Asia Pasific Prostate Society (APPS) March 04, 2011 Seoul

 $\hat{\mathbf{D}}$ 



# The burden of prostate cancer in Asia: prevalence & screening

# Yasutomo Nasu Okayama University Okayama Japan

特別史跡 閑谷(しずたに)学校(岡山県)

Asia Pasific Prostate Society (APPS) March 04, 2011 Seoul

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# The burden of prostate cancer in Asia: prevalence & screening

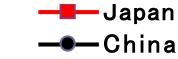
# Yasutomo Nasu Okayama University Okayama Japan

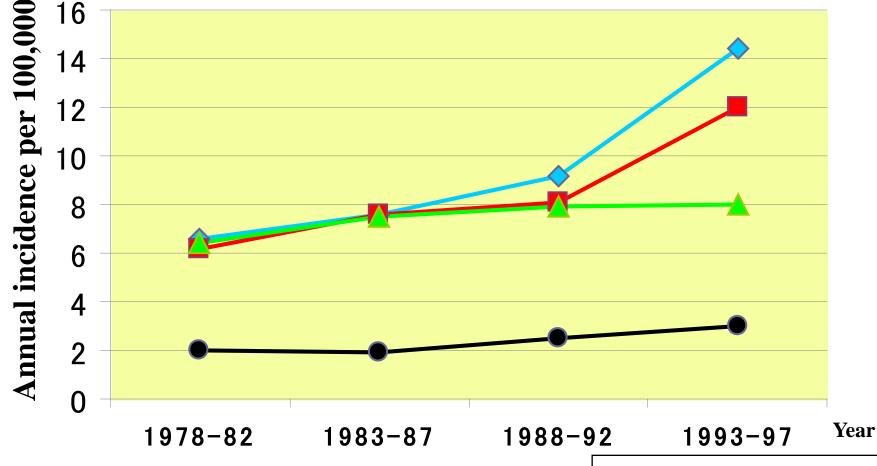
特別史跡 閑谷(しずたに)学校(岡山県)

# **Prostate Cancer (PCa) Increasing in Asia**

**Changing Morbidity of PCa in Asia** 

- Singapore - ▲ Hong Kong

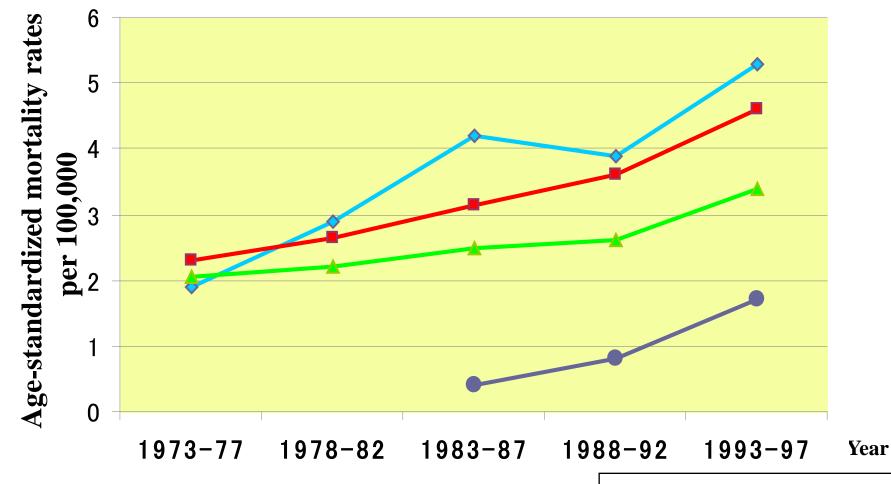




Sim HG et al. Eur J Cancer, 2005

# **Prostate Cancer (PCa) Increasing in Asia**





Sim HG et al. Eur J Cancer, 2005

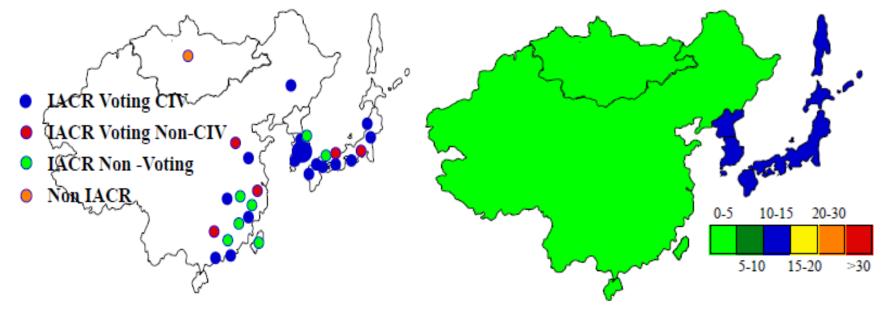
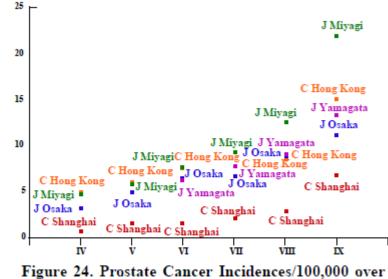


Figure 1. Cancer Registries in North-East Asia

Figure 23. Prostate Cancer Incidences/100,000 over Time(Globocan. 2002: Ferlay et al., 2004)



**Time** (Waterhouse et al., 1982; Muir et al., 1987; Parkin et al., 1992; 1997; 2002; Curado et al., 2007)

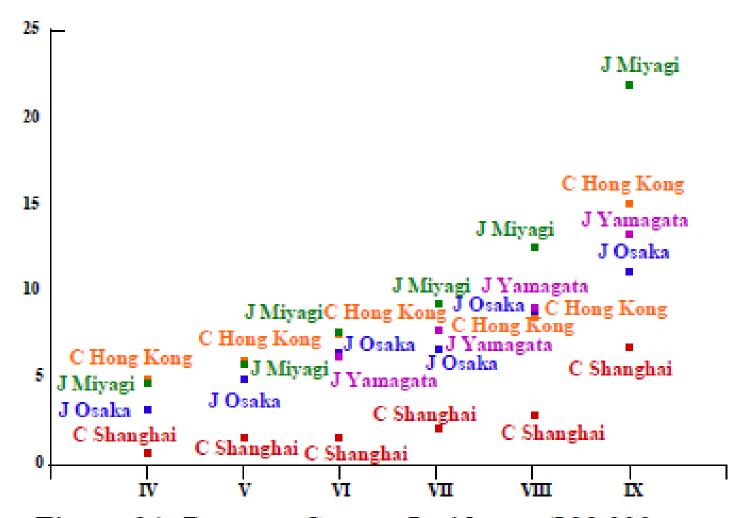


Figure 24. Prostate Cancer Incidences/100,000 over Time (Waterhouse et al., 1982; Muir et al., 1987; Parkin et al., 1992; 1997; 2002; Curado et al., 2007)

