

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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 - ① Circulating tumor cell
 - 2 Detection technology for methylated DNA
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(2) Approach for e-Health



2. Strategy & Progress of R&D

Mitsuru WATANABE Member of Managing Board and Executive Officer Head 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)
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 - (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





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





Subject of future investigation as front-runner











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





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2.(2) Progress status in launching stage

- Innovative technology in Next generation of hematology system -

 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
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2.(2) Progress status in launching stage

- Innovative technology in Next generation of hematology system -

 Blood testing technology (New approach for improvement of usability)

- New approach for improvement of usability -



Module system control technology :

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

Image:			XN-2	20		XN-1	XN-10		University ho Measurement module Sampler module
t channelMax <th></th> <th></th> <th>[A1]</th> <th>[A2]</th> <th>[B1]</th> <th>[B2]</th> <th>[B3]</th> <th>[B4]</th> <th>XN-2000</th>			[A1]	[A2]	[B1]	[B2]	[B3]	[B4]	XN-2000
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Flexible to a variety of needs !

- New approach for improvement of usability -





- New approach for improvement of usability -



 Automated accuracy control system by automatic sample delivery system



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



- New approach for improvement of usability -





- 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%





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)

%staining liquid set unit of
new product



Blood testing technology
 New approach for improvement of usability



Standardization of concentrated reagents/ preparation unit







1 Blood testing technology New approach for improvement of usability



Remote monitoring function by SNCS



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





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

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

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





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)







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





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



Requirements for counting HPC



(2) HPC measurement technology

-HPC measurement by next generated hematology system-





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

2 Measurement technology for HPC

- Evaluation result -





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)





(1) OSNA technology (rapid diagnosis for lymph node metastasis)

- Current status of introduction of OSNA and future possibilities -







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 –





2 C2P technology (breast cancer) in practical use





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 -





3 Cervical cancer screening

- Development of full-automated system -





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

⇒ Throughput capacity 20 test/h





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

Approach to analytical performance(Improvement for sensitivity): Optimizations of algorithm



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





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.



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



Clinical prediction and treatment effect of patients with prescribed biguanides*

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

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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?- Sysmex



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 - **SYSMEX**



5 Practical use of AUC



- Performance comparison between the system and conventional index -



 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



Features of protein produce technology by silk worm





- 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

Technology acquisition Impact







3. Progress status in Research stage

Kaoru ASANO

Executive Officer, Executive Vice President



(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







3. (1) Platform for personalized medicine of cancer

1 Circulating Tumor Cell





- 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

- Basic data (example for breast cancer) -





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- Efforts for practical use -





3. (1) Platform for personalized medicine of cancer

(2) Methylation detection technology





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"



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







3. (1) Platform for personalized medicine of cancer

3 DNA Chip



Approaches to "cancer diagnosis" by tissue



3 DNA chip technology

- Treatment selection by molecule sub typing -





Molecule sub typing



Classification by gene expression Objective diagnosis



(3) DNA chip technology

- Sub type classification of colon cancer -





Esophageal cancer

3 DNA chip technology

•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

Collaborative research with National Cancer Center





3. (2) Approach 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*)





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





Drug effect prediction system



DMET[™] Plus



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クラウド・ コンピューティング Knowledge based on

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

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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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