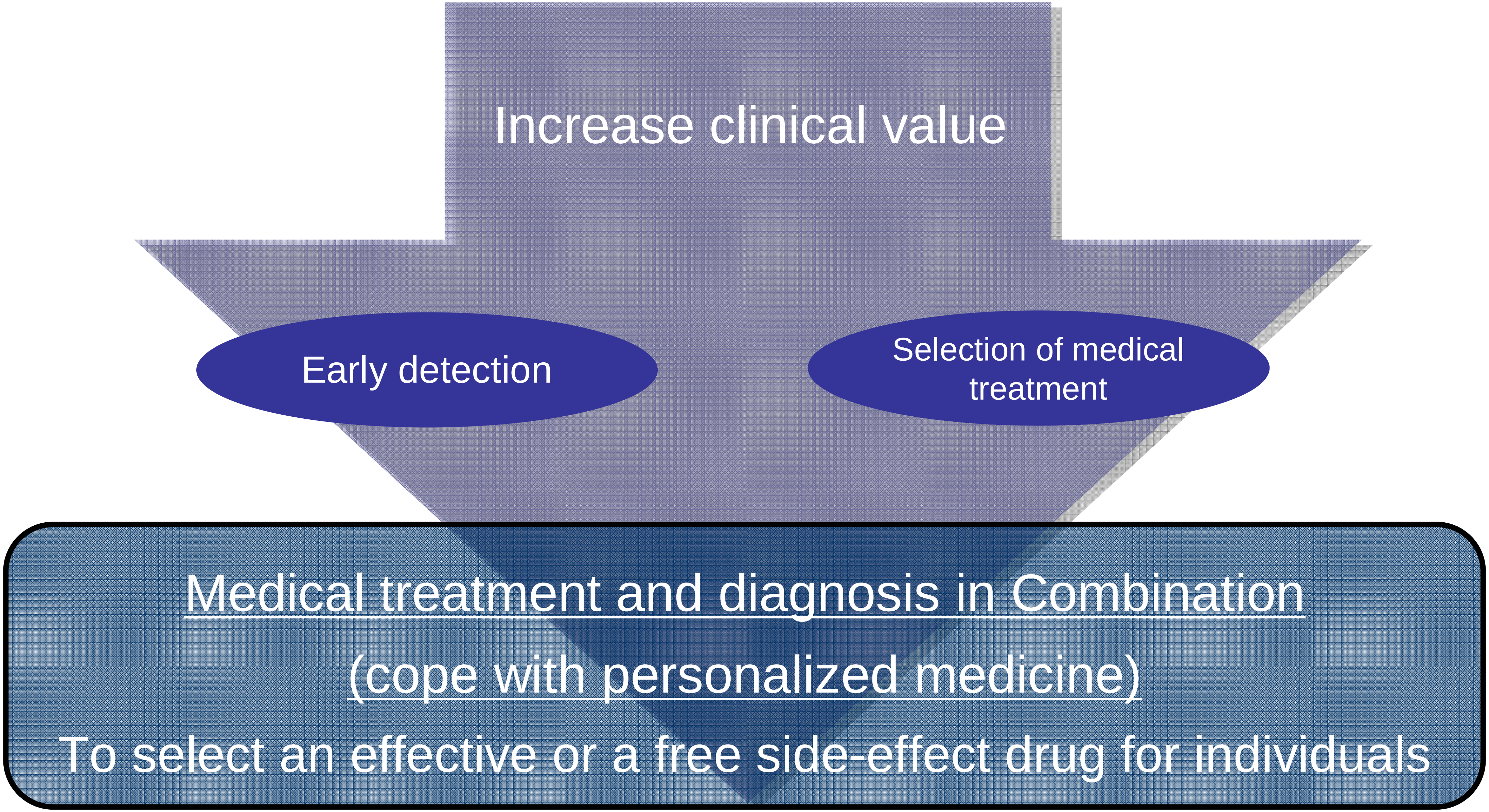
GE **Philips** **SIEMENS** **SAMSUNG** **SONY**

Advanced IT and usability technology with huge capital

Aim for innovative usability improvement besides increase of clinical value


Early detection
Selection of medical treatment
Clinical value
Incomparable solution
sysmex
Environmental friendliness
Quality
Usability
Operability
Efficiency

Outline of Technology Strategy（1）



Increase clinical value

Early detection

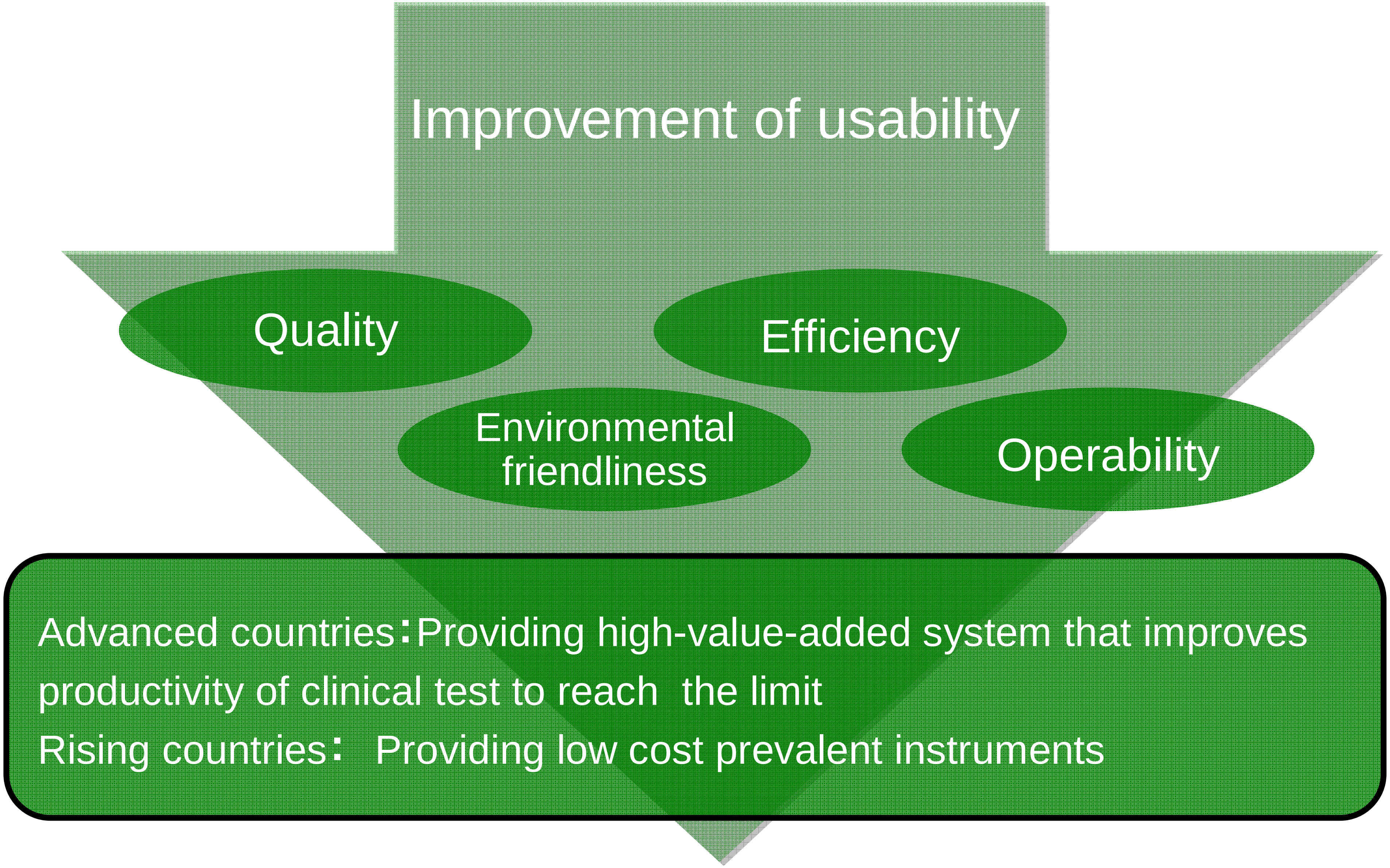
Selection of medical treatment

Medical treatment and diagnosis in Combination

(cope with personalized medicine)

To select an effective or a free side-effect drug for individuals

Outline of Technology Strategy（1）



Improvement of usability

Quality

Efficiency

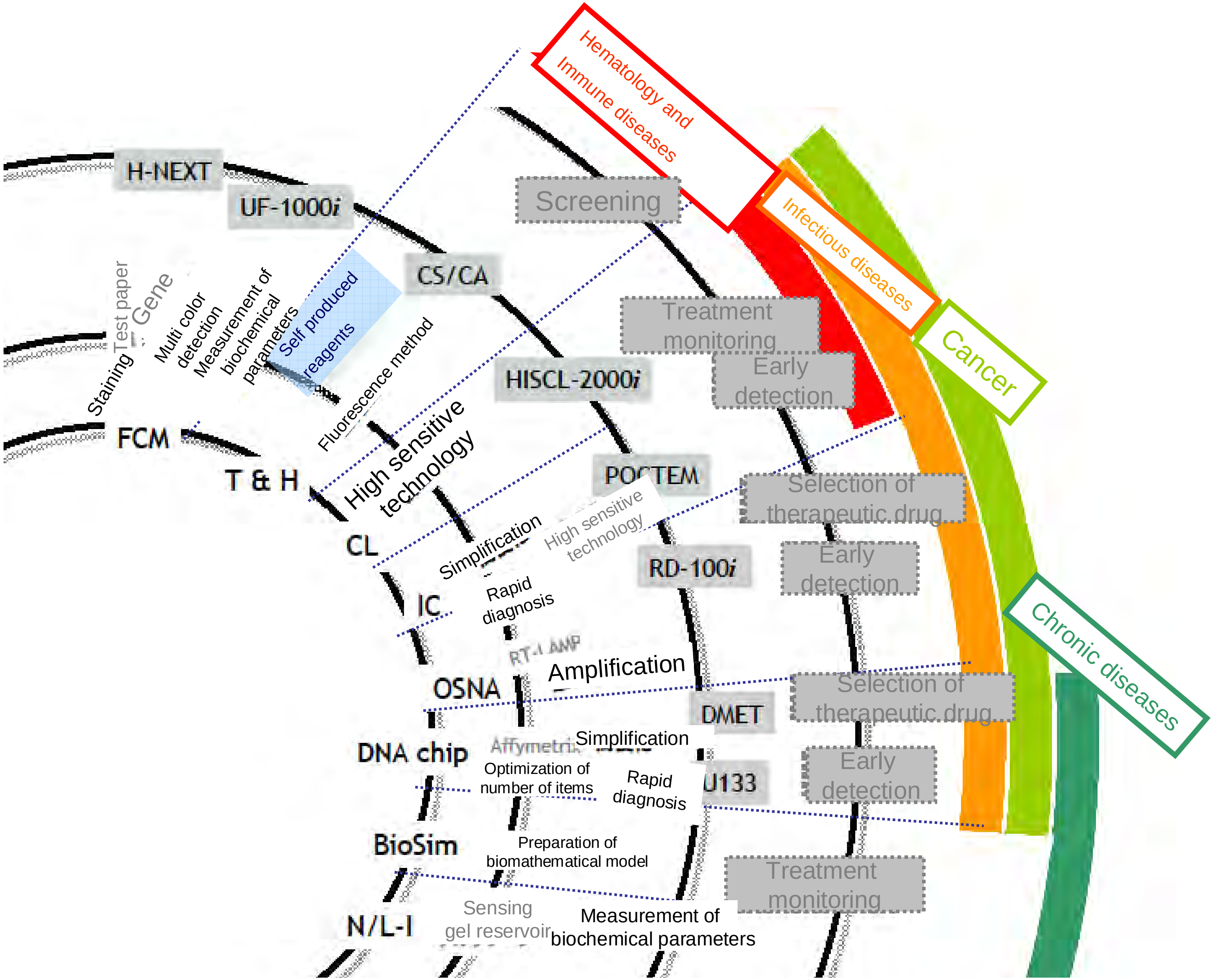
Environmental friendliness

Operability

Advanced countries：Providing high-value-added system that improves productivity of clinical test to reach the limit

Rising countries： Providing low cost prevalent instruments

Technology platform


H-NEXT
UF-1000i
CS/CA
HISCL-2000i
POCTEM
RD-100i
DMET
U133
FCM
T & H
CL
IC
OSNA
DNA chip
BioSim
N/L-I
Staining
Test paper
Gene
Multi color detection
Measurement of biochemical parameters
Self produced reagents
Fluorescence method
High sensitive technology
Simplification
High sensitive technology
Rapid diagnosis
RT-LAMP
Amplification
Affymetri
Simplification
Optimization of number of items
Rapid diagnosis
Preparation of biomathematical model
Sensing gel reservoir
Measurement of biochemical parameters
Screening
Treatment monitoring
Early detection
Selection of therapeutic drug
Early detection
Selection of therapeutic drug
Early detection
Treatment monitoring
Hematology and Immune diseases
Infectious diseases
Cancer
Chronic diseases

2.(2) Progress status in launching stage

- Innovative technology in Next generation of hematology system -

① Blood testing technology
(New approach for improvement of usability)

② New platelet counting technology
(Enhanced accuracy by platelet specific staining)

③ High accurate measurement technology of leukocyte

④ Measurement technology for Hematopoietic Cell (HPC)

2.(2) Progress status in launching stage

- Innovative technology in Next generation of hematology system -

① Blood testing technology

(New approach for improvement of usability)

① Blood testing technology
- New approach for improvement of usability -

Module system control technology :

To establish device configuration meeting various customer’s needs by combining device module

Measurement channel and measurement mode

		XN-20		XN-10			
		[A1]	[A2]	[B1]	[B2]	[B3]	[B4]
Measurement channel	WNR	✔	✔	✔	✔	✔	✔
	RBC/PLT	✔	✔	✔	✔	✔	✔
	HGB	✔	✔	✔	✔	✔	✔
	WDF	✔	✔	✔	✔	✔	✔
	WPC	✔	✔				
	RET	✔	✔	(✔)		(✔)	
	PLT-F	(✔)	−	(✔)	(✔)	−	−
Measurement mode	WB、LW、PD	✔	✔	✔	✔	✔	✔
	BF	▲	▲	▲	▲	▲	▲

【Ex.】

Measurement module Sampler module

University hospital

XN-2000

XN-20 X 2 + SA-20 =

Max: 200 test/hr

Medium scale hospital

XN-1000

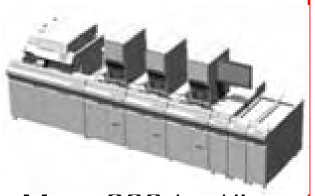
XN-10 X 1 + SA-10 =

Max: 100 test/hr

XN-9000

Testing center

XN-10 X 4
XN-20 X 2 + CV-50 =

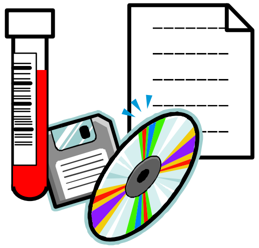
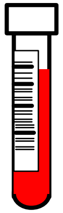
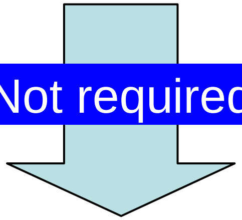
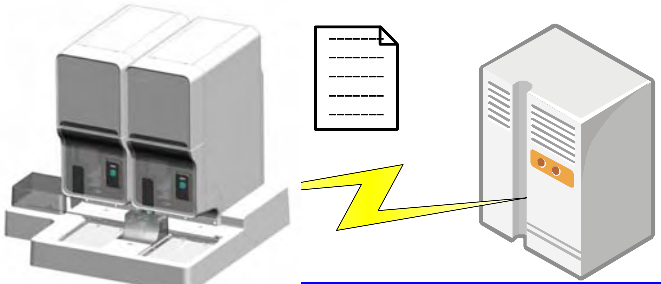


Max: 900 test/hr

Flexible to a variety of needs！

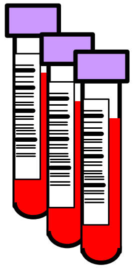
① Blood testing technology
- New approach for improvement of usability -

Automated accuracy control system

	XE series	New generation system
1. Delivery of a new lot control to the customers	 Delivery with standard value in media	
2. Record a standard count to a device by customers		 Not required
3. Quality control material measurement	 Require a manual accuracy control	 Network delivery of standard count Automated record at measurement time （no require operations）

① Blood testing technology
- New approach for improvement of usability -

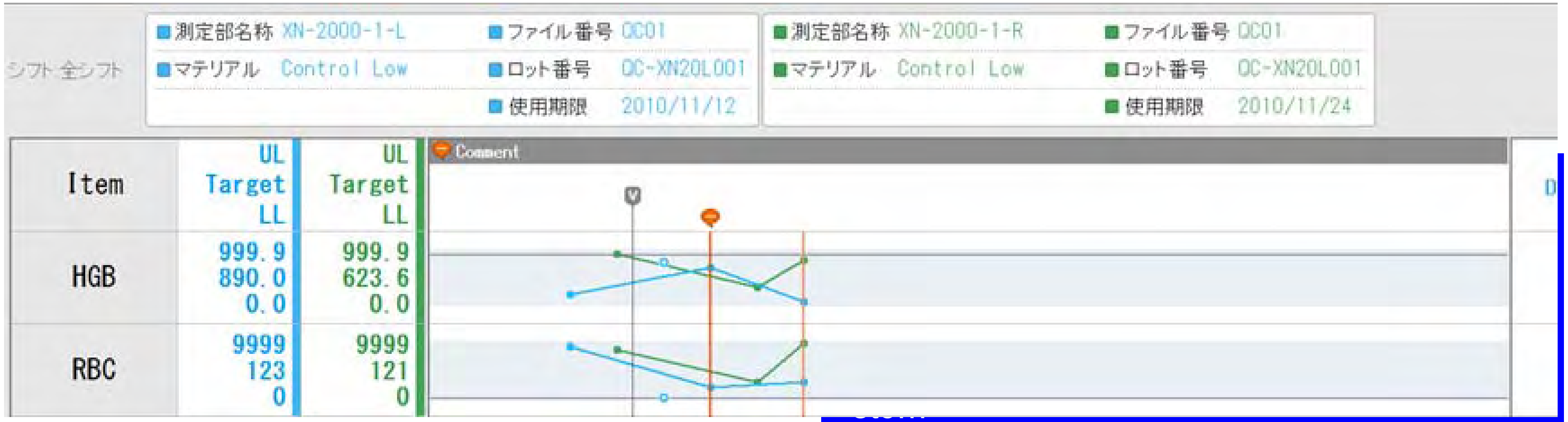
- Automated accuracy control system by automatic sample delivery system



＜test sample＞
Automated delivery to either measurement module with measurement parameter

＜control＞
Automated delivery to both measurement module

- Improvement of operability/user-friendliness of an accuracy control panel



シフト 全シフト

■測定部名称 XN-2000-1-L ■ファイル番号 QC01
■マテリアル Control Low ■ロット番号 QC-XN20L001
■使用期限 2010/11/12

■測定部名称 XN-2000-1-R ■ファイル番号 QC01
■マテリアル Control Low ■ロット番号 QC-XN20L001
■使用期限 2010/11/24

Item	UL Target LL	UL Target LL
HGB	999.9 890.0 0.0	999.9 623.6 0.0
RBC	9999 123 0	9999 121 0