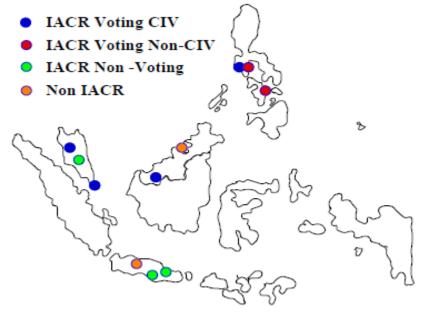


Figure 1. Cancer Registries in Peninsular and Island South East Asia

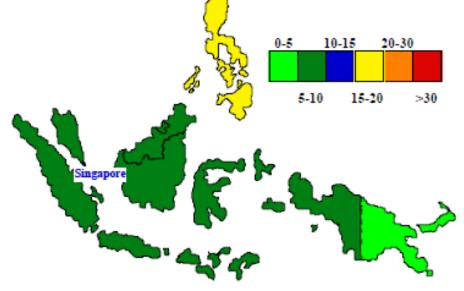


Figure 15. Prostate Cancer Incidences/100,000 (Globocan, 2002: Ferlay et al., 2004)

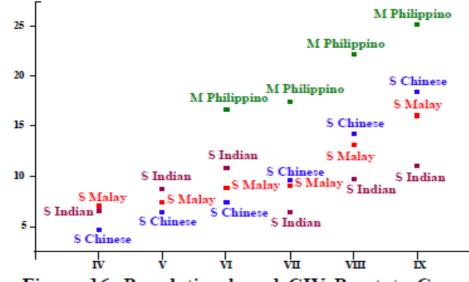


Figure 16. Population-based CIV Prostate Cancel Incidence Rates over Time (Waterhouse et al., 1982; Mui et al., 1987; Parkin et al., 1992; 1997; 2002; Curado et al., 2007

education (Sun et al., 2002).

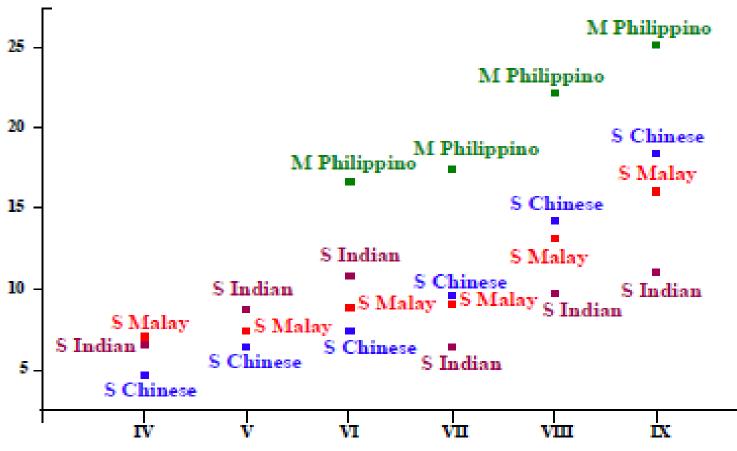


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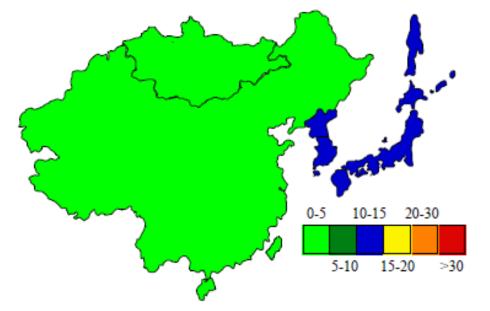


Figure 23. Prostate Cancer Incidences/100,000 over "Globocan, 2002: Ferlay et al., 2004)

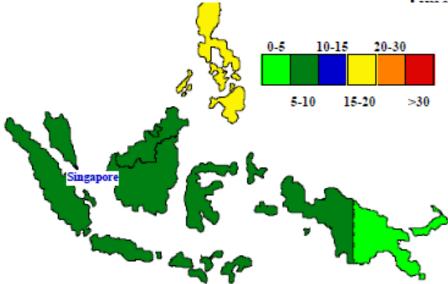


Figure 15. Prostate Cancer Incidences/100,000 (Globocan, 2002: Ferlay et al., 2004)



				Chinese	•			Korea				an Figure	1. Cancer Registries in Nort
	HK≇	Zhong	Jiashang	g Shangh	ai Harbii	n Taiwan	Hawaii	Seoul	Pusan	Osaka	Yama l	Miyagi	Hawaii
Lip	0.1	0.1	0.1	0.6	0.1	0.7	0.1	0.1	0.0	0.0	0.1	0.1	0.0
Tongue	1.7	1.9	0.6	0.6	0.5	5.1	2.2	1.0	1.0	1.6	1.5	1.5	3.0
Mouth	1.6	1.3	0.6	0.8	0.4	9.3	1.5	1.4	1.3	1.4	1.2	1.3	1.2
Nasopharynx	17.8	26.9	4.0	4.1	1.3	13.6	9.9	1.1	0.8	0.5	0.4	0.5	0.6
Hypopharynx	1.4	0.8	0.5	0.2	0.3	-	2.1	1.2	1.0	1.5	1.1	1.4	1.7
Oesophagus	9.5	16.5	20.2	9.2	10.3	7.9	5.4	7.1	8.1	10.8	13.0	15.4	6.0
Stomach	14.7	9.4	32.1	34.1	24.8	18.6	4.6	63.7	59.9	51.3	79.4	65.8	17.2
Colon	23.8	8.5	9.8	15.8	9.4	15.1	21.6	18.7	12.7	23.6	33.9	36.0	31.9
Rectum	7.0	8.7	10.7	11.2	8.6	13.7	11.4	17.4	12.6	13.5	21.7	22.4	21.8
Liver	29.5	25.7	33.8	25.9	30.3	51.9	13.9	44.1	49.8	35.6	14.3	16.4	8.5
Gallbladder	2.9	4.4	2.2	3.2	2.1	2.6	1.2	8.0	9.3	5.7	8.4	6.9	2.4
Pancreas	4.5	2.6	7.1	7.5	7.5	4.7	8.2	8.7	7.7	9.3	9.9	10.1	7.8
Larynx	4.4	5.1	1.1	2.8	3.8	3.5	3.1	4.7	4.9	2.4	2.9	3.3	3.2
Trachea, lung	57.9	34.0	46.7	51.5	55.5	38.2	28.6	49.7	46.2	43.3	38.2	40.6	31.0
Penis	0.2	0.6	0.9	0.3	0.3	0.5	0.0	0.2	0.2	0.1	0.2	0.3	0.2
Prostate	15.0	2.2	1.4	6.9	2.1	11.9	69.1	12.7	7.3	11.3	13.4	22.0	74.2
Kidney	3.3	1.8	1.6	4.8	3.2	5.7	6.2	5.6	4.9	3.9	3.4	6.6	8.4
Bladder	10.9	5.0	5.9	8.1	6.2	8.9	7.5	11.0	10.2	7.9	7.4	10.6	13.0
Brain	3.4	1.9	4.0	5.7	5.6	3.8	1.7	3.5	3.0	2.5	2.4	2.7	3.2
Thyroid	2.2	0.9	1.0	1.4	0.7	1.5	1.6	2.5	2.2	1.3	1.5	2.0	1.8
Non-Hodgkin	8.1	4.3	3.4	5.5	3.1	5.8	13.9	6.8	4.5	6.2	5.7	7.4	11.1
Leukemia	5.5	4.8	3.1	3.6	2.7	4.9	5.9	5.2	4.6	5.7	4.0	4.9	8.7
Total	265	181	205	226	194	250	239	298	274	256	281	302	286