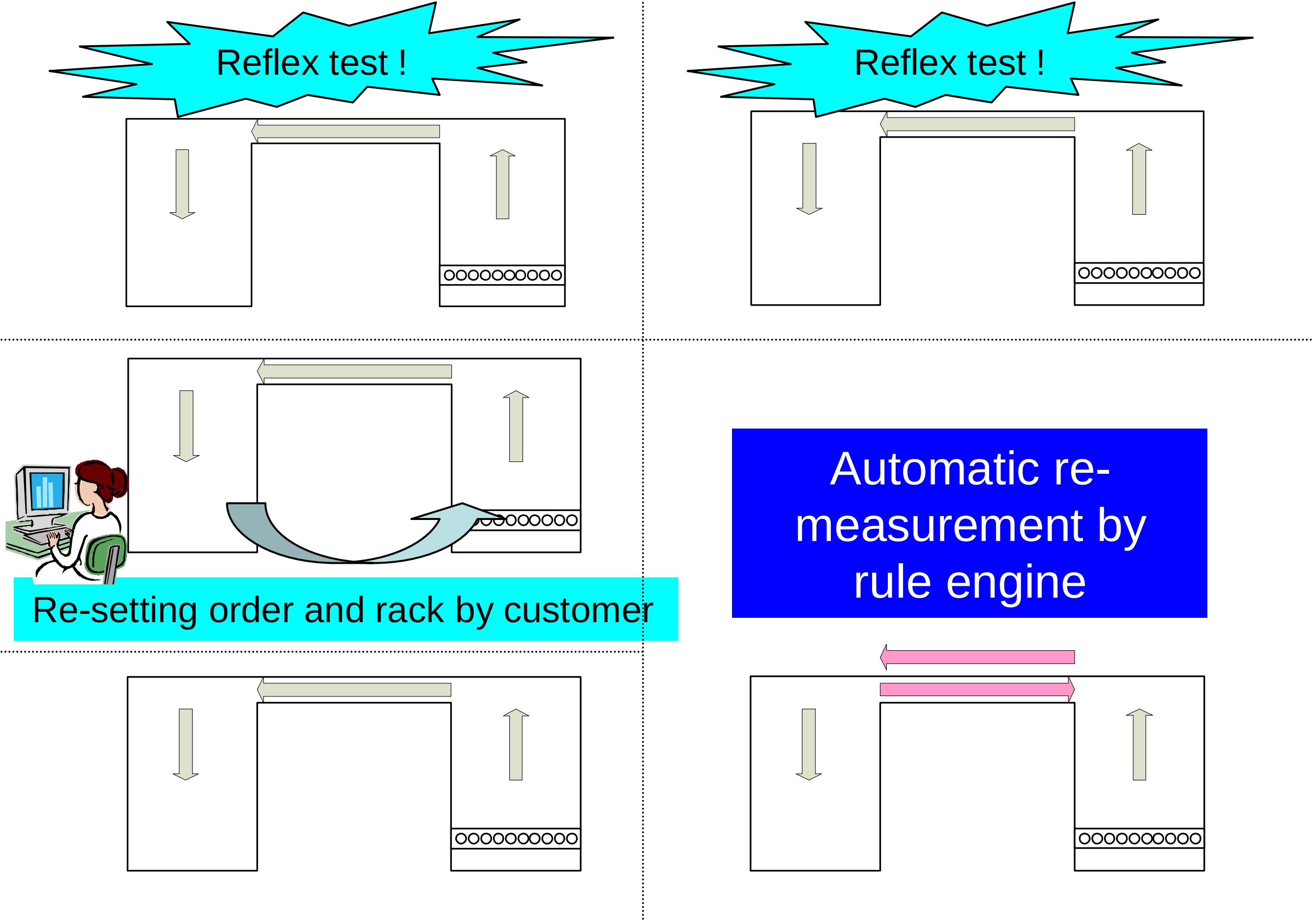
Ex. Quality control chart display

① Blood testing technology
- New approach for improvement of usability -

Automatization for re-measurement

Conventional series

New-generation system



Reflex test !
Reflex test !
Re-setting order and rack by customer
Automatic re-measurement by rule engine

1. First test

2. Sample pickup and re-setting order

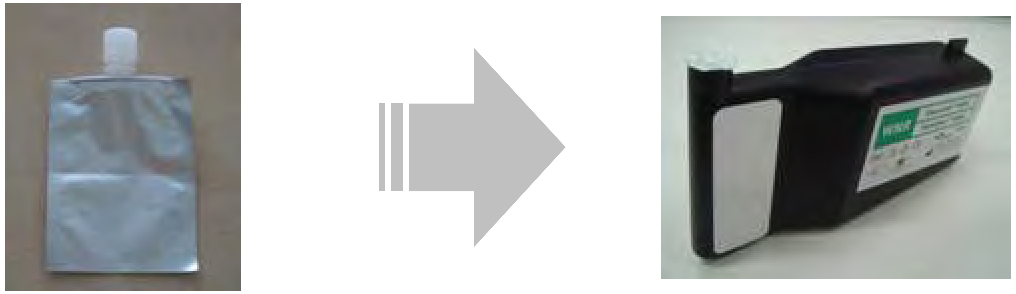
3. Re-test / additional measurement

① Blood testing technology
- New approach for improvement of usability -

Reagent cartridge loading and automated recognition by RF-ID technology

- Improvement of connect-ability (one-touch replace)

⇒reduce replacing time in 25%



※staining liquid set unit of
new product

- Reagent control function by RF-ID technology (wireless tag)

(Reagents name, lot number, number of tests etc.)

Read lot number/expire date etc. with setting reagent by RF-ID technology

RF-ID: Radio Frequency Identification (Individual identification by radio waves)

① Blood testing technology
New approach for improvement of usability

Standardization of concentrated reagents/ preparation unit

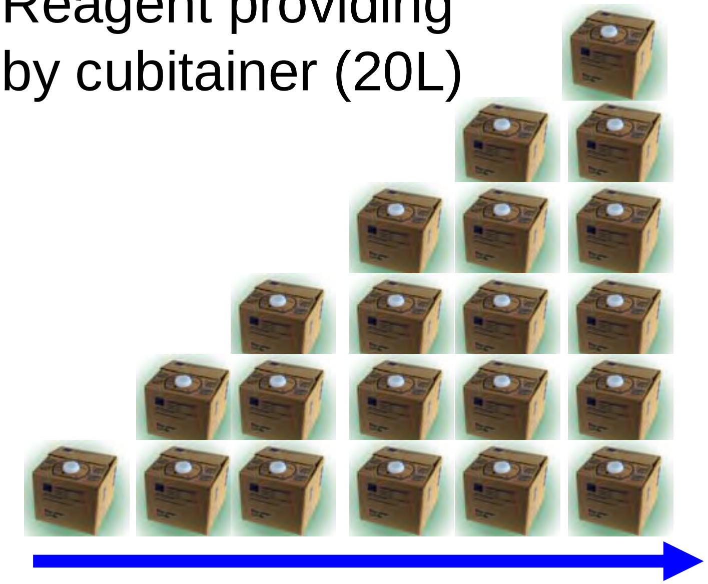
Conventional device

Device

+

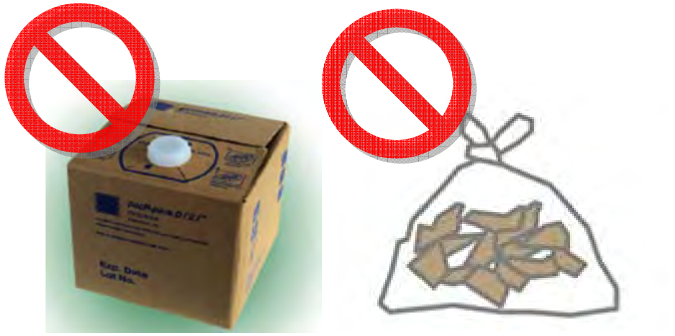
Reagent (cubitainer etc.)

Reagent providing by cubitainer (20L)



Increasing workload as growing the number of tests (man-hour/space)

Realization of reagent supply system



Automation / simplification of testing work
Reduction of waste

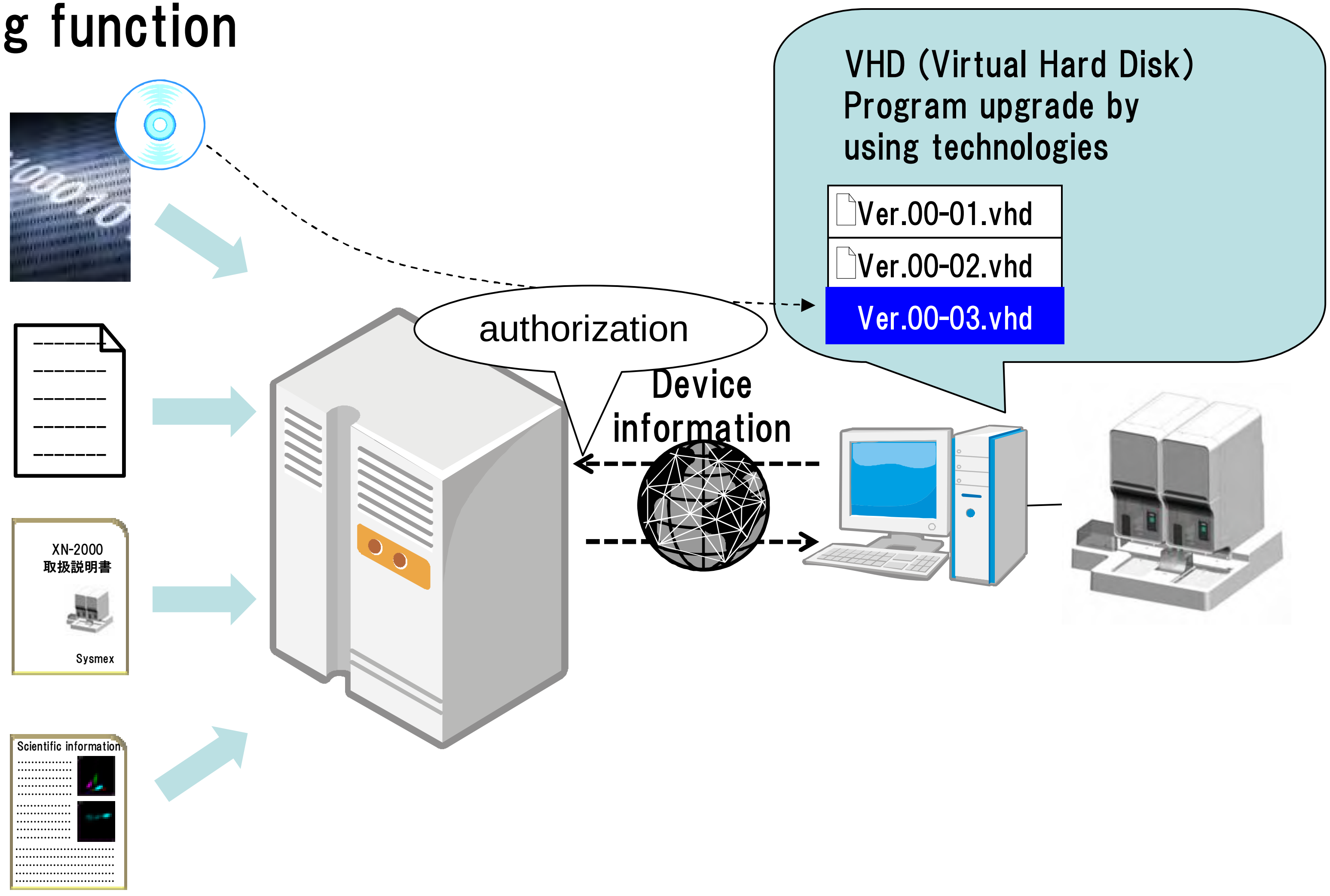
Reagent providing to XN system

Preparation unit

Concentrated reagent

① Blood testing technology
New approach for improvement of usability

Online up-dating function


XN-2000
取扱説明書
Sysmex
Scientific information

Program

Control/Std
value

Manual

Academic
information
(plan)

authorization

Device
information

VHD (Virtual Hard Disk)
Program upgrade by
using technologies

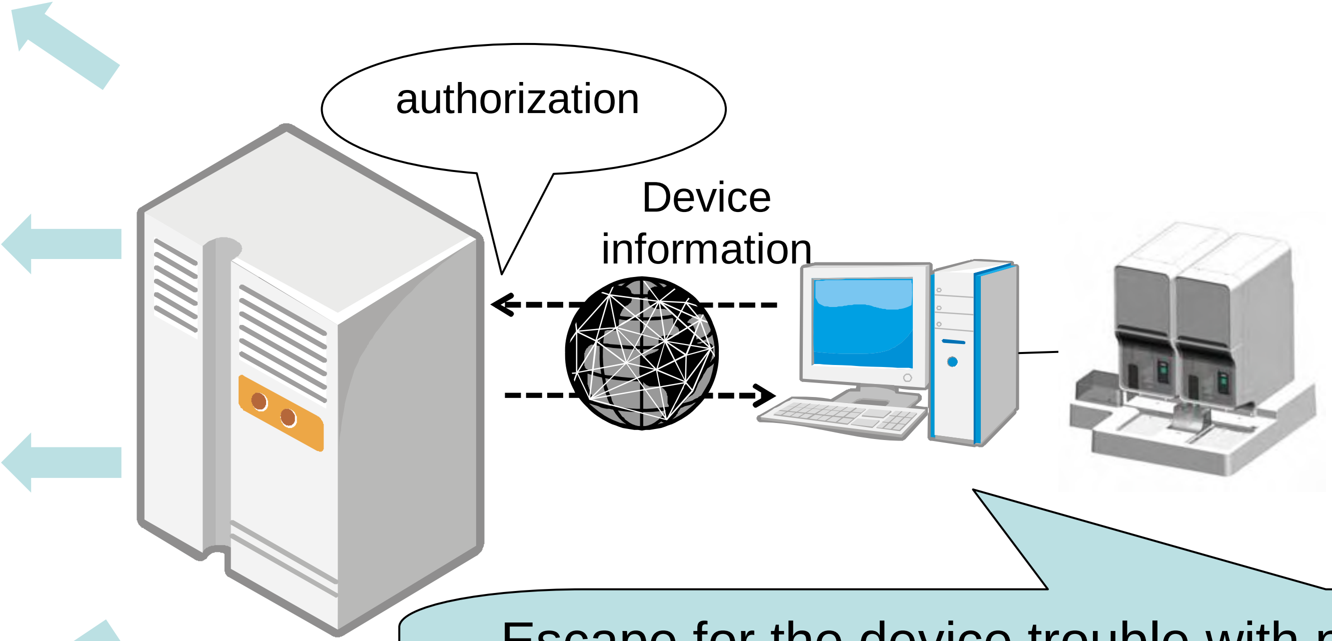
Ver.00-01.vhd
Ver.00-02.vhd
Ver.00-03.vhd

Currently developing
delivery system

① Blood testing technology
New approach for improvement of usability

Remote monitoring function by SNCS

After service → Pre-maintenance service



Time monitoring for temperature and presser stable state

Condition of each sensor

Error records

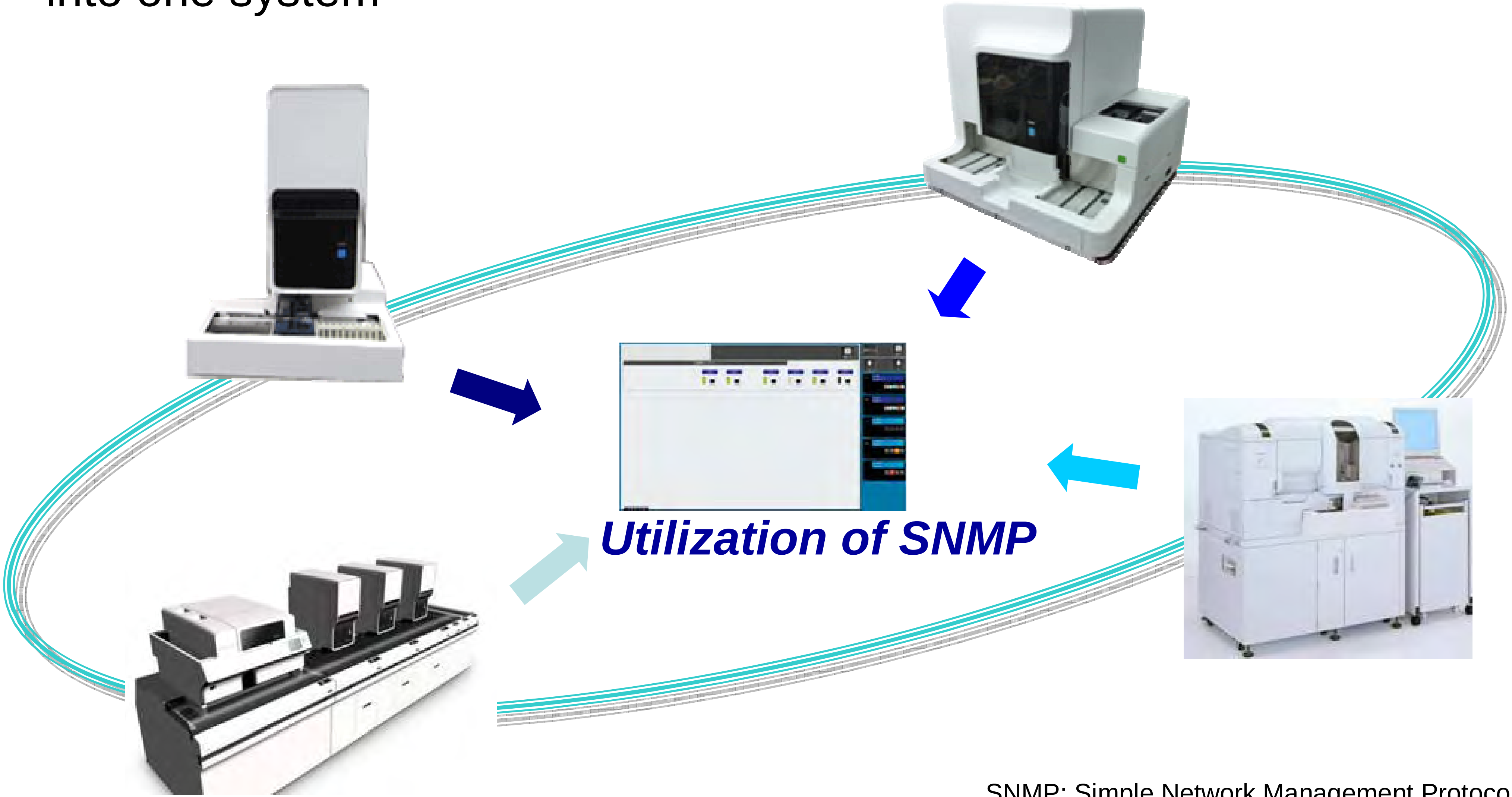
Back up of setting

Escape for the device trouble with pre-maintenance for protect by regular state remote monitoring system

Currently developing
delivery system

① Blood testing technology
– New approach for improvement of usability –

- Improvement of usability by integrating information from each device into one system



Utilization of SNMP

SNMP: Simple Network Management Protocol

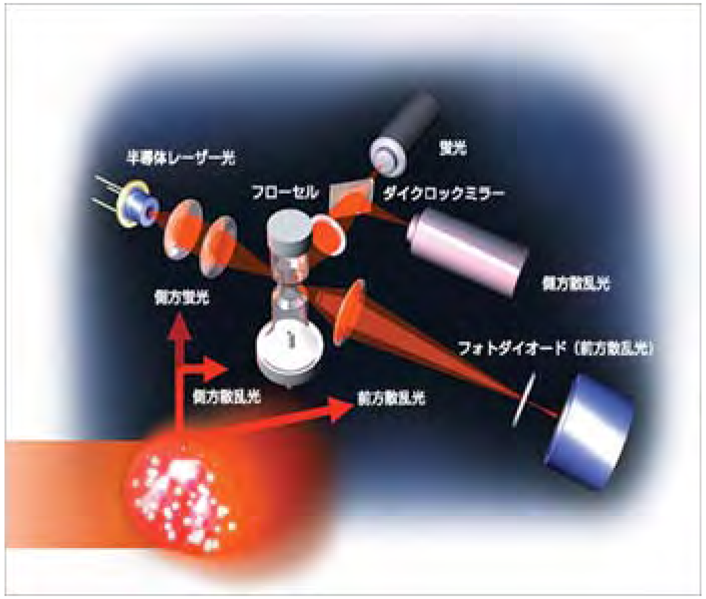
2.（2）Progress status in launching stage

- Innovative technology in Next generation of hematology system -

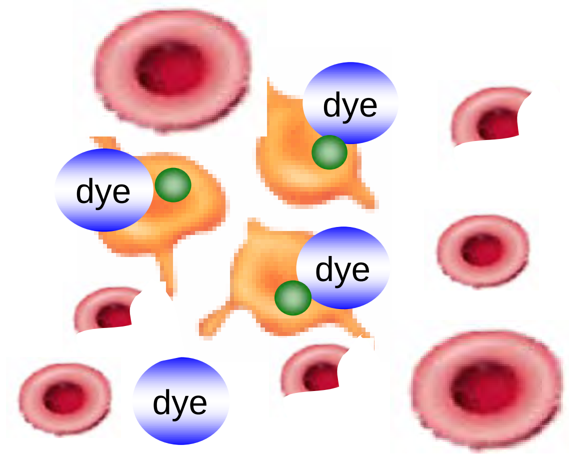
② New platelet counting technology (Enhanced accuracy by platelet specific staining)

② New platelet counting technology (Enhanced accuracy by platelet specific staining)

method：Flow-cytometry

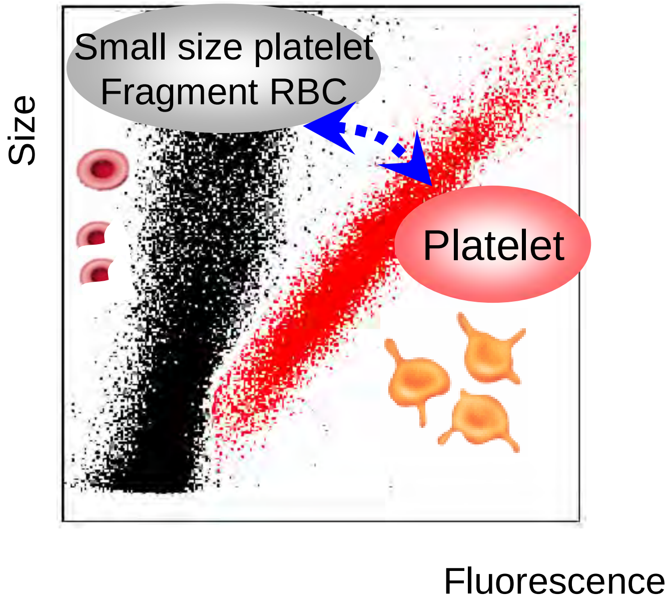

半導体レーザー光
蛍光
フローセル
ダイクロックミラー
側方散乱光
側方蛍光
フォトダイオード（前方散乱光）
側方散乱光
前方散乱光

platelet specific staining


dye
dye
dye
dye

Realization of platelet specific staining by low cost Fluorescent dye

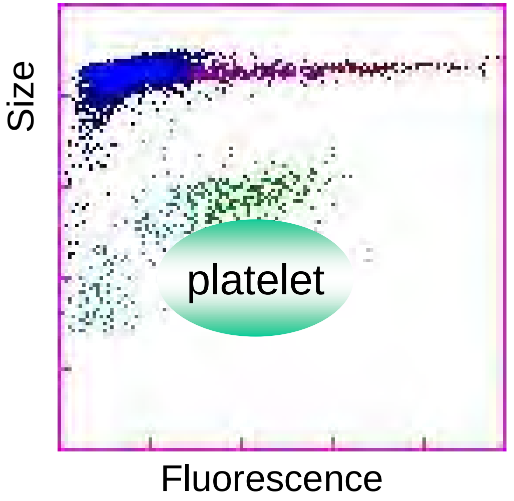
Example data



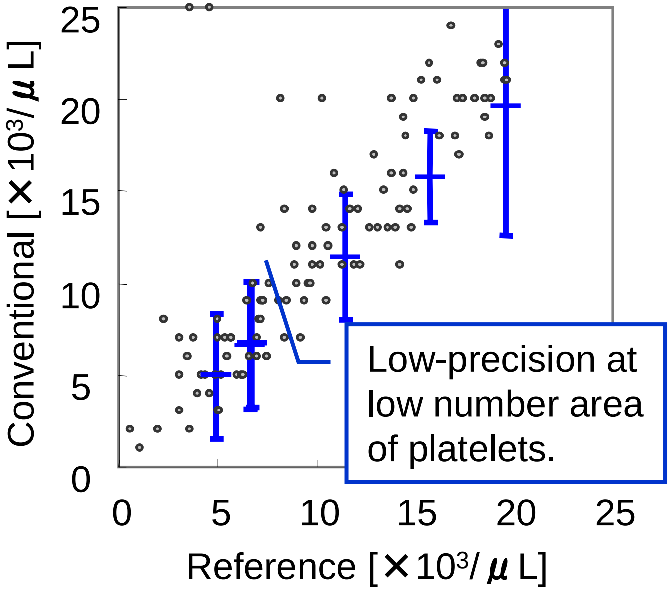
Adequate platelet blood transfusion is enabled by realizing specificity and sensitivity around the value that were the index of the platelet blood transfusion.

② New platelet counting technology (Enhanced accuracy by platelet specific staining)

Conventional

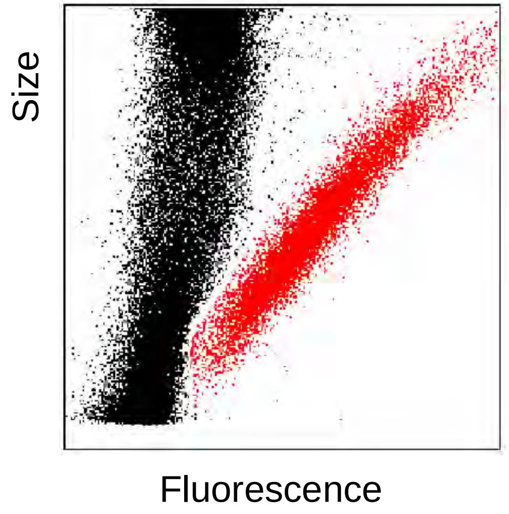


Correlation with comparison method

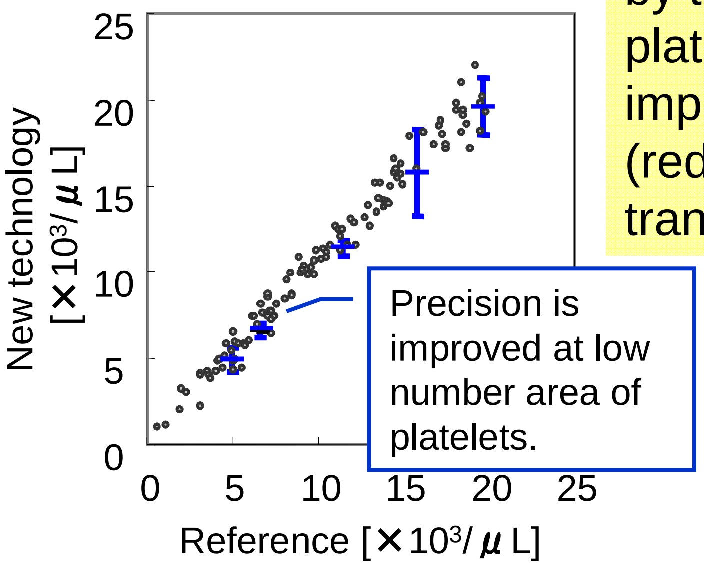


Low-precision at low number area of platelets.

New



Correlation with comparison method



Precision is improved at low number area of platelets.

Adequate platelet blood transfusion is enabled by realizing specificity and sensitivity around the value that were the index of the platelet blood transfusion.

It will contribute to the reduction of medical expenses by the reduction of the preventive platelet blood transfusion and improvement of the patient QOL (reduce the side effect of blood transfusion).

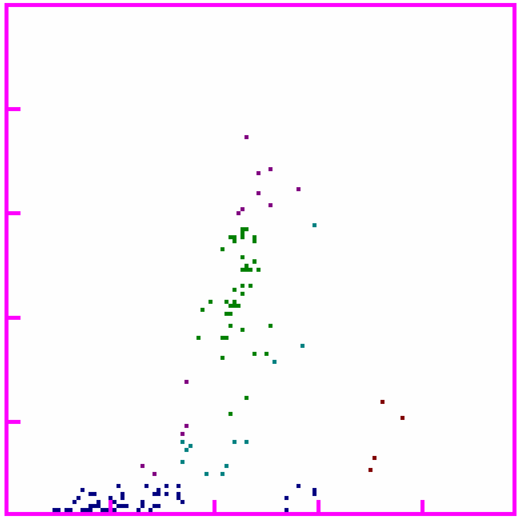
2.（2） Progress status in launching stage
- Innovative technology in Next generation of hematology system -

③ High accurate measurement technology of leukocyte

④ Measurement technology for Hematopoietic Cell（HPC）

③ High accurate measurement technology of leukocyte

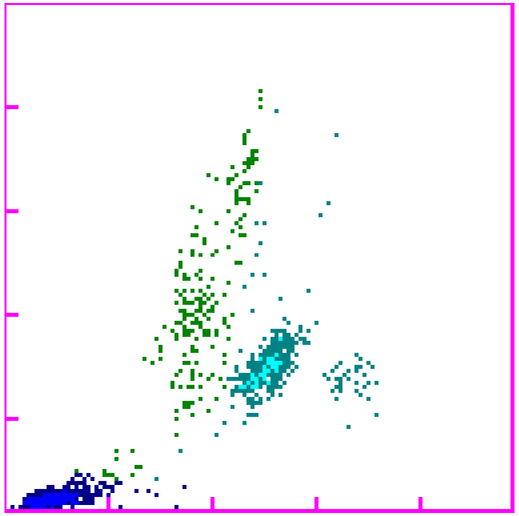
Conventional



The WBCs with a few numbers can not be classified.

Change the blood aspiration method
Increase quantity of blood analysis

New



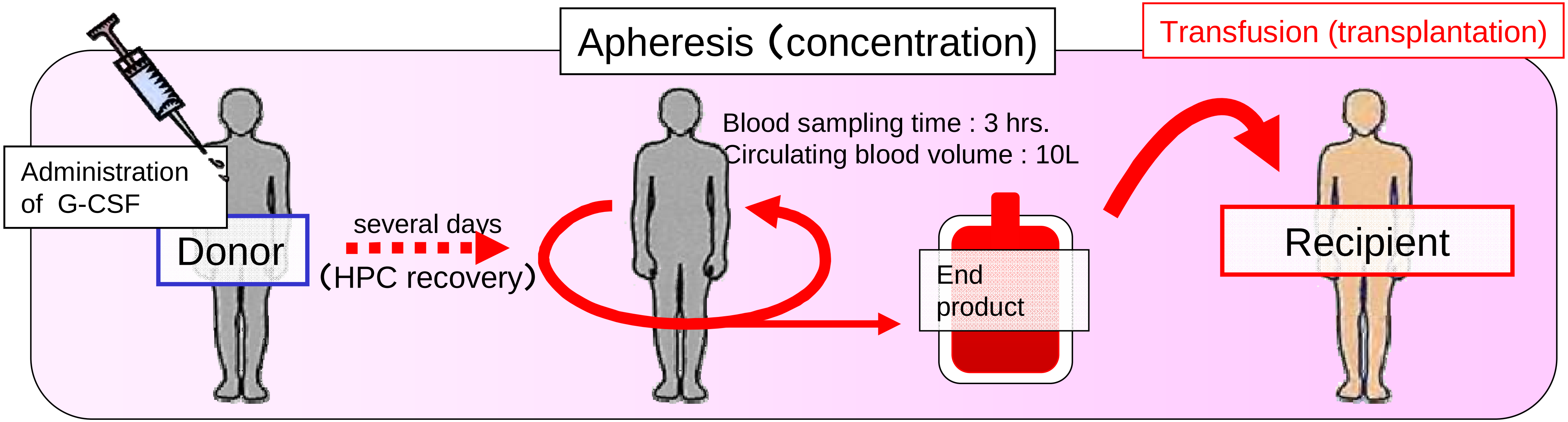
WBCs can be classified.

Specific analysis mode to automatically recognize and reanalyze the sample with a little number of WBC.
To classify the sample with low number of WBC after having reduced the volume of blood necessary by changing the aspiration method (from SRV method to pipetting method), by increasing quantity of blood analysis.

② Measurement technology for Hematopoietic stem cell (HPC)
– Application for HPC transplantation –

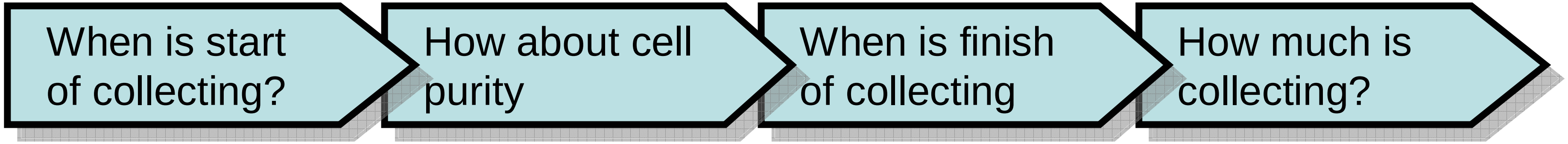
HPC transplantation：transplant HPC which is donated by donors

Treatment results strongly depends on number of HPC



Apheresis（concentration)
Transfusion (transplantation)
Administration of G-CSF
Donor
several days
（HPC recovery）
Blood sampling time : 3 hrs.
Circulating blood volume : 10L
End product
Recipient

Requirements for counting HPC

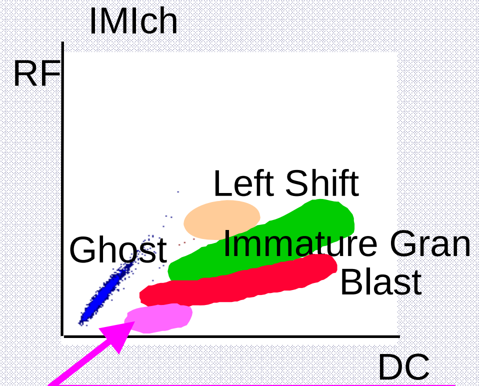


When is start of collecting?
How about cell purity
When is finish of collecting
How much is collecting?

② HPC measurement technology
–HPC measurement by next generated hematology system–

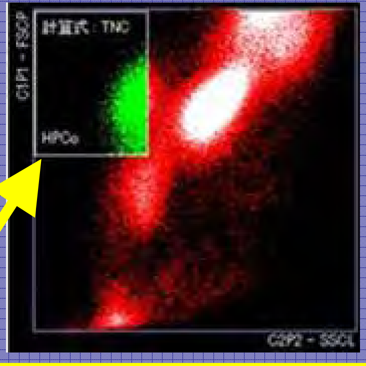
XE-2100/5000

XE-5000



HPC detection area

XN system



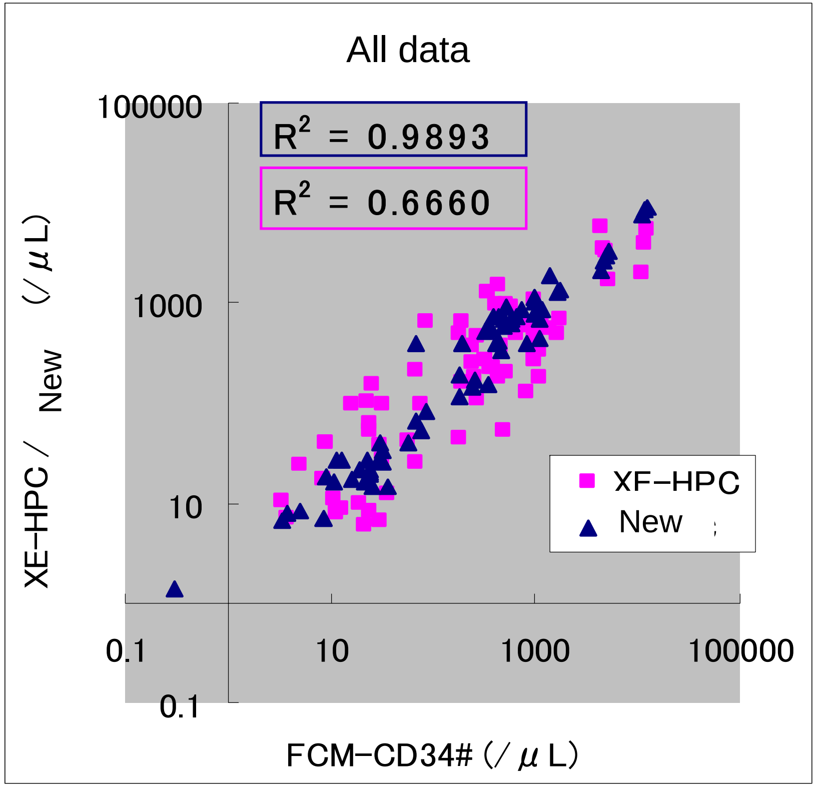
Detection area by new HPC

Product name	XE-HPC (Conventional system)	New HPC (XN series)	Characteristics of next-generation system Provision of a performance as the same as FCM method by enhancement of measurement theory and reagent technology •Possible to test at any center •Low cost and user-friendly
Measurement theory	Electric type (DC/RF)	Optical type(FCM)	
Reagent	Hemolysis reagent	Hemolysis reagent + Staining solution	
Dilution rate	250 times	50 times	
Others	–	Possible repeat test	

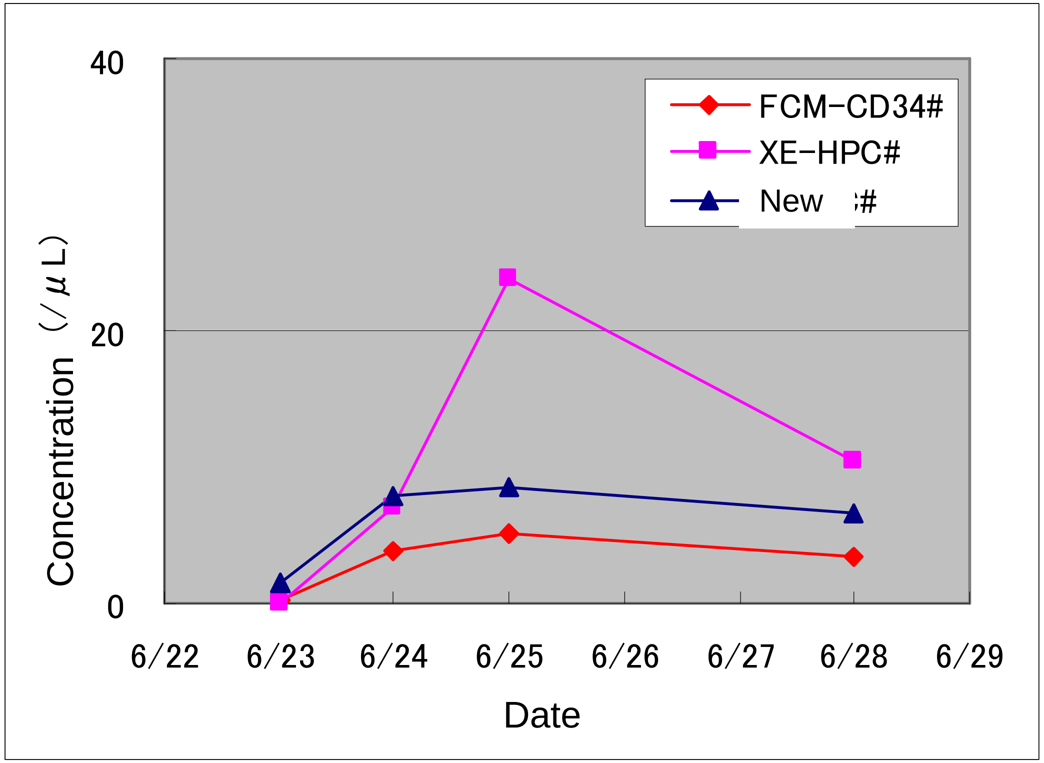
② Measurement technology for HPC

－ Evaluation result －

Allo-doner / Self transplantation 15 patients (N=59)



Self transplantation cases



New technology is positively correlated with FCM-CD34.

Sequential changes of HPC concentration new and conventional FCM-CD34.