#### Table 2. Population-based Cancer Incidences/100,000 for North-East Asians - Males\*

\*Data from Curado et al, 2007, except for Taiwan, Parkin et al., 2002; #Hong Kong; Zhong, Zhongshan; Yama, Yamagata



	Malay	Malaysians		gaporeans		Bruneiians <sup>+</sup>	Philippinos		
	Penang	Sarawak	Chinese	Malay	Indian		Manila	In Hawaii	
Lip	0.2	0.1	0.0	0.0	0.0	0.0	0.0	0.0	
Tongue	1.4	1.1	1.7	1.4	1.7	0.0	1.8	0.7	
Mouth	1.7	1.0	1.5	0.5	2.8	0.2	1.8	1.2	
Nasopharynx	9.3	15.0	12.8	5.5	1.8	13.0	5.8	3.3	
Hypopharynx	1.3	0.6	1.0	0.7	1.4	0.4	0.4	0.9	
Oesophagus	2.5	2.2	5.8	1.7	3.3	0.5	3.1	1.7	
Stomach	12.5	12.3	21.5	6.5	7.8	14.5	7.9	8.7	
Colon	13.9	7.3	26.5	10.5	7.4	15.0	14.5	20.6	
Rectum	9.9	6.3	19.1	11.6	7.9	9.4	9.5	17.6	
Liver	10.6	9.1	21.3	12.3	8.1	12.7	21.7	10.2	
Gallbladder	1.0	0.6	2.1	1.4	2.3	0.7	1.2	2.1	
Pancreas	3.4	2.3	5.4	3.9	3.1	5.5	4.3	5.9	
Larynx	4.7	2.1	4.9	3.0	2.4	3.1	5.5	1.9	
Trachea, lung	39.0	21.0	51.8	34.8	12.1	43.6	51.7	48.7	
Penis	0.4	0.9	0.5	0.0	0.4	0.7	0.6	0.3	
Prostate	11.3	5.8	18.6	16.1	11.1	18.6	25.3	78.0	
Kidney	3.6	2.0	5.3	3.0	1.7	5.0	4.6	6.7	
Bladder	7.3	3.1	8.0	7.9	4.6	3.3	4.7	6.5	
Brain	3.5	1.6	2.3	1.4	2.7	2.2	2.8	2.7	
Thyroid	1.1	1.1	2.0	2.3	1.3	2.8	2.9	5.7	
Non-Hodgkin	7.0	6.6	8.1	11.9	3.3	4.7	6.8	10.9	
Leukemia	6.0	4.4	5.8	6.2	4.5	4.1	4.9	6.6	
Total	185	129	257	167	108	160	213	271	

Table 2. Population-based Cancer Registry Data for Peninsular and Island South-East Asia - Males<sup>\*</sup> Figure 1. Carer Registry and the

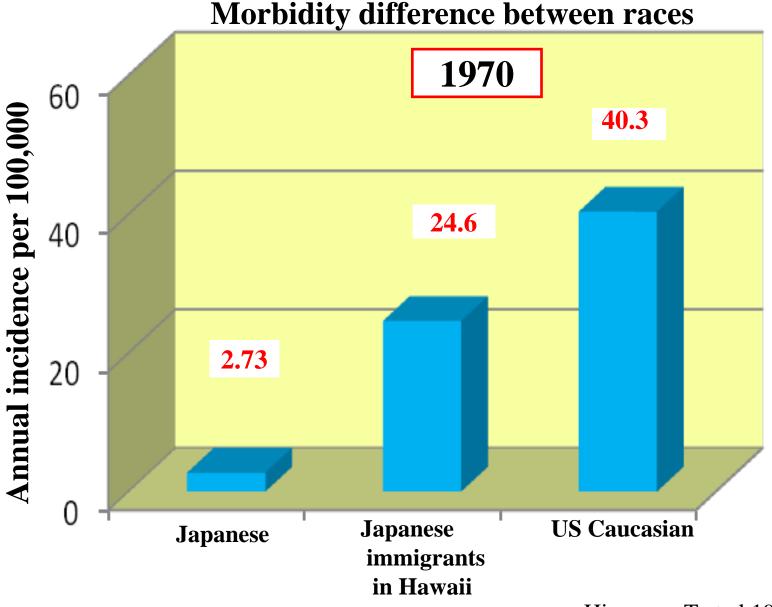
\*Data (/100 000) from Curado et al 2007: \*Nvunt et al personal communication

		T	hailand			Viet Nam				
	Chiang Mai*	Lampang*	Khon Kae	en# Bangkok#	Songkla*	Hanoi# H	Io Chi Minh <sup>#</sup>			
Lip	0.2	0.3	0.3	0.0	0.2	0.2	0.0			
Tongue	2.1	0.9	0.7	2.4	4.4	1.2	2.0			
Mouth	2.0	1.3	1.4	2.1	4.6	0.8	1.9 / LACR Voting CIV			
Nasopharynx	3.9	2.5	3.7	7.4	2.7	12.8	8.3			
Hypopharynx	1.4	0.5	-	-	2.7	-	-			
Oesophagus	2.2	1.6	1.6	4.4	7.8	2.9	4.4			
Stomach	5.9	5.3	3.2	4.9	2.7	27.0	18.7 Figure 1. Cancer Registries in Mainland South-East			
Colon	5.0	7.9	4.8	10.3	5.3	5.5	7.5			
Rectum	4.6	3.9	2.7	6.3	4.4	5.2	5.5			
Liver	18.4	32.3	88.0	14.4	8.6	20.0	27.1			
Gallbladder	1.7	2.9	1.9	1.3	0.8	0.5	1.6			
Pancreas	1.4	2.0	1.0	1.8	1.8	1.4	2.4			
Larynx	3.0	1.9	1.4	4.1	3.8	1.5	4.6			
Trachea, lung	32.6	51.7	18.5	25.7	15.4	34.4	26.9			
Penis	1.7	1.6	1.6	0.9	2.2	2.3	1.4			
Prostate	5.3	4.9	2.4	6.4	4.6	1.5	3.8			
Kidney	1.7	0.8	1.4	2.0	0.7	0.5	1.3			
Bladder	5.1	5.6	3.3	6.8	4.4	3.1	3.0			
Brain	1.6	1.1	2.7	2.4	1.5	0.7	2.3			
Thyroid	1.1	0.8	0.9	1.3	1.7	1.3	1.3			
Non-Hodgkin	7.1	6.0	3.7	5.0	5.5	7.2	3.2			
Leukemia	4.2	4.1	4.2	3.9	3.2	4.5	3.9			
Total	148	166	179	144	109	155	147			