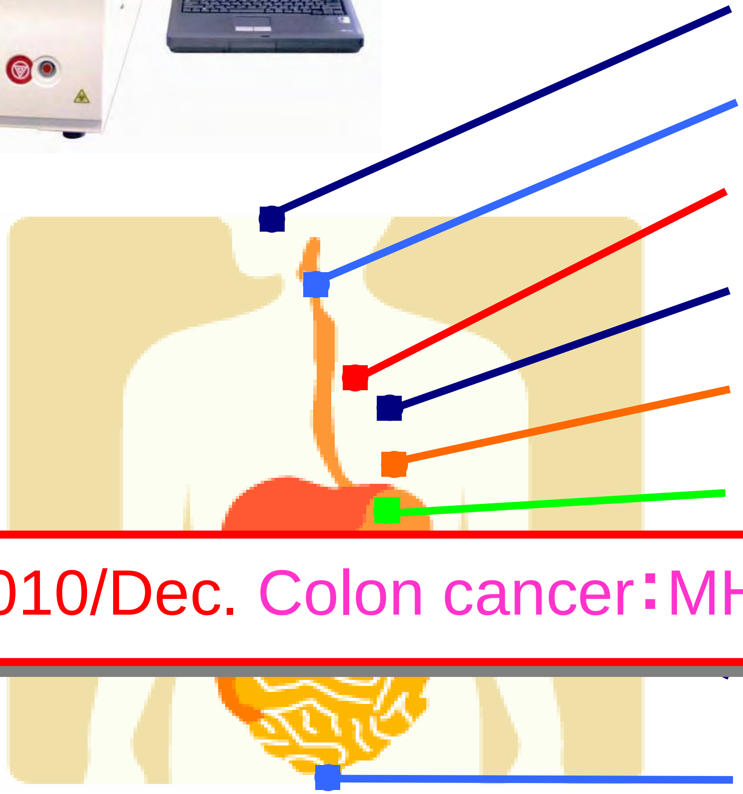
2. 3）Progress status in practical stage

① OSNA（Rapid diagnosis of lymph node metastasis detection technology）

① OSNA technology（rapid diagnosis for lymph node metastasis）

Gene amplification detection technology RD-100i

Activities aimed at expanding application



Oral cancer：Clinical study

Esophagus cancer：Clinical study

Breast cancer： Launched (Japan)

Lung cancer: Clinical study

Stomach cancer:Completed clinical evaluation

Peripheral metastasis： Clinical study

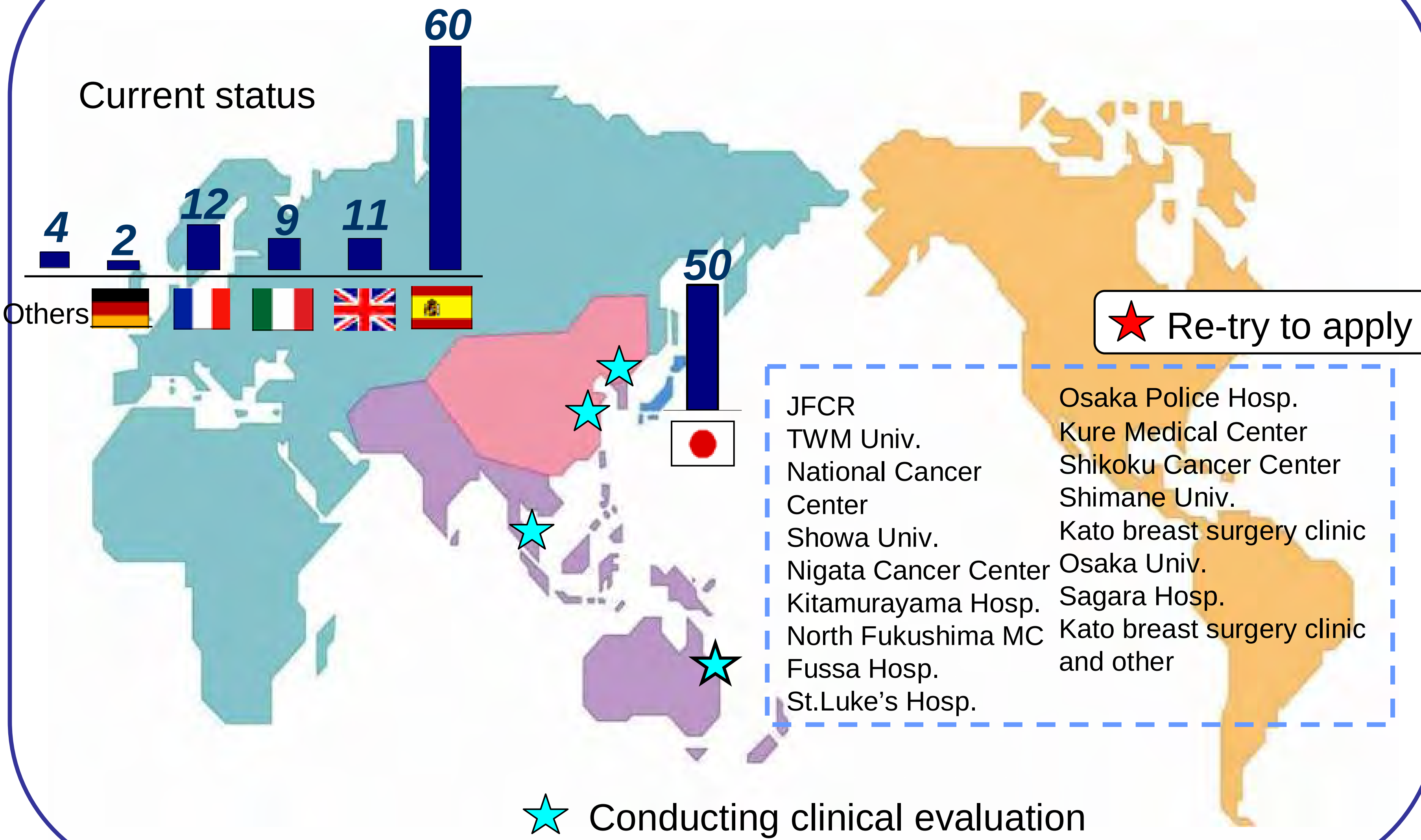
2010/Dec. Colon cancer：MHLW approval（Japan）

Melanoma： Under study

Cervical cancer： Under study

① OSNA technology（rapid diagnosis for lymph node metastasis）

– Current status of introduction of OSNA and future possibilities –



★ Re-try to apply for FDA

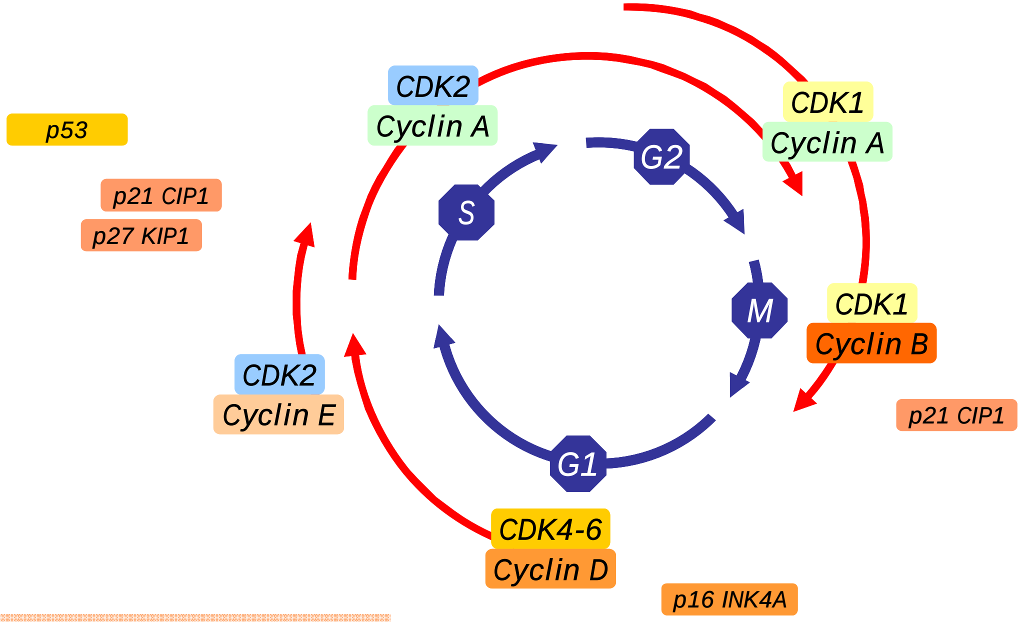
- JFCR
- TWM Univ.
- National Cancer Center
- Showa Univ.
- Nigata Cancer Center
- Kitamurayama Hosp.
- North Fukushima MC
- Fussa Hosp.
- St.Luke’s Hosp.
- Osaka Police Hosp.
- Kure Medical Center
- Shikoku Cancer Center
- Shimane Univ.
- Kato breast surgery clinic
- Osaka Univ.
- Sagara Hosp.
- Kato breast surgery clinic and other

☆ Conducting clinical evaluation

2.（3）Progress status in practical stage

② C2P（Breast cancer recurrence prediction）

② Practical application of C2P technology (breast cancer) – Cell-cycle profiling(C2P) technology –


p53
p21 CIP1
p27 KIP1
CDK2
Cyclin A
S
G2
CDK1
Cyclin A
M
CDK1
Cyclin B
p21 CIP1
CDK2
Cyclin E
G1
CDK4-6
Cyclin D
p16 INK4A

Measurement for expression level

Measurement for kinase activity

Cell proliferation dynamics
（CDK2 specific activity/CDK1 specific activity）

Clinical value

- Decision of treatment method

Hormonal treatment or chemotherapy treatment?

- Decision of anticancer drug

Which chemotherapy is effective?

Prediction of a cancer recurrence after surgery

Prediction of anticancer treatment sensitivity

Aiming for the establishment of optimized medical treatment for each patients

② C2P technology (breast cancer) in practical use

Clinical performance test

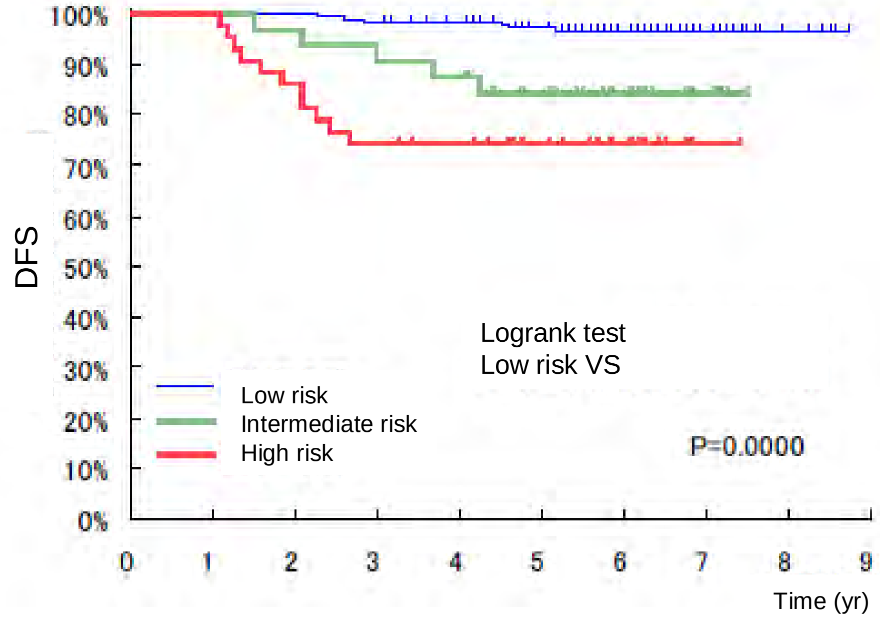
Objective:

Verify the fact that risk evaluation for C2P breast cancer recurrence with high-sensitivity method is clinical use as a factor for predicting recurrence.

Result:

C2P technology showed that statistically-significant differences, as clinical benefit, among each risk group in point of cumulative recurrence free survival ratio.

Kaplan Meier analysis



Future plan

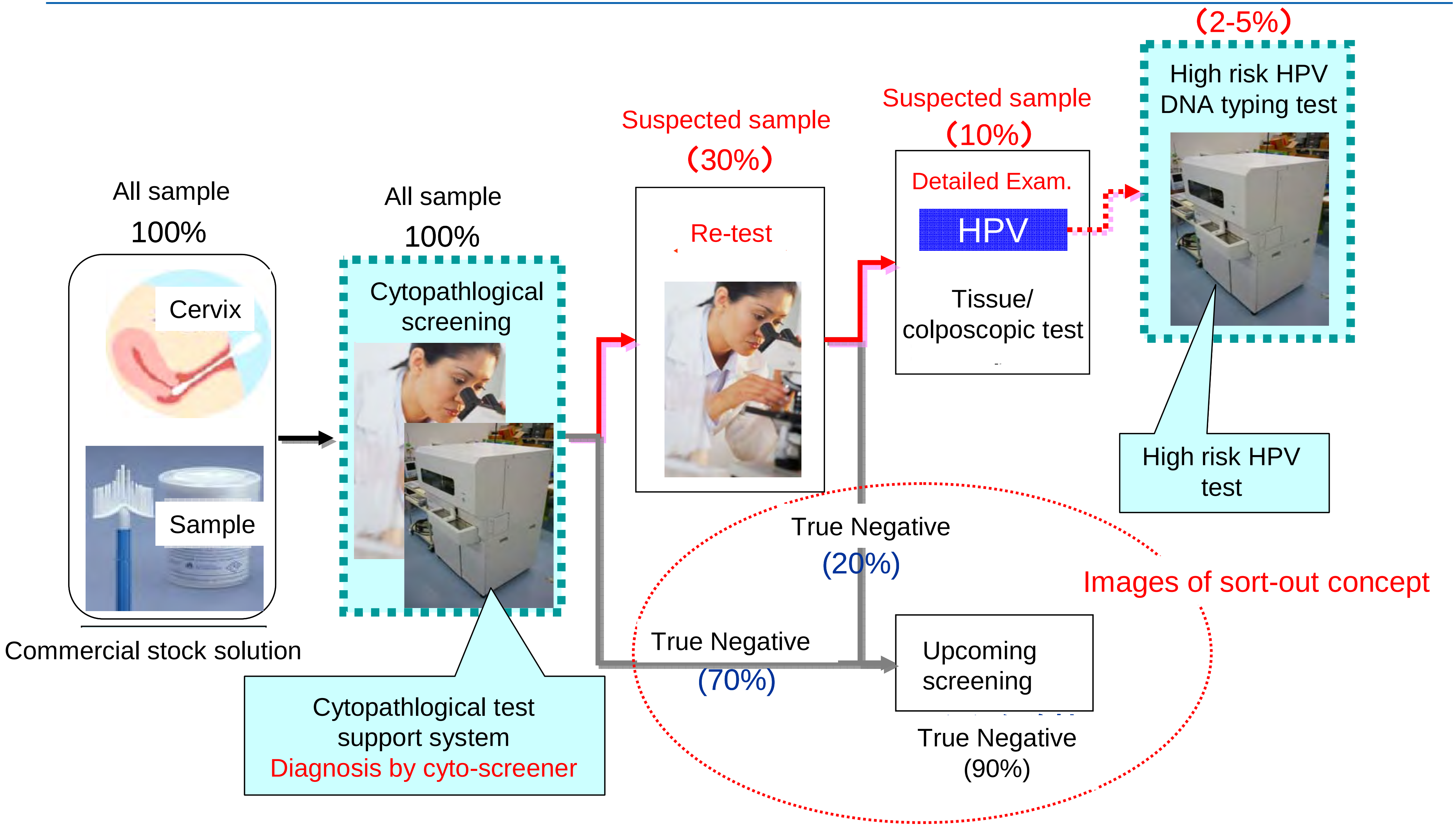
- Achieve the target results and publish the papers on clinical evaluation results and academics presentation from the members of study team.
- Development of Lab-assay business (JPN) with manual methods by the end of this year.
- Verify the clinical impact of C2P profiling for assess a create plan to full scale business.

2. (3) Progress status in practical stage

③ Cervical cancer screening

③ Cervical cancer screening

- Cervical cancer test flow -



All sample
100%

Cervix

Sample

Commercial stock solution

All sample
100%

Cytopathlogical screening

Cytopathlogical test support system
Diagnosis by cyto-screener

Suspected sample
(30%)

Re-test

Suspected sample
(10%)

Detailed Exam.

HPV

Tissue/ colposcopic test

(2-5%)

High risk HPV DNA typing test

High risk HPV test

True Negative
(20%)

True Negative
(70%)

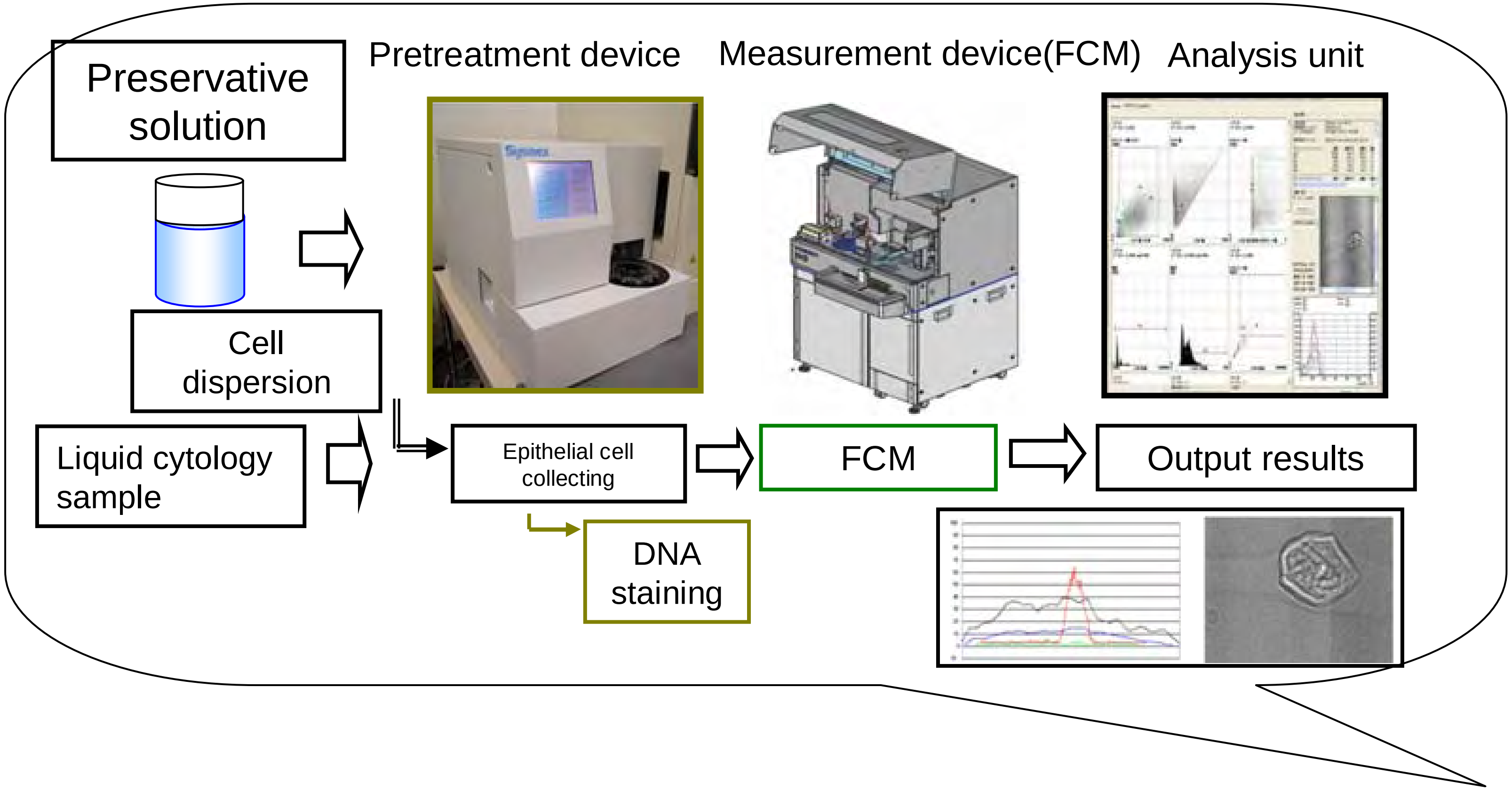
Upcoming screening

True Negative
(90%)

Images of sort-out concept

③ Cervical cancer screening

– Development of full-automated system –



Preservative solution

Cell dispersion

Liquid cytology sample

Pretreatment device

Measurement device(FCM)

Analysis unit

Epithelial cell collecting

DNA staining

FCM

Output results

Completion of prototype development of full-automated and high-speed system

⇒ Throughput capacity 20 test/h

③ Cervical cancer screening

Pretreatment:

Improvement of reagent, dispersion protocol (chemical, mechanical, physical treatment)

Approach to analytical performance（Improvement for sensitivity）:

Optimizations of algorithm

n=296

	sensitivity	specificity
Practical system	92 %	63 %

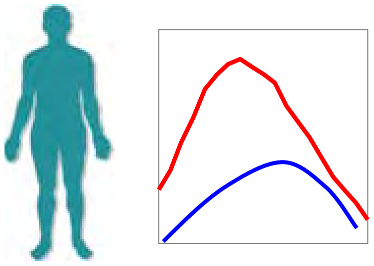
Future plan
▪ Produce the prototype device for market evaluation, verify the clinical performance and feasibility of sort-out concept in JP, US, EU, China within FY2011. ▪ Initiate the development of unique technology for high-risk HPV typing based on common technological platform.

2. (3) Progress status in practical stage

④ Disease status simulation technology for diabetes

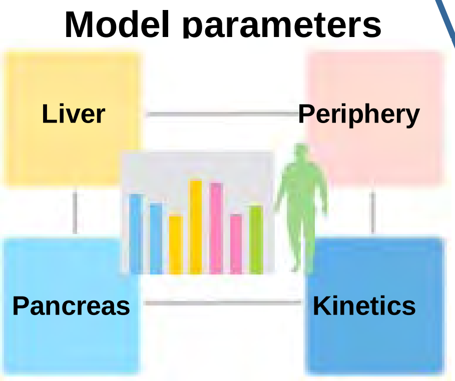
④ Disease state simulation technology for diabetes

Input



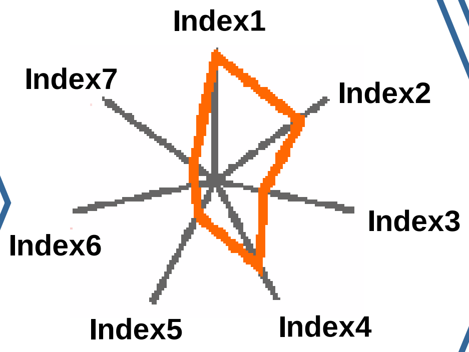
Input of test values of type 2 diabetes

Analysis


Model parameters
Liver
Periphery
Pancreas
Kinetics

Analysis of clinical conditions from the view point of insulin secretion and action

Output



Output of disease profiles as analysis results

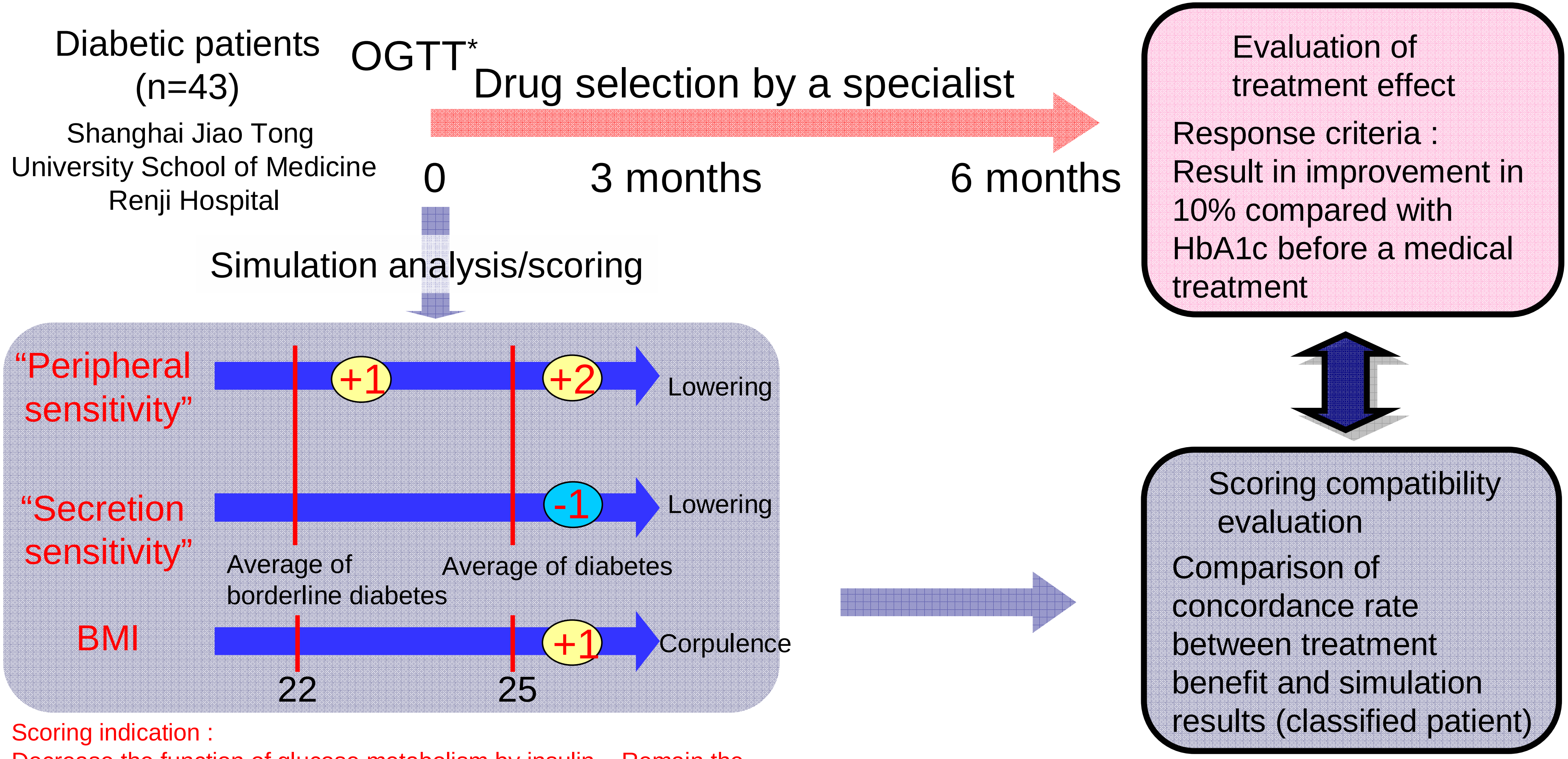
Treatment

Decision support information for personalized therapeutic strategies

Quantification of individual’s disease state by simulation of “pancreas function”, “insulin function” and “sugar metabolism”

④ Diabetes simulation system -clinical research design-

Comparison of concordance rate between treatment efficacy (changes of HbA1c) and simulation results by using the parameters from pre-treatment status.



Diabetic patients
(n=43)

Shanghai Jiao Tong
University School of Medicine
Renji Hospital

OGTT*

Drug selection by a specialist

Simulation analysis/scoring

Evaluation of treatment effect

Response criteria : Result in improvement in 10% compared with HbA1c before a medical treatment

Scoring compatibility evaluation

Comparison of concordance rate between treatment benefit and simulation results (classified patient)

0
3 months
6 months
“Peripheral sensitivity”
+1
+2
Lowering
“Secretion sensitivity”
-1
Lowering
Average of borderline diabetes
Average of diabetes
BMI
+1
Corpulence
22
25

Scoring indication :
Decrease the function of glucose metabolism by insulin, Remain the function of insulin secretion
(BMI : corrective factor of obesity)

＊OGTT：Oral glucose tolerance test

④ Simulation system for diabetes – Intermediate results of clinical evaluation -

Clinical prediction and treatment effect of patients with prescribed biguanides*

	Score 0	Score 1 or more
Number of case	5	15
HbA1c (%) Pre-treatment⇒ Post-treatment ※average	6.8 ⇒ 6.5	7.0 ⇒ 6.2

*In hyperinsulinemia, biguanides can lower fasting levels of insulin in plasma. Their therapeutic uses derive from their tendency to reduce gluconeogenesis in the liver, and, as a result, reduce the level of glucose in the blood. Biguanides also tend to make the cells of the body more willing to absorb glucose already present in the blood stream, and there again reducing the level of glucose in the plasma.

Improvement effect of HbA1c

score 0： Low drug efficacy (0.3 % improvement)

score 1 or more： High drug efficacy (0.8% improvement)

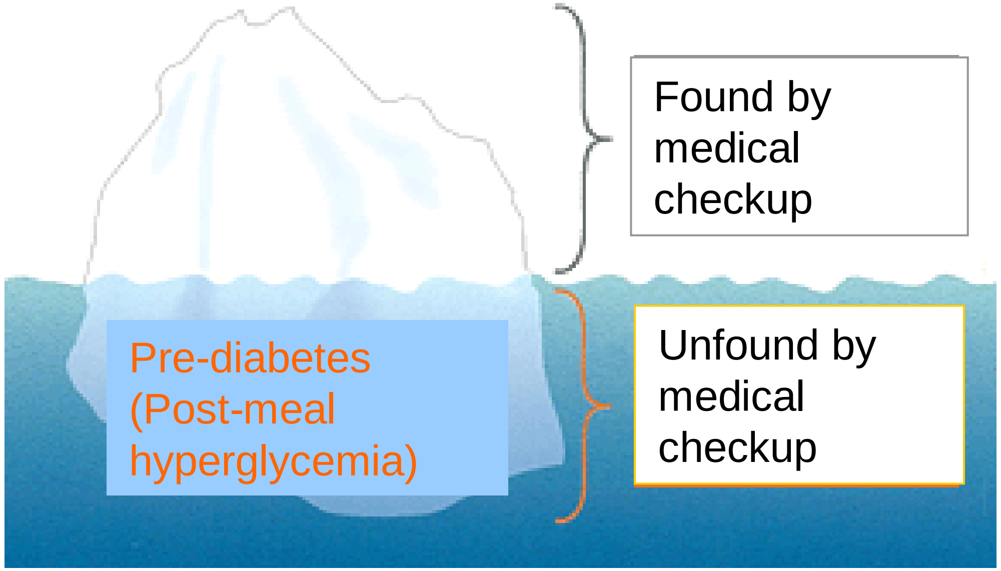
Future plan

- Implementation of market evaluation in main area at FY2011, follow by China market evaluation
- Business plan for 2013 including a new business model development (ex. Screening system) under discussion

2. (3) Progress status in practical stage

⑤ Measurement of glucose AUC by minimum invasive fluid extraction technology - Practical of AUC -

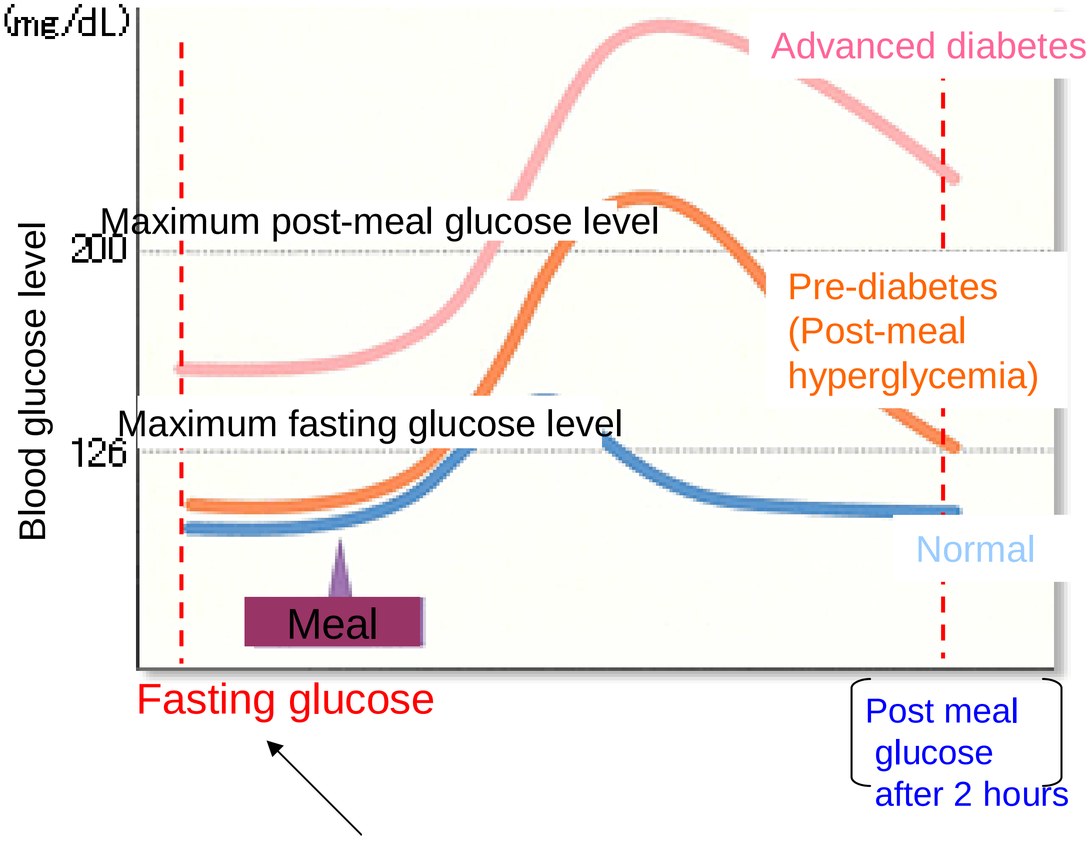
⑤ Practical use of AUC* -What is post-meal hyperglycemia?-



Found by medical checkup

Unfound by medical checkup

Pre-diabetes (Post-meal hyperglycemia)



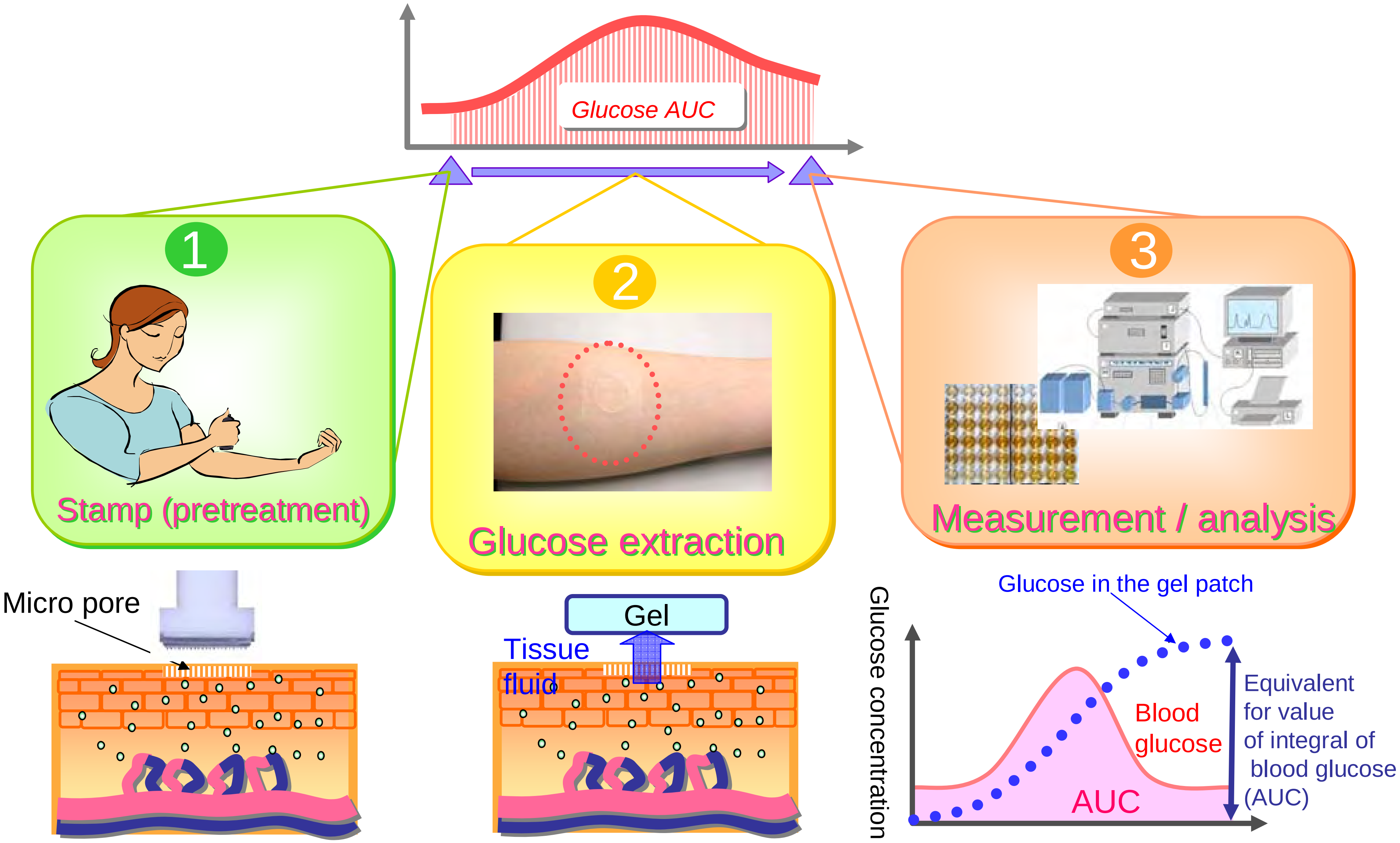
Normal medical checkup

Post-meal hyperglycemia : risk factor of large vessel disease (cerebral accident, myocardial infarction)

Expected development of device which enables us to simple and exactly monitor monitor post-meal hyperglycemia

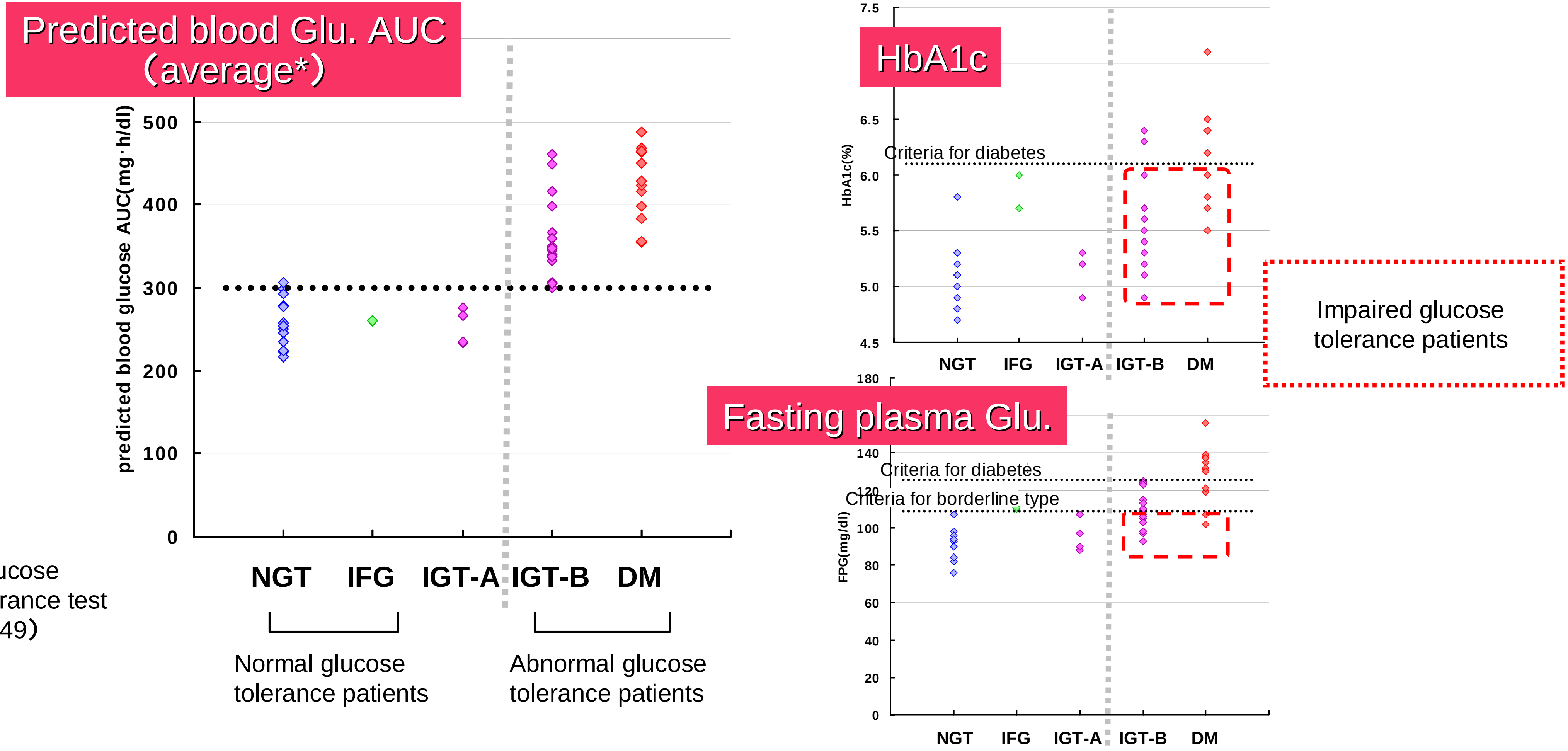
＊AUC：Area Under the Curve

⑤ Practical use of AUC - extraction technology for tissue fluid -


Glucose AUC
1
Stamp (pretreatment)
2
Glucose extraction
3
Measurement / analysis
Micro pore
Gel
Tissue fluid
Glucose in the gel patch
Glucose concentration
Blood glucose
AUC
Equivalent for value of integral of blood glucose (AUC)

⑤ Practical use of AUC

– Performance comparison between the system and conventional index –



*Glucose tolerance test (n=49)

Future plan

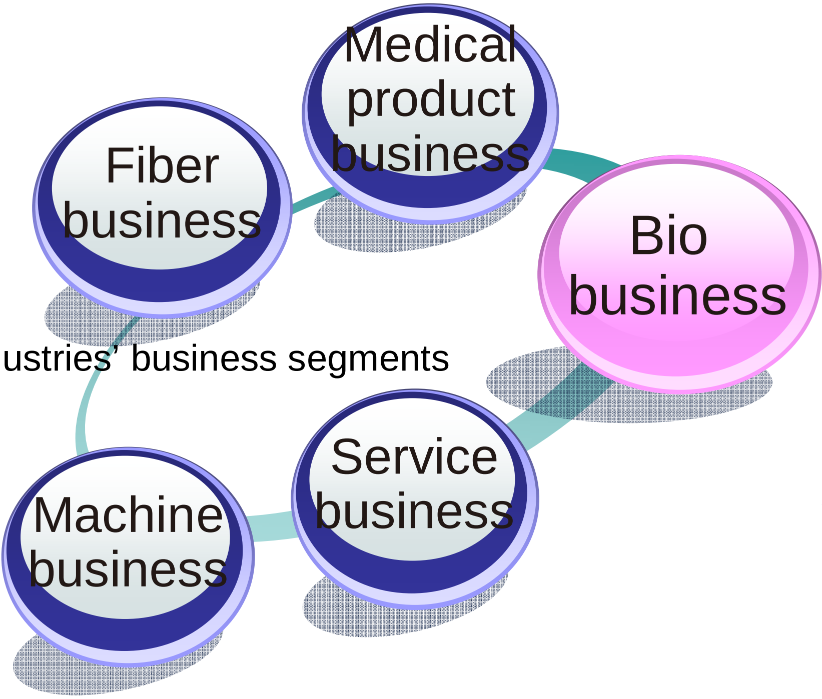
- Start the recognizing action of AUC at many academic conferences as novel diagnosis parameter of early stage of diabetes.
- Initiate the development of system for medical device approval and entry to market within 2 years.