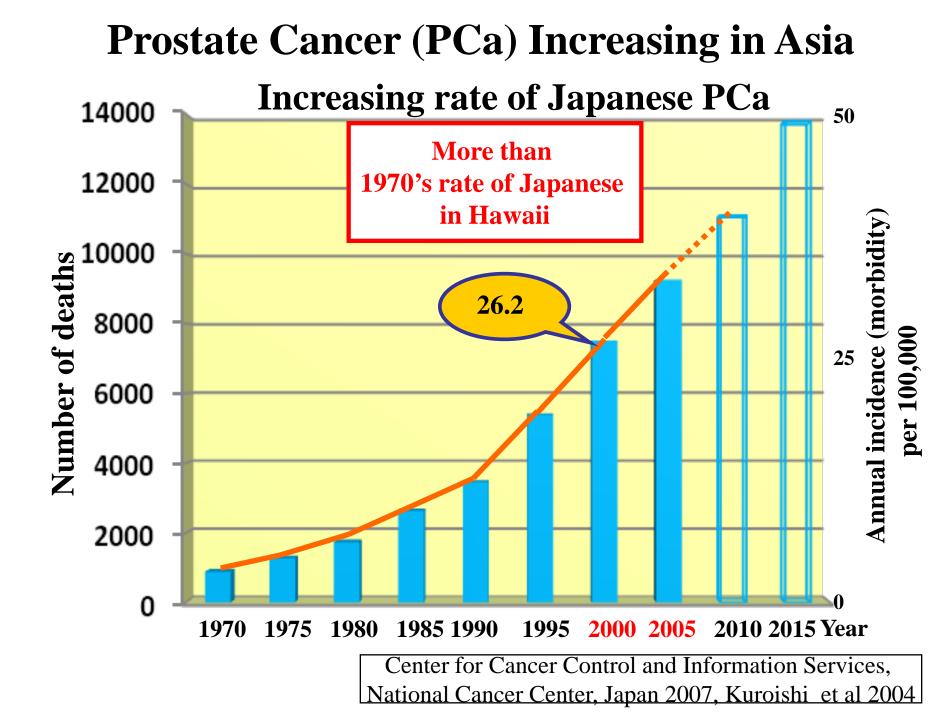
Table 2. Age-standardized Population-based Cancer Incidence Data for Mainland South-East Asian Countries - Males

\*Curado et al., 2007; \*Parkin et al., 2002

# **Prostate Cancer (PCa) Increasing in Asia**



Hirayama T et al. 1979



# References:

- Long N, Moore MA, Chen W, Gao CM, Lai MS, Mizoue T, Oyunchimeg D, Park S, Shin HR, Tajima K, Yoo KY, Sobue T. Cancer epidemiology and control in peninsular and island South-East Asia - past, present and future.AsianPac J Cancer Prev. 2010;11 Suppl 2:107-48. Review.
- 2. Moore MA, Manan AA, Chow KY, Cornain SF, Devi CR, Triningsih FX, Laudico A, Mapua CA, Mirasol-Lumague MR, Noorwati S, Nyunt K, Othman NH, Shah SA, Sinuraya ES, Yip CH, Sobue T. Cancer epidemiology and control in peninsular and island South-East Asia - past, present and future. Asian Pac J Cancer Prev. 2010;11 Suppl 2:81-98. Review.
- Moore MA, Attasara P, Khuhaprema T, Le TN, Nguyen TH, Raingsey PP, Sriamporn S, Sriplung H, Srivanatanakul P, Bui DT, Wiangnon S, Sobue T. Cancer epidemiology in mainland South-East Asia - past, present and future. Asian Pac J Cancer Prev. 2010;11 Suppl 2:67-80. Review.

Asia Pasific Prostate Society (APPS) March 04, 2011 Seoul

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# The burden of prostate cancer in Asia: prevalence & screening

# Yasutomo Nasu Okayama University Okayama Japan

特別史跡 閑谷(しずたに)学校(岡山県)

ORIGINAL ARTICLE



### PCa screening can reduce deaths by 20%

Prostate cancer is the scientific number one topic at the 24th Annual EAU Congress. At the EAU press conference Prof. Freddie Hamdy reported about congress highlights and also mentioned the European Randomized Study of Screening for Prostate Cancer. Only a few hours it was reported that screening for prostate cancer can reduce deaths by 20%, according to the results of the European Randomized Study of Screening for Prostate Cancer (ERSPC) published online by the New England Journal of Medicine.



ERSPC is the world's largest prostate cancer screening study. The findings were also unveiled at the 24th Annual EAU Congress in Stockholm.

## Screening and Prostate-Cancer Mortality in a Randomized European Study

Fritz H. Schröder, M.D., Jonas Hugosson, M.D., Monique J. Roobol, Ph.D., Teuvo L.J. Tammela, M.D., Stefano Ciatto, M.D., Vera Nelen, M.D., Maciej Kwiatkowski, M.D., Marcos Lujan, M.D., Hans Lilja, M.D., Marco Zappa, Ph.D., Louis J. Denis, M.D., Franz Recker, M.D.,
Antonio Berenguer, M.D., Liisa Määttänen, Ph.D., Chris H. Bangma, M.D., Gunnar Aus, M.D., Arnauld Villers, M.D., Xavier Rebillard, M.D.,
Theodorus van der Kwast, M.D., Bert G. Blijenberg, Ph.D., Sue M. Moss, Ph.D.,
Harry J. de Koning, M.D., and Anssi Auvinen, M.D., for the ERSPC Investigators\*

Swedish TV star Hasse Aro

ORIGINAL ARTICLE

#### Screening and Prostate-Cancer Mortality in a Randomized European Study

Fritz H. Schröder, M.D., Jonas Hugosson, M.D., Monique J. Roobol, Ph.D., Teuvo L.J. Tammela, M.D., Stefano Ciatto, M.D., Vera Nelen, M.D., Maciej Kwiatkowski, M.D., Marcos Lujan, M.D., Hans Lilja, M.D., Marco Zappa, Ph.D., Louis J. Denis, M.D., Franz Recker, M.D., Antonio Berenguer, M.D., Liisa Määttänen, Ph.D., Chris H. Bangma, M.D., Gunnar Aus, M.D., Arnauld Villers, M.D., Xavier Rebillard, M.D., Theodorus van der Kwast, M.D., Bert G. Blijenberg, Ph.D. Suc M. Moss, Dh.D. Harry J. de Koning, M.D., and Anssi Auvinen, M.D., for th ERSPC: Positive data for PSA screening

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

#### PLCO: Negative data for PSA screening

#### Mortality Results from a Randomized Prostate-Cancer Screening Trial

Gerald L. Andriole, M.D., Robert L. Grubb III, M.D., Saundra S. Buys, M.D., David Chia, Ph.D., Timothy R. Church, Ph.D., Mona N. Fouad, M.D., Edward P. Gelmann, M.D., Paul A. Kvale, M.D., Douglas J. Reding, M.D., Joel L. Weissfeld, M.D., Lance A. Yokochi, M.D., E. David Crawford, M.D., Barbara O'Brien, M.P.H., Jonathan D. Clapp, B.S., Joshua M. Rathmell, M.S., Thomas L. Riley, B.S., Richard B. Hayes, Ph.D., Barnett S. Kramer, M.D., Grant Izmirlian, Ph.D., Anthony B. Miller, M.B., Paul F. Pinsky, Ph.D., Philip C. Prorok, Ph.D., John K. Gohagan, Ph.D., and Christine D. Berg, M.D., for the PLCO Project Team\*