2.（4）Strengthening of bio-material (protein) production technology

Transferred protein production business from Katakura Industries Co., Ltd

- Signing date　2011 March 3rd
- Effective date　2011 April 1st
- Contract details　Katakura Industries Co., Ltd. Bioscience laboratory（excl. Matsumoto bunshitsu）

  Contract manufacturing service by silk worm


Medical product business
Fiber business
Bio business
Service business
Machine business

Katakura Industries' business segments

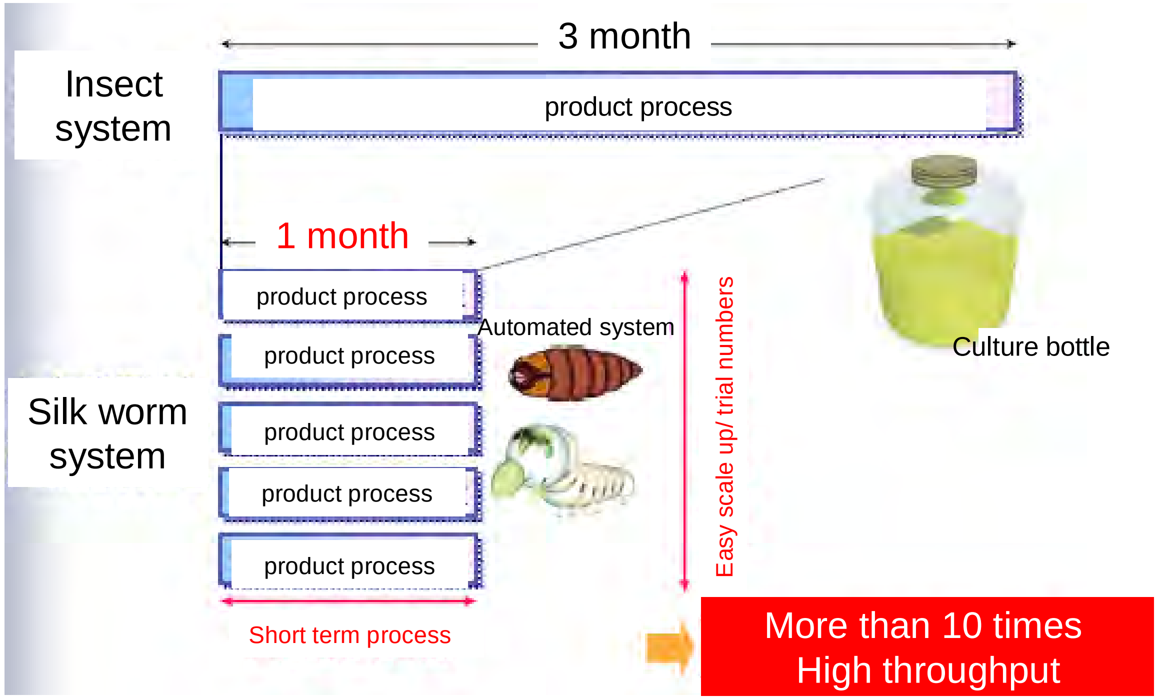
Application to Bio-business for Silkworm protein synthesis "efficient" technology

Features of protein produce technology by silk worm

High productivity/stability/rapid production/flexibility of scale-up

1. High production capability by using a powerful expression promoter
2. Keeping to native proteomic characters (glycosylation, conformation, phosphorylation, antigenecity)
3. Simple purification process（possible collection as soluble protein）
4. Easy scale-up as no need of investment in facilities

Ex.) High throughput production system by silkworm



3 month

Insect system

product process

1 month

Silk worm system

product process

product process

product process

product process

product process

Short term process

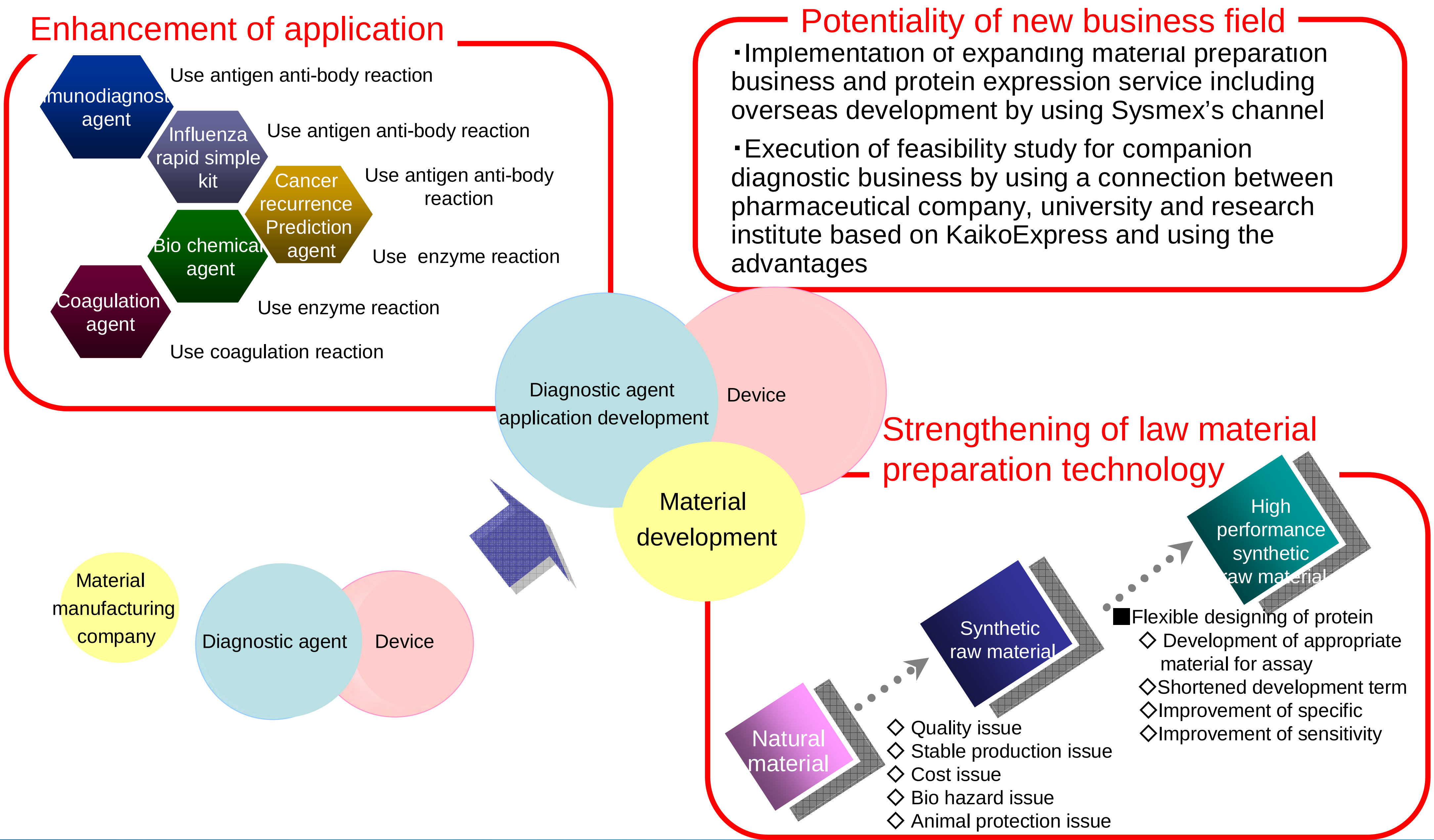
Automated system

Easy scale up/ trial numbers

Culture bottle

More than 10 times
High throughput

Technology acquisition Impact



Enhancement of application

munodiagnost
agent
Influenza rapid simple kit
Cancer recurrence Prediction agent
Bio chemical agent
Coagulation agent

Use antigen anti-body reaction

Use antigen anti-body reaction

Use antigen anti-body reaction

Use enzyme reaction

Use enzyme reaction

Use coagulation reaction

Potentiality of new business field

・Implementation of expanding material preparation business and protein expression service including overseas development by using Sysmex's channel

・Execution of feasibility study for companion diagnostic business by using a connection between pharmaceutical company, university and research institute based on KaikoExpress and using the advantages

Diagnostic agent application development
Device
Material development
Material manufacturing company
Diagnostic agent
Device

Strengthening of law material preparation technology

Natural material
Synthetic raw material
High performance synthetic
aw material

◇ Quality issue
◇ Stable production issue
◇ Cost issue
◇ Bio hazard issue
◇ Animal protection issue

■Flexible designing of protein
◇ Development of appropriate material for assay
◇Shortened development term
◇Improvement of specific
◇Improvement of sensitivity

3. Progress status in Research stage

Kaoru ASANO

Executive Officer, Executive Vice President

3. Progress status in research stage

(1) New technology

  ① Circulating tumor cell

  ② Detection technology for methylated DNA

  ③ DNA chip

(2) Approach for e-Health

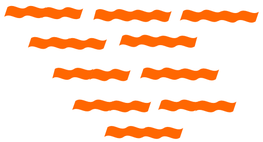
Platform for personalized medicine of cancer

Platform

Gene

•Genetic mutation/ polymorphism		*DNA chip*	*SNPs, DMET*
•Acquired modification		*Methylation detection*	*Early detection*

mRNA

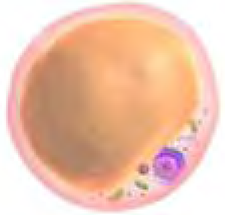


•Quantitative alteration	*OSNA*	*Lymph node metastasis*
	DNA chip	*Treatment selection*

Protein

•Quantitative alteration •Qualitative alteration	*HISCL*	*Tumor marker*
	C2P	*Prognosis*

Cell



•Quantitative alteration	*FCM*	*Cytological diagnosis*
•Qualitative alteration (functional)	*CTC*	*Early detection* *Treatment selection*

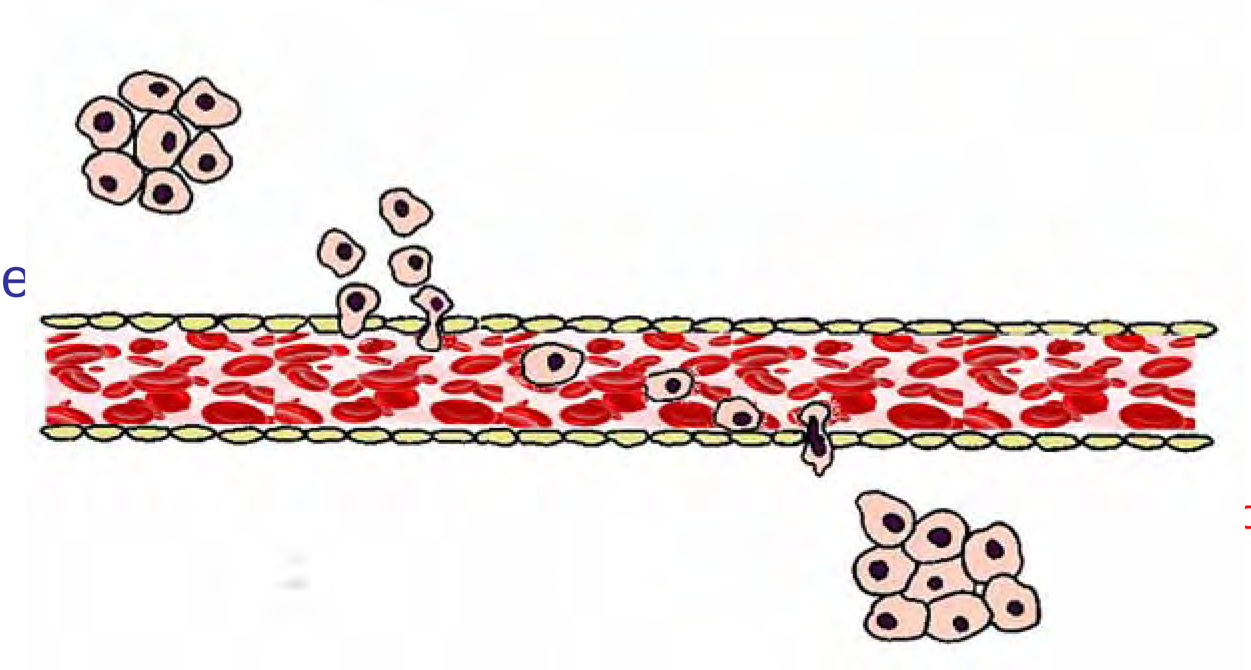
SNP **s** : Single Nucleotide Polymorphism
DMET: Drug metabolism / transporter

3. (1) Platform for personalized medicine of cancer

① Circulating Tumor Cell

① Circulating tumor cells (CTC) detection technology

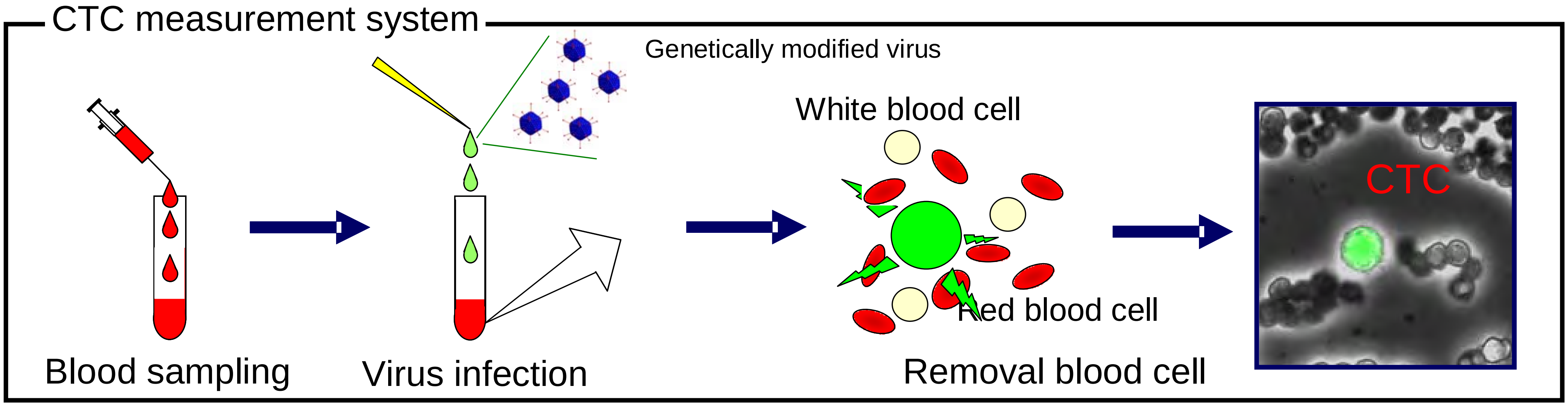
Blood ve



Tumor Cells

ɔr more cancer cells in 10ml blood

(metastasis)



CTC measurement system

Genetically modified virus
White blood cell
CTC
Red blood cell
Blood sampling
Virus infection
Removal blood cell

① Circulating tumor cells (CTC) detection technology
- Promoting collaborative research-

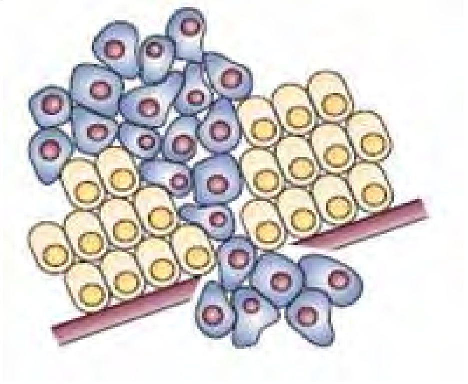
GFP positive rate in type of cancer

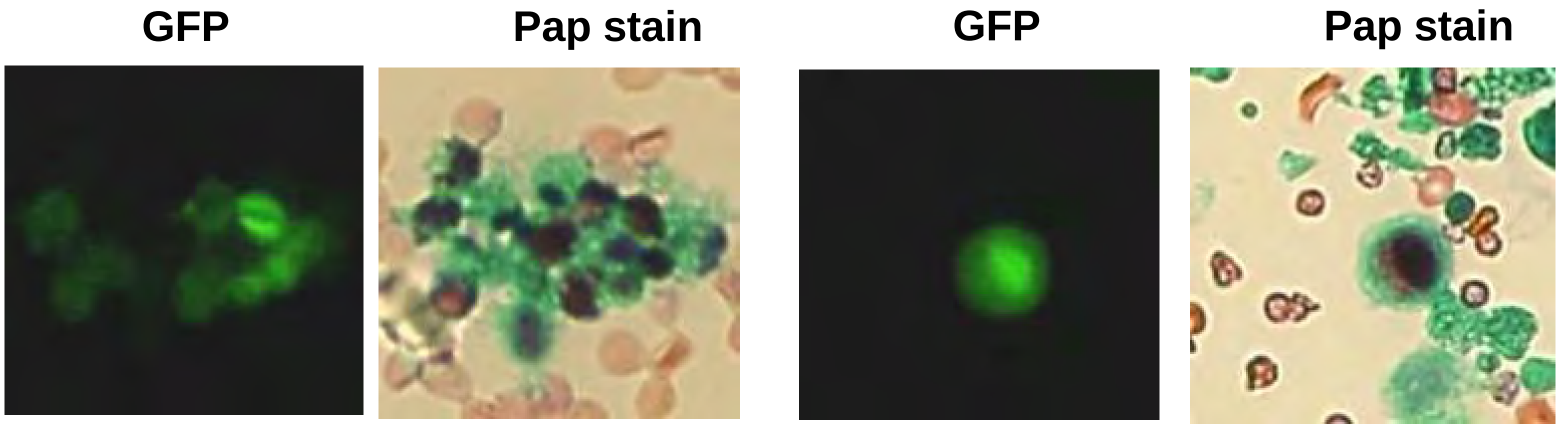
Type of cancer	Cases	GFP positive rate(%) (GFP positive cell≧1)
Breast cancer	**70**	**53% (37/70)**
Stomach cancer	**82**	**76% (63/82)**
Lung cancer	**79**	**87% (69/79)**
Colon cancer	**18**	**50% (9/18)**
Esophageal cancer	**10**	**70% (7/10)**
Pancreas cancer	**12**	**42% (5/12)**
Hepatocellular carcinoma	**21**	**33% (7/21)**

Suggest potential for applying stomach cancer and lung cancer

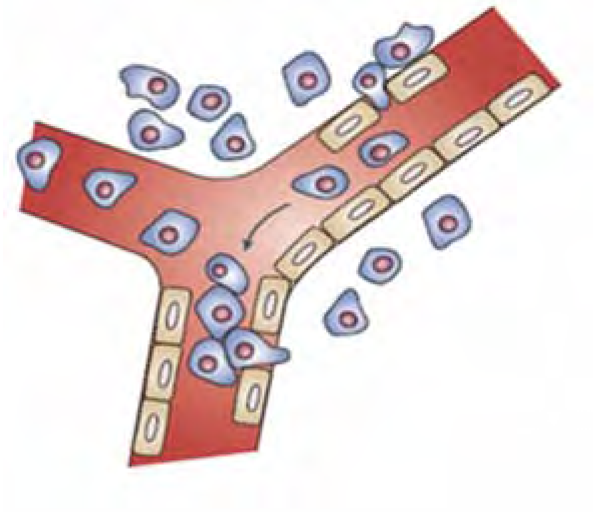
① Circulating tumor cells (CTC) detection technology
- Basic data（example for breast cancer）-

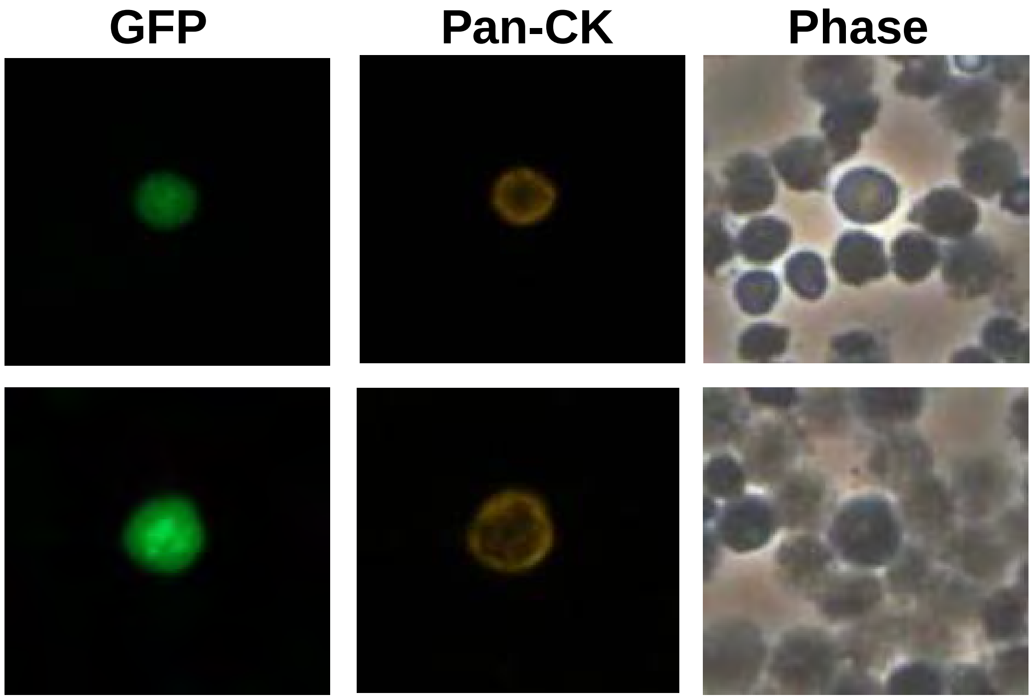
Primary tumor



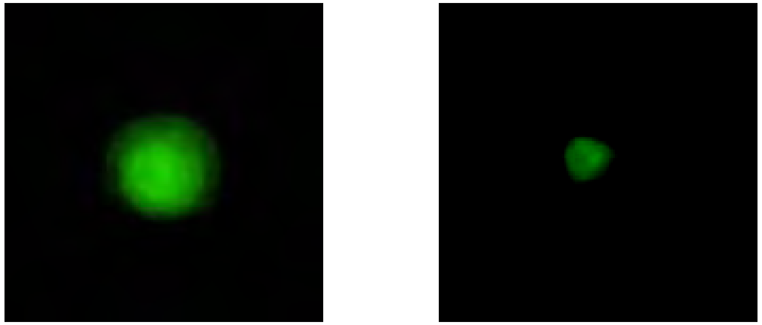

GFP
Pap stain
GFP
Pap stain

Hematogenous metastasis




GFP
Pan-CK
Phase

① Circulating tumor cells (CTC) detection technology
- Efforts for practical use -