## JUA official statement for ERSP vs PLCO

## PLCO :

Contamination in control group Less valid as a RCT study Less scientific value

### ERSPC:

High scientific standard Highest level of evicence 20% reduction of death rate

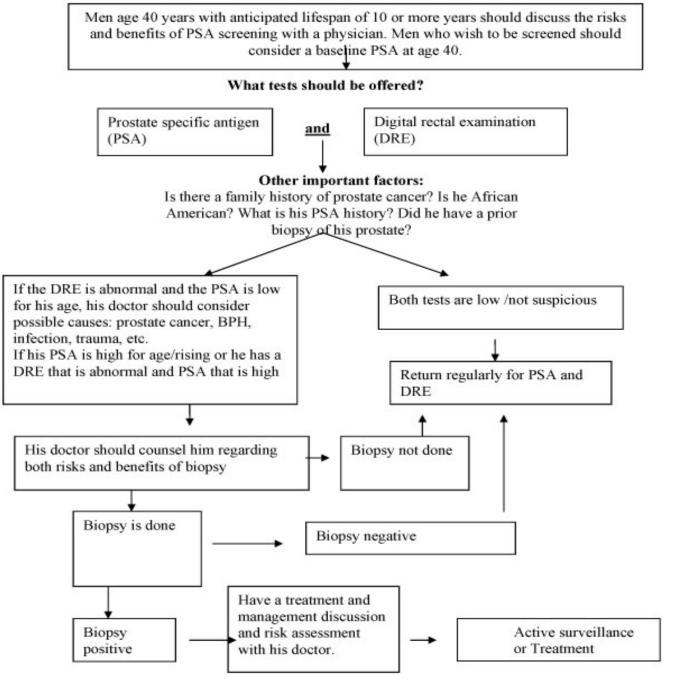
 In Japan: Based on ERSPC result Promotion of PSA screening Social recognition of PSA screening

# For whom might a PSA screening test be recommended?



The American Urological Association (AUA) issued new guidelines recommends that well informed men aged 40 and over who have a life expectancy of at least 10 years should be offered the prostate-specific antigen (PSA) test in order to establish a baseline reading and that PSA testing should be individualized rather than a blanket annual test for any man aged 50 and over.

> Prostate-specific antigen (PSA) best practice statement: 2009 update. American Urological Association 2009 (AUA)



Prostate-specific antigen (PSA) best practice statement: 2009 update. AUA

# EAU Guidelines on PSA Coll European Screening of Urology

# A baseline PSA determination at age 40 years has been suggested upon which the subsequent screening interval may then be based.

Tab. 1Übersicht über Einstiegsalter in die Früherkennung (in Klammern Alter bei Männern mit erhöhtem Risiko), PSA-Grenzwert zur Biopsie und Untersuchungsintervall in den<br/>Leitlinien von vier internationalen Fachgesellschaften

	Beginn	Grenzwert	Intervall
EAU 2009	Individuell, ggf. 50 Jahre	Individuell, ggf. >0,6 ng/ml/y	Individuell
American Cancer Society 2001	50 (45) Jahre	2,5 ng/ml	Jährlich
AUA Best Practice Policy 2009	40 Jahre	Individuell	Jährlich
National Comprehensive Cancer Network 2007	40 Jahre	2,6 ng/ml oder >0,35 ng/ml/y	<0,6 ng/ml: 45, 50, 51 >0,6 ng/ml: jährlich

(in German)

Guidelines on Prostate Cancer 2010 update. EAU Asia Pasific Prostate Society (APPS) March 04, 2011 Seoul



# The burden of prostate cancer in Asia: prevalence & screening

# Formation of research network on PCa

特別史跡 閑谷(しずたに)学校(岡山県)

Special Coordination Funds for Promoting Science and Technology in 2008-2010 FY Asia S&T Strategic Cooperation Promotion Program ~International Joint R&D~

An Asia-wide translational research on high-risk group detection based on ms-SNP and IL-12 immunogene therapy for prostate cancer

> Project leader: Hiromi Kumon Okayama University

#### Medical innovations

## Creation of advanced medical technology and global standard for TR

Established research seeds Immune Gene Therapy Analysis of Genetic **Predisposition for Cancer** 







Translational research (TR) Setting up of **Academic Society** in East Asia



#### Advisory board by outside experts

(1) Global standard

- 2 Ethics, Personal info.
- ③ Intellectual properties/

**Birth of** Medical innovation

**Academia** network based Okayama on University's long-lasting nartnarahin

KAYAMA

**Project Organization** 

#### **Expeditious implementation** (Global) Advisory Board **♦**Leading gene therapy for clinical study TR researchers in Japan, **Prof. Liping XIA** Prof. Yungun NA Beijing Univ. **US**, and **Europe** Zhejiang Univ. President for Chinese Urological Assoc. ♦ China Board of Science Head of Urology. China Rep. of China-Japan **♦**Leader in Global relation **Zhejiang University Urological Conference ♦**Leader in ethics 1<sup>st</sup> Hospital Prof. Ming LI **Beijing Cancer Hospital ♦** Specialist in global IP **♦** Leader in CRO industry Prof. Hiromi KUMON Okayama Univ. Chairman for Japanese Urological Assoc. (FY2009) Japan Rep. of China-Japan Urological Conference Chairman for Korea-Japan Urological Conference (FY2008) Prof. Shiro BABA Kitazato Univ. Dean, Medical School, Kitazato University <u>(</u>:: 11 Utilization of accumulated 12 Race diversity and data in the first Prostate leading ability in advanced **Bank in Asia** medical application Prof. Tae-Kon HWANG Korea Catholic Univ. **Prof. Christopher CHEN** President for Korean Urological Assoc. Head of Urology, Singapore SGH **Former Chairman for** Dr. Ji Youl LEE Singapore Urological Assoc. **President, Korea Prostate Bank**

### **Post-Genome Genetic Analyses**

Human Genome Project [1990~2003]

Mapping of entire human genome (3 billion bps)

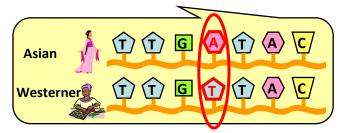
Everyone in the world shares "Human Genome" database

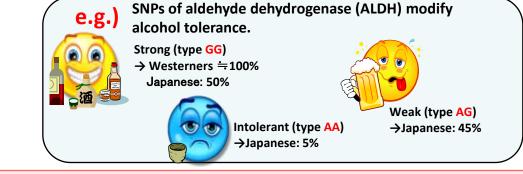
#### **Post-Genomic Era**

**Discovery of SNPs (Single Nucleotide Polymorphism)** 

**SNP** is a DNA sequence variation with a single nucleotide occurred in the genome between members of a species.

#### SNPs can affect ethnic/individual constitution





#### Genetic predisposition for cancer and its application to personalized medicine

- Cancer risk
- Cancer progression/recurrence risk
- Drug sensitivity/toxicity

SNPs provide new cancer medicine!!