Cancer cell White blood cell

GFP positive cell

＝ Cancer cell＋Contaminated false positive cells

Efforts in regard to practical use issue

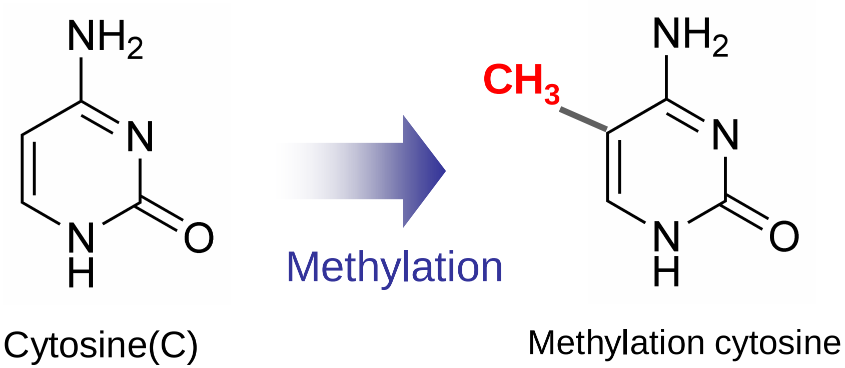
- Technologies for quality control of virus infectivity
  - Quality assurance of virus, internal standard substance
- Marker addition for identifying species
  - Cell size, double stain with CD45 etc,

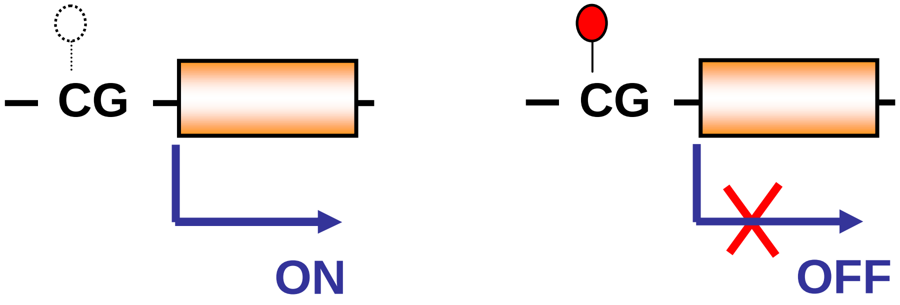
3. (1) Platform for personalized medicine of cancer

② Methylation detection technology

② Methylation detection technology

DNA methylation





Application for cancer diagnosis
i) confirmative diagnosis
ii) Risk diagnosis
iii) Disease state diagnosis

i)Colon cancer screening from the blood

- Construction of measurement system for methylation (OS-MSP)

Construction of rapid and simple measurement system for methylation

- Colon cancer marker(SEPT9)

Collaborative research with Epigenomics

ii)Evaluation of cervical cancer stage

- Study relations between precancerous lesion of cervical cancer and methylation

iii)Search diagnosis methylation marker

- Participation in “basic technology development for new drugs utilizing mechanism of acquired genome modification”

② Methylation detection technology

ⅰ) Localizing diagnosis of cancer clinical study for colon cancer screening

◆ Large scale clinical study in USA (Epigenomics)

Marker： SEPT9

Completed major clinical study in USA in 2010 (7,940 case)
Sensitivity 67%, Specificity 88%

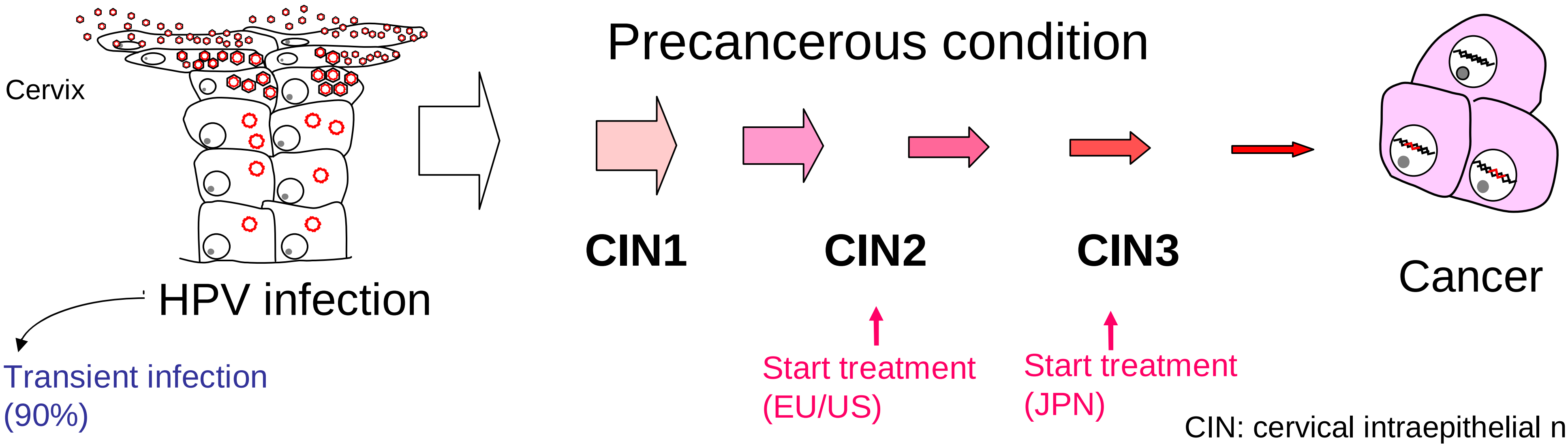
◆ Clinical study in JPN （progress）

	Positive	Negative
Patients with colon cancer	**28**	**13**
Healthy people	**5**	**40**

Sensitivity ：68%
Specificity ：88%

100 analyses have completed until now and clinical study has been on-going for achieving 200 cases.

② Methylation detection technology
ii) Risk diagnosis of cervical cancer progression



Cervix

HPV infection

Transient infection
(90%)

Precancerous condition

CIN1

CIN2

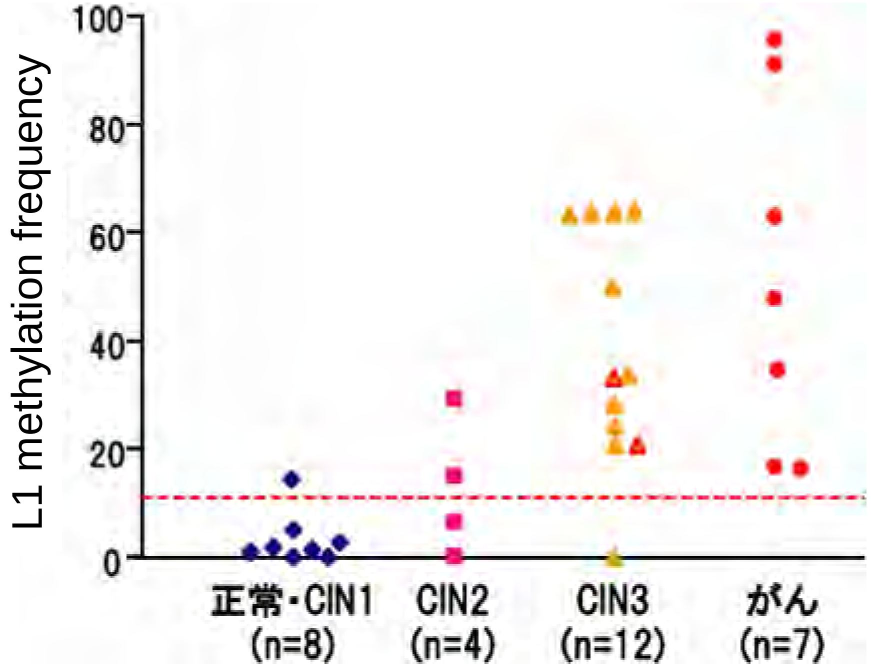
CIN3

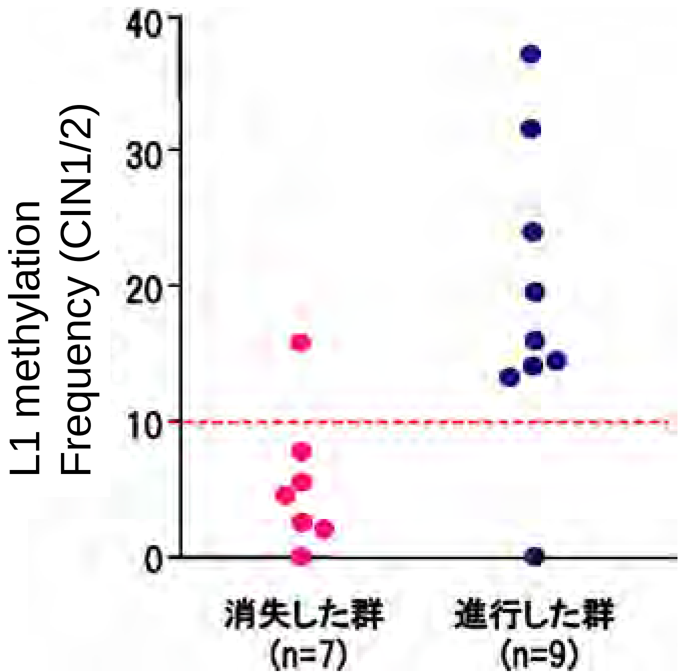
Cancer

Start treatment
(EU/US)

Start treatment
(JPN)

CIN: cervical intraepithelial neoplasia





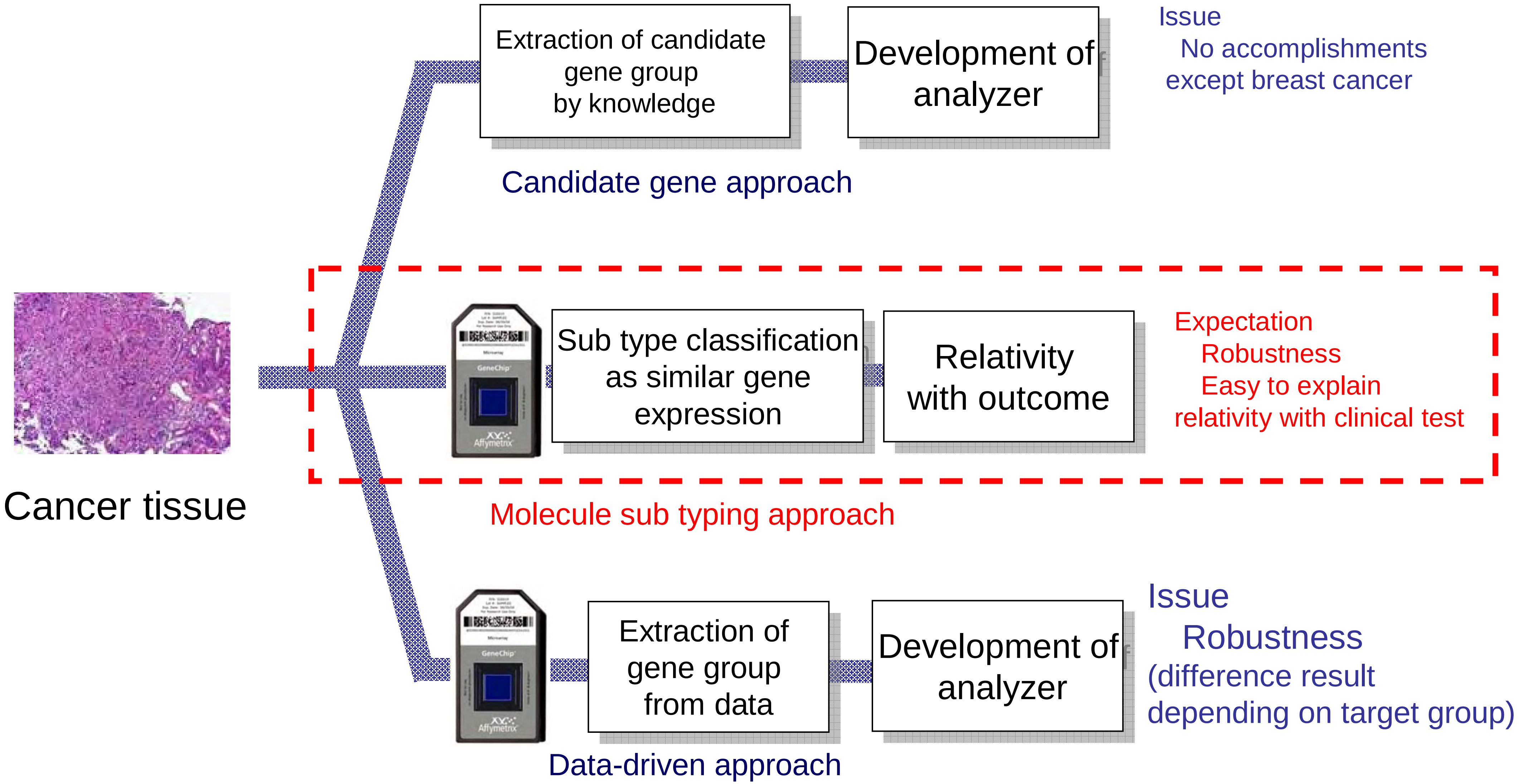
Collaborative research
with Hyogo cancer center

3. (1) Platform for personalized medicine of cancer

③ DNA Chip

③ DNA chip technology

Approaches to “cancer diagnosis” by tissue



Extraction of candidate gene group by knowledge

Development of analyzer

Candidate gene approach

Issue
No accomplishments except breast cancer

Sub type classification as similar gene expression

Relativity with outcome

Molecule sub typing approach

Expectation
Robustness
Easy to explain relativity with clinical test

Cancer tissue

Extraction of gene group from data

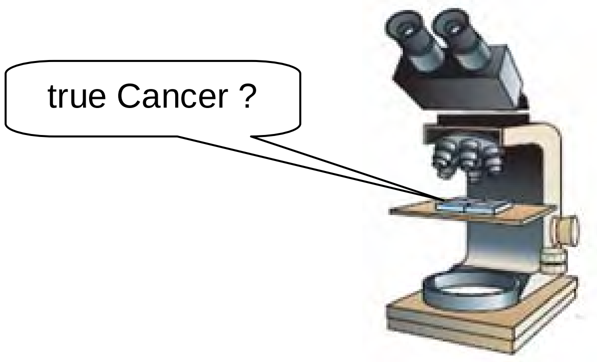
Development of analyzer

Data-driven approach

Issue
Robustness
(difference result depending on target group)

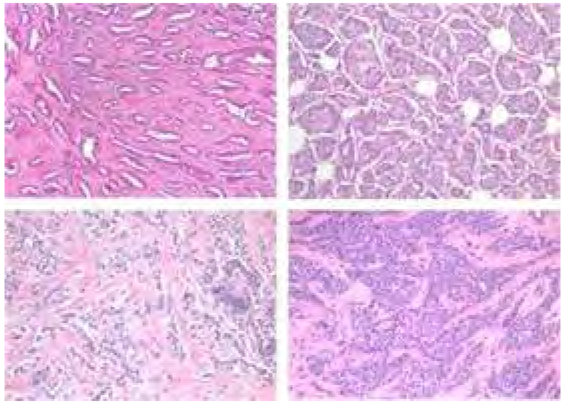
③ DNA chip technology
- Treatment selection by molecule sub typing -

Pathological diagnosis


true Cancer ?

Morphological classification

Subjective diagnosis by a pathologist



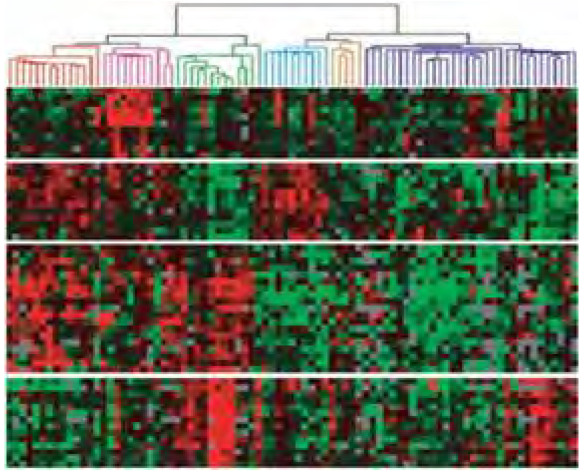
Clinical outcome
(Treatment effect)

Molecule sub typing

GeneChip
Affymetrix

Classification by gene expression

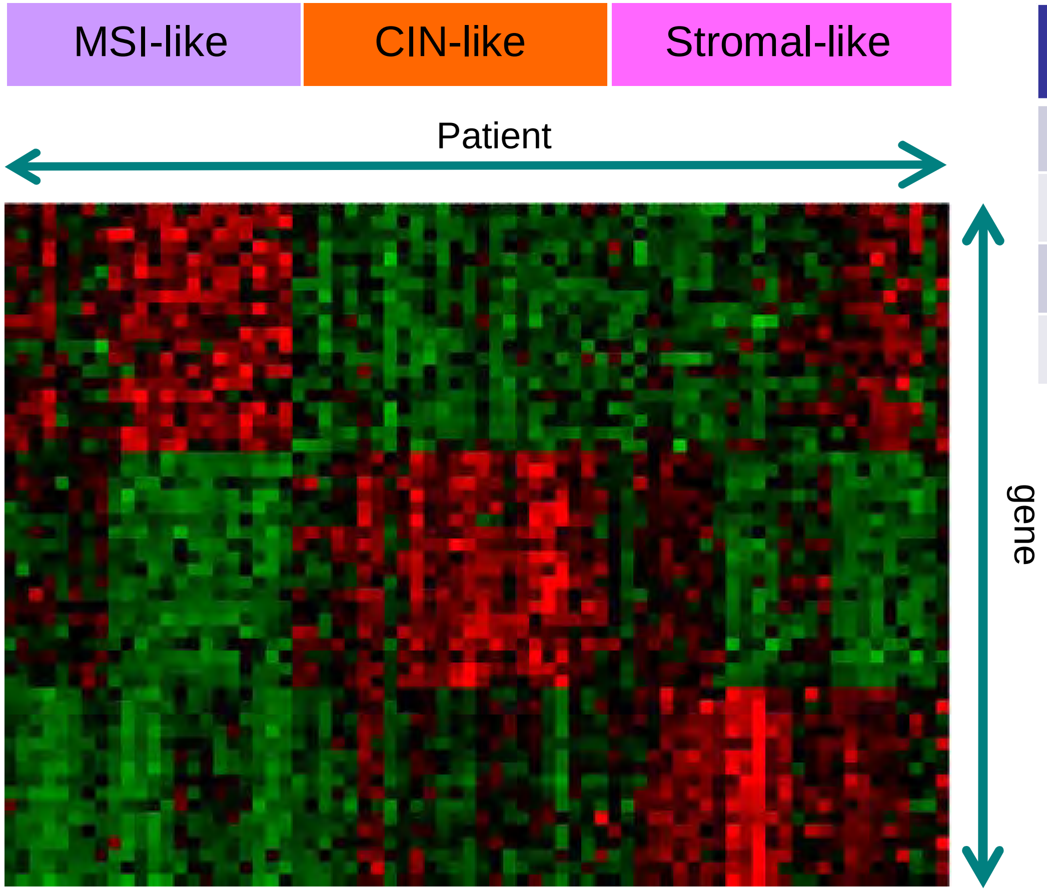
Objective diagnosis



Clinical outcome
(Treatment effect)

③ DNA chip technology

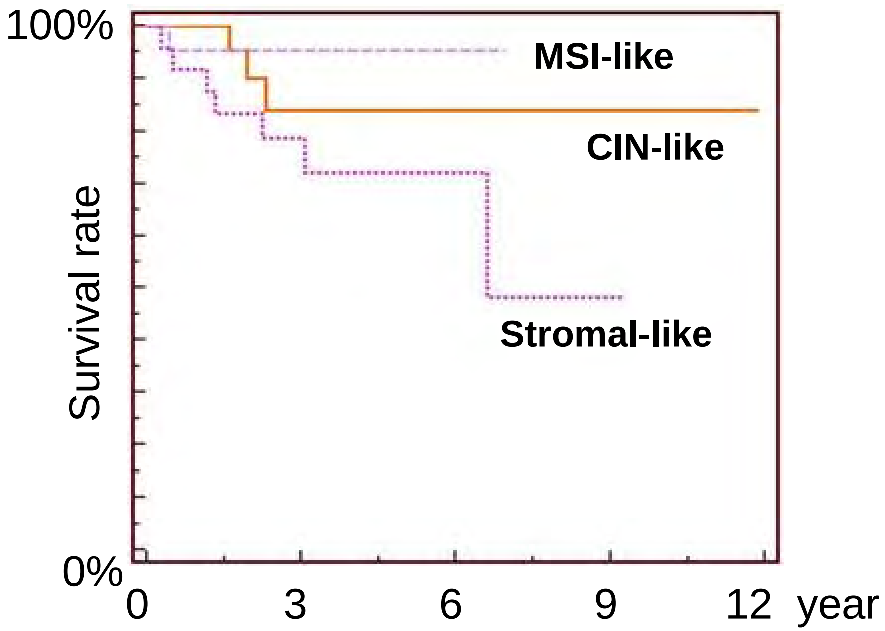
- Sub type classification of colon cancer -