Determination of cancer-predisposition by using multiple ms-SNPs, taking the initiative in the world by Prof. Shimizu, Okayama Univ.



#### Asia-wide Analysis of SNPs based on Japanese Data

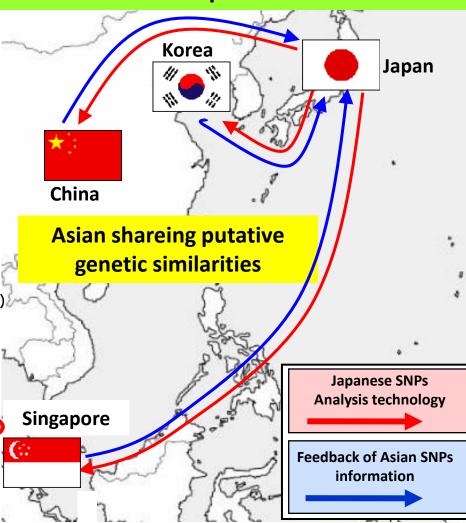
#### Prostate cancer-related missense SNPs

	<b>Okayama Univ.</b> 107-193981)				
Gene	Amino acid		Freque		corrected
Gene	permutation		Healthy	Cance	Odds Ratio
chromosome separation A	isoleucine →phenylalani	ne	39	52	1.77
chromosome separation B	arginine →glutamine		22	47	3.43
Cancer suppressor A	glutamine →histidine		39	56	1.95
Cancer suppressor B	glutamine →proline		21	37	1.90
Metabolic enzyme	glutamic acid →lysine		43	56	1.74
Apoptosis	arginine →glycine		43	54	1.87

#### Simultaneous analysis

0	Accumulated	Number o	f cases (%)	
Canc	number of high risk gene	Healthy	Cancer	Odds Ratio
er Healthy	<u> </u>	63 (46.7)	24 (14.8)	1.00 (ref.)
<b>Healiny</b>	s) 2	33 (24.4)	40 (24.7)	3.18
VS	3	25 (18.5)	45 (27.8)	4.73
V.S. Prostate	4	10 (7.4)	35 (21.6)	9.19
	≥ 5	4 (3.0)	18 (11.1)	11.8
Cancer	\$) _24	14 (10.	453 (32)	79.94
		•	• •	

#### Preventive/therapeutic strategies for prostate cancer From Japan to Asia



Accumulation of 4 or more high-risk genes leads to 10-fold higher incidence of prostate cancer.

**Development/Standardization of Japan-oriented Seeds** 

# **Samples Collected for SNPs Research**

Conutry	PCa	Control	
Japan	619	1565	
China	150	114	
Singapore	143	150	
Korea	100	100(BPH)	
TOTAL	1012	1929	2941

# **Implementation of Genotyping Work**

Samples Collection	DNA Extraction	First PCR	Second PCR	Analysis
Japan	Japan	Japan	Japan	Japan
China	China	China	China	Japan
Singapore	Singapore	Singapore	Japan	Japan
Korea	Korea	Japan	Japan	Japan

China: Transportation of human DNA and PCR products is forbidden Singapore: Transportation of PCR products permitted Korean: Transportation of human DNA permitted

# Highlights for SNPs Analysis Results (Japan)

#### Ethnic difference for distribution of the 42 ms-SNPs

1、8 SNPs in 6 genes associated with PCa risk;

Risk SNPs different for people <70 years compared with  $\geq$  70yrs;

- 2、An MOR method we established was useful in predicting risk of PCa;
- Associations between SNPs and clinical characteristics (PSA, Gleason Score and Stage) were specified;
- 4 、6 SNPs were found to be significantly associated with latent PCa;
- 5、 A few SNPs were found to be underlying prognosis marker after PCa radical therapy or Brachy therapy.

# Highlights for SNPs Analysis Results (Asia)

#### Ethnic difference for distribution of the 21 ms-SNPs

- 1. Genetic background of Japanese is similar to Korean, Chinese and Malay;
- 2、At least 3-4 Risk SNPs, which are useful in Japanese, might be effective in Korean and Chinese.

Gene         SNP (AN)         SNP (NU)         O kayama         Korean         Chinese         Chinese         Malay         Indian         Caucasian         A           Chromesoms Seg, # 1         P/S         C/T         0.88/0.12         0.78/0.22         0.78/0.24         0.72/0.28         0.88/0.14         0.86/0.43         0.68/0.43         0.68/0.43         0.68/0.41         0.68/0.41         0.68/0.44         0.68/0.42         0.68/0.44         0.68/0.42         0.68/0.44         0.68/0.42         0.68/0.43         0.68/0.43         0.68/0.43         0.68/0.42         0.68/0.42         0.68/0.43         0.68/0.43         0.68/0.43         0.68/0.43         0.68/0.43         0.68/0.43         0.68/0.43         0.68/0.43         0.68/0.43         0.68/0.43         0.68/0.43         0.68/0.43         0.68/0.43         0.68/0.43         0.68/0.43         0.68/0.43         0.68/0.43 </th <th></th> <th></th> <th>Nation</th> <th>Japan</th> <th>Korea</th> <th>China (Pekin)</th> <th></th> <th>Singapore</th> <th></th> <th>Europe</th> <th>Sub-Sahara</th> <th></th>			Nation	Japan	Korea	China (Pekin)		Singapore		Europe	Sub-Sahara	
Chromosome Seg. # 1 Chromosome Seg. # 1 P/S Chromosome Seg. # 2 V/H Gr/A 0.56/0.45 0.57/0.43 0.56/0.45 0.57/0.43 0.56/0.44 0.66/0.40 0.6			Males	n = 474	n = 100	n = 114	n = 50	n = 50	n = 50	n = 120	n = 120	
Cell Cycle #1 R/H G/A 0.5570.45 0.5170.49 0.6070.40 0.6770.33 0.6570.35 0.5770.43 0.570.43 0.570.45 0.770.43 0.570.45 0.770.43 0.570.45 0.770.43 0.570.45 0.770.43 0.570.45 0.770.43 0.570.45 0.5770.45 0.570.45 0	Gene	SNP (AA)	SNP (Nuc)	Okayama	Korean	Chinese	Chinese	Malay	Indian	Caucasian	African	
Repair # 1         R/Q         G/A         0.59/0.41         0.58/0.44         0.58/0.44         0.58/0.45         0.58/0.41	romosom e Seg. #1	P/S	C/T	0.88/0.12	0.83/0.17	0.78/0.22	0.76/0.24	0.72/0.28	0.86/0.14	0.57/0.43	0.93/0.07	
Repair #2         V/M         G/A         0.63/0.37         0.68/0.34         0.68/0.32         0.68/0.34         0.68/0.34         0.68/0.34         0.68/0.34         0.68/0.34         0.68/0.34         0.68/0.34         0.68/0.34         0.68/0.34         0.68/0.34         0.68/0.34         0.68/0.34         0.68/0.34<	oll Cycle # 1	R/H	G/A	0.55/0.45	0.51/0.49	0.60/0.40	0.60/0.40	0.67/0.33	0.65/0.35	0.57/0.43	0.86/0.14	
Repair # 3a         P/L         C/T         0.67/0.43         0.58/0.42         0.68/0.40         0.52/0.48         0.80/0.10         0.83/0.17         0.00           Tumor Suppressor #1         R/P         G/C         0.63/0.37         0.65/0.35         0.52/0.48         0.52/0.48         0.30/0.50         0.56/0.38         0.52/0.48         0.56/0.50         0.56/0.45	opair#1	R/Q	G/A	0.59/0.41	0.62/0.38	0.59/0.41	0.56/0.44	0.50/0.50	0.15/0.85	0.23/0.77	0.27/0.73	
Chromosome Seg.# 2       I/F       A/T       0.67/0.32       0.67/0.32       0.62/0.38	pair # 2	V/M	G/A	0.63/0.37	0.74/0.26	0.66/0.34	0.66/0.34	0.68/0.32	0.92/0.08	0.84/0.16	0.97/0.03	
Tumor Suppressor #1         R/P         G/C         0.8/0.37         0.66/0.36         0.52/0.48         0.50/0.50         0	opair#3a	P/L	С/Т	0.57/0.43	0.58/0.42	0.60/0.40	0.54/0.46	0.52/0.48	0.90/0.10	0.83/0.17	0.78/0.22	
Tum or Suppressor #1         R/P         G/C         0.68/0.37         0.66/0.36         0.52/0.48         0.50/0.50         0.50/0.50         0.50/0.50         0.50/0.50         0.50/0.50         0.50/0.50         0.50/0.50         0.50/0.50         0.50/0.50         0.50/0.50         0.50/0.50         0.50/0.50         0.50/0.50         0.50/0.50         0.65/0.35         0.52/0.28         0.50/0.50         0.60/0.50         0.66/0.34         0.65/0.35         0.62/0.38         0.66/0.34         0.65/0.55         0.62/0.38         0.66/0.34         0.65/0.45         0.66/0.34         0.66/0.34         0.66/0.34         0.66/0.34         0.66/0.34         0.65/0.41         0.66/0.45         0.66/0.45         0.66/0.45         0.66/0.45         0.65/0.41         0.66/0.45 <th< td=""><td>romosom e Seg.#2</td><td>I/F</td><td>A/T</td><td>0.65/0.35</td><td>0.68/0.32</td><td>0.71/0.29</td><td>0.62/0.38</td><td>0.62/0.38</td><td>0.31/0.69</td><td>0.98/0.02</td><td>0.98/0.02</td><td></td></th<>	romosom e Seg.#2	I/F	A/T	0.65/0.35	0.68/0.32	0.71/0.29	0.62/0.38	0.62/0.38	0.31/0.69	0.98/0.02	0.98/0.02	
Spoptosis*1         V/A         T/C         0.64/0.38         0.54/0.46         0.63/0.37         0.66/0.34         0.52/0.48         0.60/0.50         0.46/0.52         0.0           Vertabolic*1         E/K         G/A         0.77/0.23         0.67/0.13         0.61/0.19         0.01/0.09         0.90/0.01         1.00/0         0.71/0.22         0.65/0.31         0.62/0.38         0.46/0.54         0.46/0.54         0.46/0.54         0.46/0.54         0.46/0.55         0.47/0.55         0.46/0.55         0.47/0.55         0.46/0.55         0.47/0.55         0.46/0.55         0.47/0.55         0.46/0.55         0.47/0.55         0.46/0.55         0.47/0.55         0.46/0.55         0.46/0.55         0.46/0.55         0.46/0.		R/P	G/C	0.63/0.37	0.65/0.35	0.52/0.48	0.50/0.50	0.50/0.50	0.59/0.41	0.77/0.23	0.33/0.67	
poptosis#1         V/A         T/C         0.64/0.38         0.64/0.48         0.63/0.31         0.66/0.34         0.52/0.48         0.60/0.50         0.46/0.52         0.0           Vatabolic#1         E/K         G/A         0.77/0.23         0.67/0.43         0.61/0.19         0.61/0.09         0.69/0.01         1.00/0         1.00/	mor Suppressor #2	Q/H	G/T	0.72/0.28	0.69/0.31	0.65/0.35	0.72/0.28	0.59/0.41	0.81/0.19	0.78/0.22	0.55/0.45	
istabilic #1         E/K         G/A         0.77/0.23         0.77/0.23         0.87/0.13         0.81/0.19         0.99/0.01         1.00/0		V/A	т/с	0.64/0.36	0.54/0.46	0.63/0.37	0.66/0.34		0.50/0.50	0.48/0.52	0.69/0.31	
Tum or Suppressor # 3 brapin # 4 brapin # 4 brapin # 4 brapin # 5 brapin # 5 bra 5 brapin # 5 brapin # 5 brapin # 5 brapin # 5 brap			G/A	0.75/0.25							1.00/0	
Sepair # 1         L/R         T/G         0.77/0.29         0.57/0.43         0.68/0.31         0.76/0.24         0.68/0.32         0.68/0.32         0.68/0.32         0.68/0.40         0.68/0.44         0.68/0.45         0.58/0.41	mor Suppressor # 3	P/S	С/Т	0.70/0.30	0.74/0.26				0.46/0.54		0.98/0.02	
Stepair # 5         F/L         T/G         0.58/0.41         0.68/0.42         0.62/0.38         0.59/0.41         0.41/0.58         0.19/0.81         0.45/0.55         0.0           hromosome Seg.# 3         A/V         C/T         0.76/0.24         0.77/0.28         0.77/0.28         0.73/0.27         0.76/0.24         0.75/0.27         0.66/0.45         0.57/0.48         0.75/0.27         0.65/0.48         0.75/0.27         0.58/0.41         0.5         0.57/0.48         0.75/0.27         0.58/0.41         0.5         0.57/0.48         0.61/0.38         0.57/0.48         0.61/0.40         0.49/0.05         0.99/0.01         0.99/0.01         0.99/0.01         0.99/0.01         0.99/0.01         0.99/0.01         0.99/0.01         0.97/0.28         0.58/0.41         0.5         0.57/0.48         0.55/0.44         0.63/0.47         0.58/0.44         0.63/0.47         0.58/0.44         0.63/0.47         0.58/0.44         0.63/0.47         0.58/0.41		L/R									0.98/0.02	