MSI：	Microsatellite Instability
CIN：	Chromosomal instability
Stromal：	Stromal tumor

	Survival rate	Recurrence rate	Left hand : Right hand
MSI	30.6% (22)	4.5% (1)	8 : 14
CIN	33.3% (24)	12.5% (3)	17: 7
Stromal	36.1% (26)	23.1% (6)	13 : 13
total	100% (72)	13.9% (10)	38 : 34

Disease-free survival curve



③ DNA chip technology

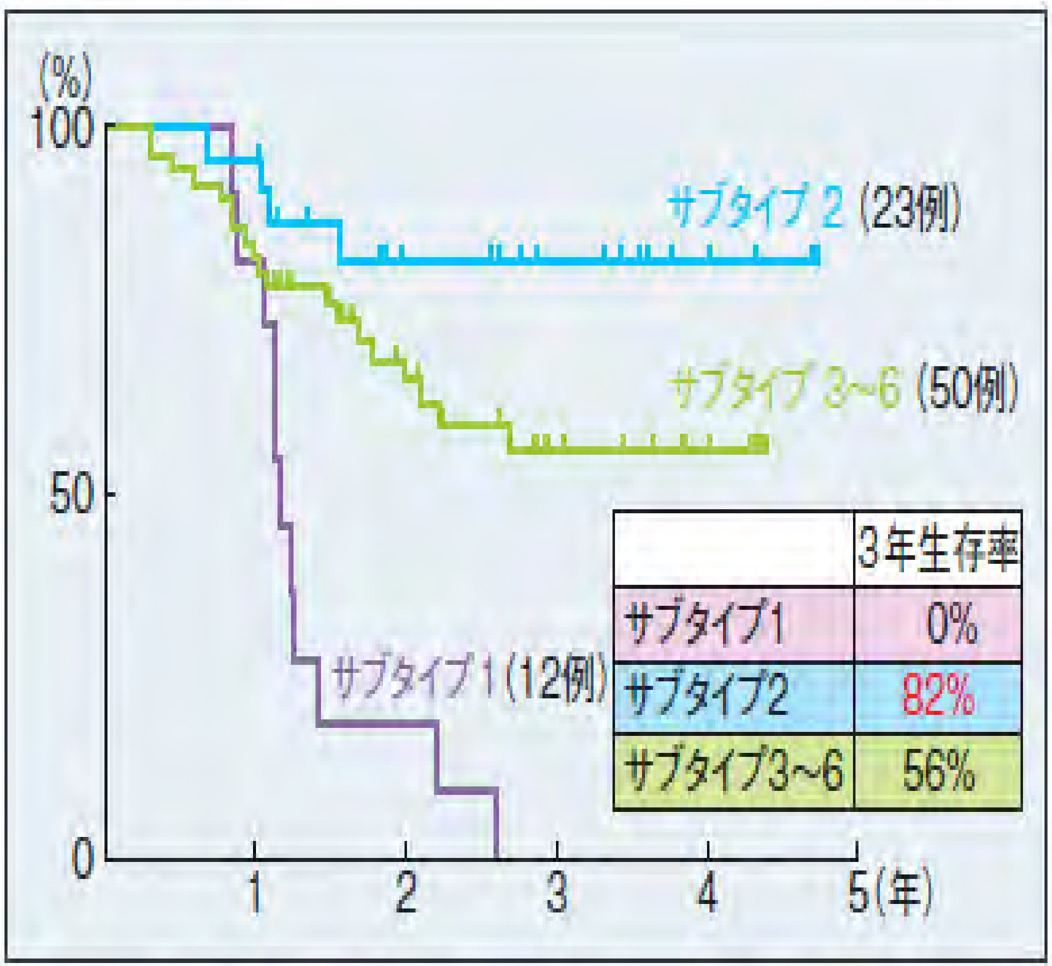
-Prediction of chemoradiation therapy effect for esophageal cancer -

Esophageal cancer

- Morbidity rate (vs. 100,000 people)
  - Man： 23.8 （rank:6）
  - Woman： 4.1
- Mortality rate (vs. 100,000 people)
  - Man： 16.2 （rank:7）
  - Woman： 2.8
- Treatment method
  - Endoscopic therapy
  - Operation
  - Chemo/radiation
- Clinical needs
  - Radiation sensitivity prediction

National Cancer Center
Center for Cancer Control and Information Services

Chemo/radiation results of 6 sub classes



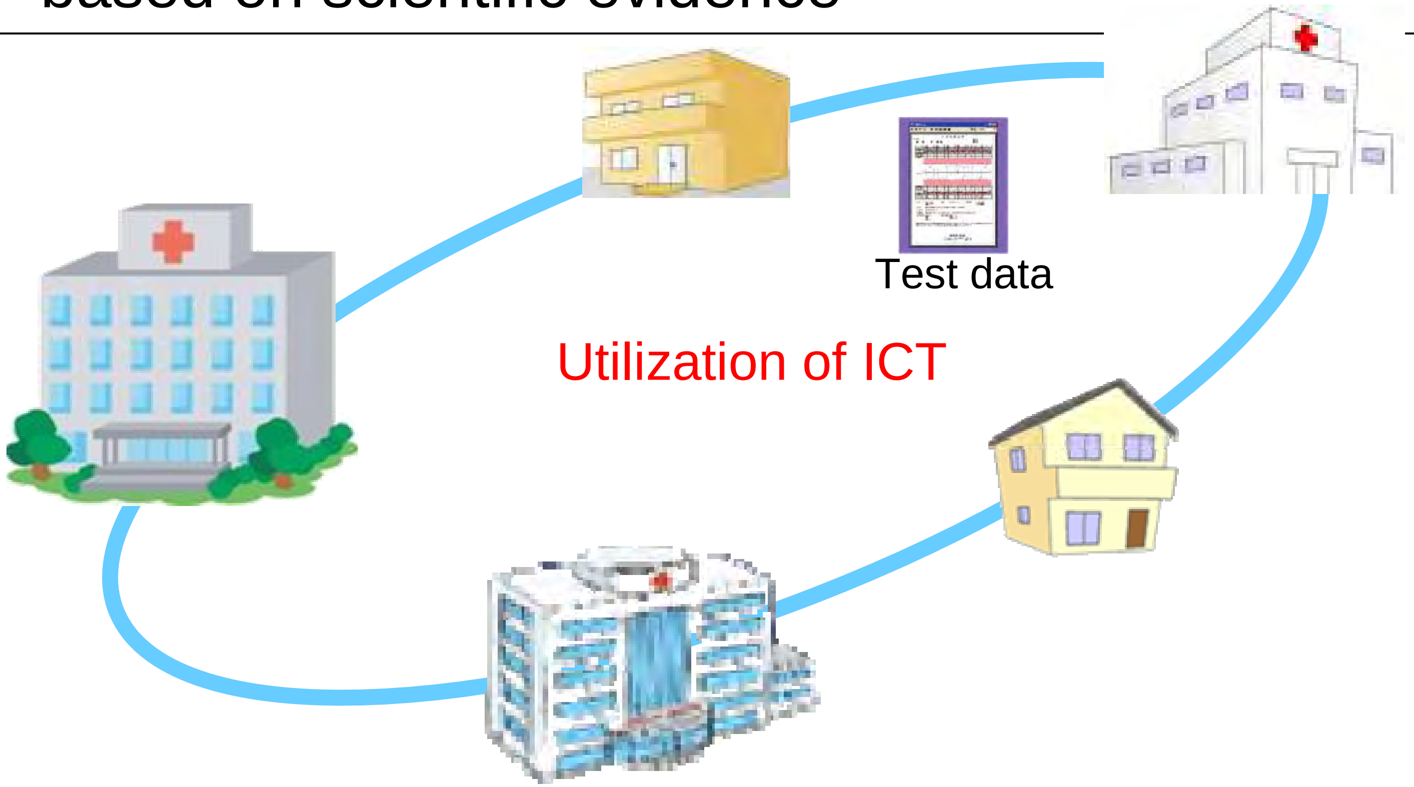
Collaborative research with National Cancer Center

3. (2) Approach for e-Health

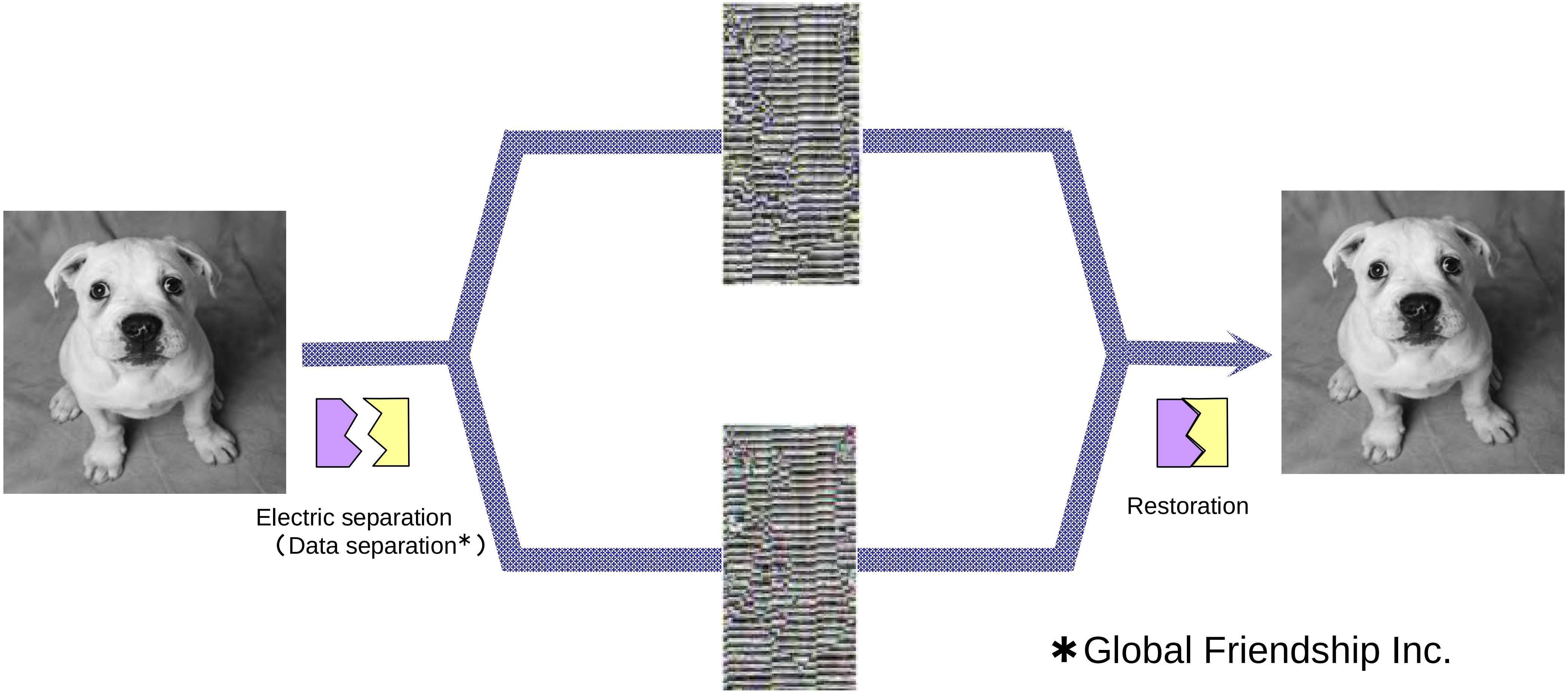
Efforts for e-Health

Sysmex's idea for e-Health

- Be secured individual test data
- In any place, easy confirmation of past test data
- Providing for medical treatment support information based on scientific evidence



Secret Sharing Scheme (Data separation*)



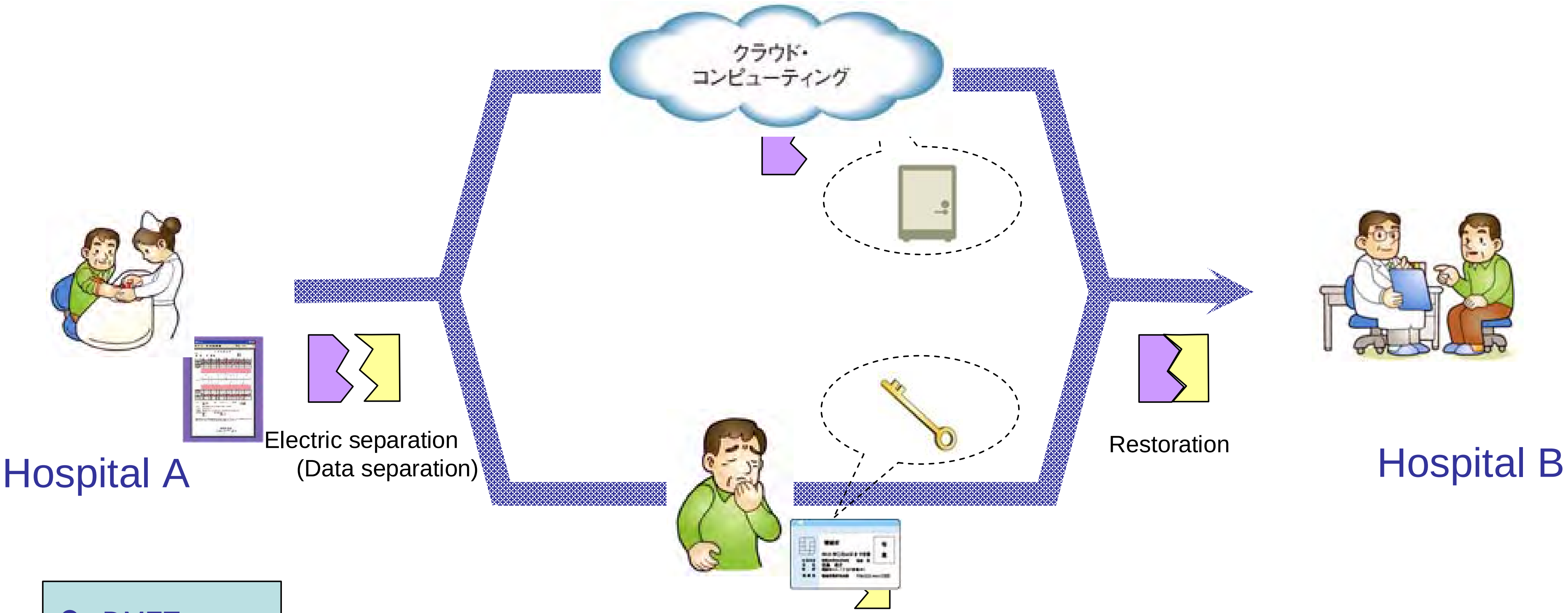
Electric separation
（Data separation＊）

Restoration

✱Global Friendship Inc.

Point： Separated data in bit level is not personal information even if original data includes personal data.

e-Health system construction with using Data Separation



Hospital A

Electric separation
(Data separation)

Restoration

Hospital B

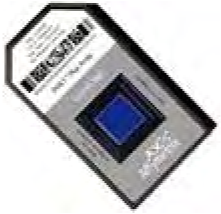
- DMET
- SNPs
- Next-generated sequence

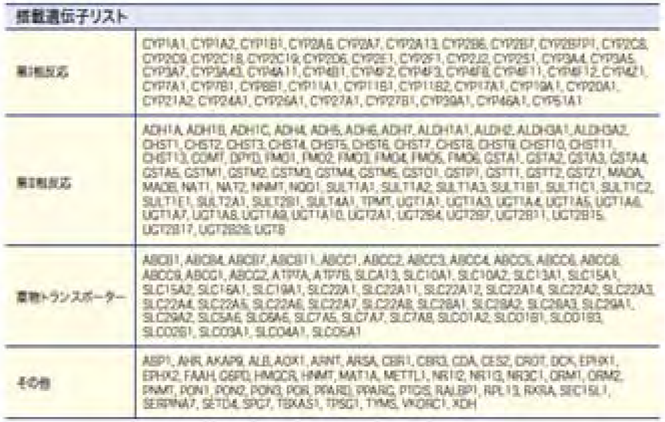
…

Point： Clinical information is managed and utilized by individual.
Cost reduction by using cloud

Drug effect prediction system

DMET^{TM} Plus

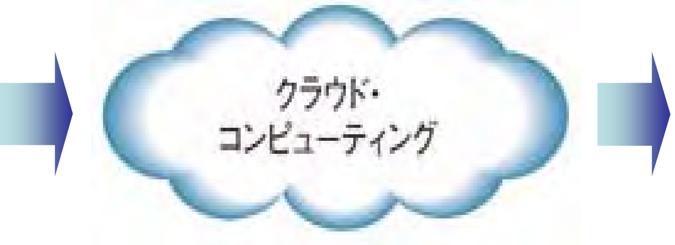




搭載遺伝子リスト

第I相反応	CYP1A1, CYP1A2, CYP1B1, CYP2A6, CYP2A7, CYP2A13, CYP2B6, CYP2B7, CYP2B7P1, CYP2C8, CYP2C9, CYP2C18, CYP2C19, CYP2D6, CYP2E1, CYP2F1, CYP2J2, CYP2S1, CYP3A4, CYP3A5, CYP3A7, CYP3A43, CYP4A11, CYP4B1, CYP4F2, CYP4F3, CYP4F8, CYP4F11, CYP4F12, CYP4Z1, CYP7A1, CYP7B1, CYP8B1, CYP11A1, CYP11B1, CYP11B2, CYP17A1, CYP19A1, CYP20A1, CYP21A2, CYP24A1, CYP26A1, CYP27A1, CYP27B1, CYP39A1, CYP46A1, CYP51A1
第II相反応	ADH1A, ADH1B, ADH1C, ADH4, ADH5, ADH6, ADH7, ALDH1A1, ALDH2, ALDH3A1, ALDH3A2, CHST1, CHST2, CHST3, CHST4, CHST5, CHST6, CHST7, CHST8, CHST9, CHST10, CHST11, CHST13, COMT, DPYD, FMO1, FMO2, FMO3, FMO4, FMO5, FMO6, GSTA1, GSTA2, GSTA3, GSTA4, GSTA5, GSTM1, GSTM2, GSTM3, GSTM4, GSTM5, GSTO1, GSTP1, GSTT1, GSTT2, GSTZ1, MAOA, MAOB, NAT1, NAT2, NNMT, NQO1, SULT1A1, SULT1A2, SULT1A3, SULT1B1, SULT1C1, SULT1C2, SULT1E1, SULT2A1, SULT2B1, SULT4A1, TPMT, UGT1A1, UGT1A3, UGT1A4, UGT1A5, UGT1A6, UGT1A7, UGT1A8, UGT1A9, UGT1A10, UGT2A1, UGT2B4, UGT2B7, UGT2B11, UGT2B15, UGT2B17, UGT2B28, UGT8
薬物トランスポーター	ABCB1, ABCB4, ABCB7, ABCB11, ABCC1, ABCC2, ABCC3, ABCC4, ABCC5, ABCC6, ABCC8, ABCC9, ABCG1, ABCG2, ATP7A, ATP7B, SLCA13, SLC10A1, SLC10A2, SLC13A1, SLC15A1, SLC15A2, SLC16A1, SLC19A1, SLC22A1, SLC22A11, SLC22A12, SLC22A14, SLC22A2, SLC22A3, SLC22A4, SLC22A5, SLC22A6, SLC22A7, SLC22A8, SLC28A1, SLC28A2, SLC28A3, SLC29A1, SLC29A2, SLC5A6, SLC6A6, SLC7A5, SLC7A7, SLC7A8, SLCO1A2, SLCO1B1, SLCO1B3, SLCO2B1, SLCO3A1, SLCO4A1, SLCO6A1
その他	ABP1, AHR, AKAP9, ALB, AOX1, ARNT, ARSA, CBR1, CBR3, CDA, CES2, CROT, DCK, EPHX1, EPHX2, FAAH, G6PD, HMGCR, HNMT, MAT1A, METTL1, NR1I2, NR1I3, NR3C1, ORM1, ORM2, PNMT, PON1, PON2, PON3, POR, PPARD, PPARG, PTGIS, RALBP1, RPL13, RXRA, SEC15L1, SERPINA7, SETD4, SPG7, TBXAS1, TPSG1, TYMS, VKORC1, XDH

Cover 225 genes and 1936 markers of drug-metabolizing enzyme /transporter



クラウド・
コンピューティング

Knowledge based on scientific evidence

Drugs	Treatment field
Aromatase Inhibitors	Breast cancer
Tamoxifen	Breast cancer
Codeine	Pain
Phenytoin	Anti epilepsy
Statins	Cholesterol
Thiopurines	Chemotherapy
Warfarin	Circulatory disease

We Believe the Possibilities.

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