https://measure.seg.#3         A/V         C/T         0.76/0.24         0.77/0.23         0.72/0.26         0.73/0.27         0.76/0.24         0.76/0.26         0.66/0.35         0.73/0.27         0.76/0.24         0.76/0.26         0.66/0.35         0.73/0.27         0.66/0.35         0.73/0.27         0.66/0.36         0.93/0.01         0.93/0.02         0.93/0.01         0.93/0.27         0.65/0.26         0.93/0.02         <	•										0.49/0.51	
bepair # 3b         T/M         C/T         0.88/0.12         0.91/0.09         0.99/0.01         0.94/0.06         0.90/0.10         0.92/0.06         1           tumor Suppressor # 6         L/V         T/G         0.54/0.46         0.67/0.33         0.52/0.48         0.61/0.39         0.73/0.27         0.59/0.01         0.73/0.27         0.59/0.41         0.73/0.27         0.59/0.41         0.73/0.27         0.59/0.41         0.73/0.27         0.59/0.41         0.73/0.27         0.59/0.41         0.73/0.27         0.59/0.41         0.73/0.27         0.59/0.41         0.73/0.27         0.59/0.41         0.73/0.27         0.59/0.41         0.73/0.27         0.59/0.41         0.73/0.27         0.59/0.41         0.73/0.27         0.59/0.41         0.73/0.27         0.59/0.41         0.73/0.27         0.59/0.41         0.57/0.43         0.55/0.45         0.53/0.47         0.55/0.45         0.53/0.47         0.52/0.48         0.64/0.36         0.44/0.16         0.89/0.11         0.55/0.45         0.53/0.47         0.55/0.45         0.77/0.23         0.64/0.16         0.89/0.11         0.55/0.45         0.77/0.23         0.64/0.16         0.89/0.11         0.55/0.45         0.77/0.23         0.64/0.16         0.89/0.11         0.55/0.45         0.77/0.23         0.64/0.16         0.89/0.11         0.55/0.45 <t< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>0.96/0.04</td><td></td></t<>											0.96/0.04	
Tumor Suppressor # 6a         Y/D         T/G         0.54/0.46         0.67/0.33         0.52/0.48         0.61/0.39         0.57/0.27         0.59/0.41         0.51/0.49           rumor Suppressor # 6b         I/M         A/G         0.52/0.48         0.61/0.39         0.51/0.49         0.56/0.44         0.49/0.51         0.61/0.39         0.51/0.49         0.56/0.44         0.61/0.39         0.51/0.49         0.51/0.49         0.51/0.49         0.61/0.39         0.51/0.49         0.51/0.49         0.51/0.49         0.61/0.39         0.51/0.49         0.51/0.49         0.61/0.39         0.51/0.49         0.51/0.49         0.61/0.39         0.51/0.49         0.51/0	-										1.00/0	
umor Suppressor # 7 umor Suppressor # 8 hromosome Seg.# 6 bincom seme Seg.# 7 bincom seme Seg.# 7 binco											0.20/0.80	
umor Suppressor # 6b         I/M         A/G         0.60/0.40         0.71/0.29         0.86/0.14         0.70/0.30         0.91/0.09         0.81/0.19         0.82/0.18           hromosome Seg.# 6         P/L         C/T         0.59/0.47         0.56/0.44         0.53/0.47         0.56/0.44         0.53/0.47         0.56/0.44         0.53/0.47         0.56/0.44         0.53/0.47         0.56/0.44         0.53/0.47         0.56/0.44         0.53/0.47         0.56/0.45         0.53/0.47         0.56/0.45         0.53/0.47         0.56/0.45         0.53/0.47         0.56/0.45         0.53/0.47         0.56/0.45         0.53/0.47         0.56/0.45         0.53/0.47         0.56/0.45         0.53/0.47         0.56/0.45         0.58/0.41         0.58/0.11         0.22/0.78         0.49/0.51         0.22/0.78         0.58/0.15         0.58/0.11         0.58/0.16         0.89/0.01         0.86/0.14         0.58/0.15         0.58/0.15         0.58/0.15         0.58/0.15         0.58/0.15         0.58/0.15         0.58/0.15         0.58/0.14         0.58/0.16         0.68/0.34         0.58/0.16         0.58/0.16         0.58/0.16         0.58/0.16         0.58/0.16         0.58/0.44         0.58/0.16         0.58/0.44         0.58/0.16         0.58/0.44         0.58/0.44         0.58/0.44         0.58/0.44         0.58/0.44 </td <td></td> <td>L/V</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>0.33/0.67</td> <td></td>		L/V									0.33/0.67	
Chromesome Seg.# 6 Repair # 9         P/L SC         C/T C/G         0.58/0.41 0.53/0.47         0.58/0.42 0.53/0.47         0.68/0.37 0.53/0.47         0.81/0.19 0.82/0.18         0.82/0.18         0.22/0.78         <											0.95/0.05	
Repair # 9         S/C         C/G         0.53/0.47         0.56/0.44         0.53/0.47         0.62/0.38         0.69/0.31         0.22/0.78         0.2           reli-Cell Inter.# 3         V/E         T/A         0.57/0.43         0.56/0.45         0.64/0.36         0.47/0.53         0.68/0.32         0.48/0.51         0.2         0.49/0.51         0.2         0.49/0.51         0.57/0.43         0.56/0.45         0.68/0.12         0.83/0.07         0.98/0.02         0.93/0.07         0.98/0.02         0.73/0.27         0.82/0.18         0.93/0.07         0.98/0.02         0.73/0.27         0.52/0.48<											0.83/0.17	
Sell-Cell Inter,#3       V/E       T/A       0.57/0.43       0.55/0.45       0.68/0.36       0.47/0.53       0.68/0.32       0.49/0.51       0.5         tepair # 6       A/V       C/T       0.83/0.17       0.83/0.17       0.98/0.02       0.84/0.16       0.84/0.16       0.88/0.12       0.84/0.16       0.88/0.12       0.84/0.16       0.88/0.17       0.98/0.007       0.86/0.14       0.86/0.14       0.88/0.12       0.85/0.15       0.83/0.17       0.94/0.06       0.8         tepair # 7       R/H       G/A       0.82/0.18       0.86/0.14       0.86/0.14       0.86/0.15       0.83/0.17       0.94/0.06       0.8       0.98/0.02       0.83/0.17       0.94/0.06       0.98/0.02       0.3         tetabolic #2       H/R       A/G       0.76/0.24       0.86/0.14	-										0.14/0.86	
tepair #6         A/V         C/T         0.83/0.17         0.83/0.17         0.77/0.23         0.84/0.16         0.89/0.11         0.85/0.15         1           tumor Suppressor #4         A/S         G/T         0.93/0.07         0.93/0.07         0.96/0.02         0.93/0.07         0.96/0.04         0.84/0.16         0.82/0.18         0.83/0.17         0.94/0.06         0.         0.93/0.07         0.96/0.04         0.84/0.16         0.93/0.07         0.96/0.04         0.84/0.16         0.93/0.07         0.94/0.06         0.         0.93/0.07         0.94/0.06         0.         0.93/0.07         0.96/0.02         0.93/0.07         0.94/0.06         0.         0.93/0.07         0.96/0.02         0.93/0.07         0.94/0.051         0.98/0.02         0.         0.         0.82/0.18         0.82/0.18         0.98/0.02         0.         0.         0.82/0.18         0.83/0.17         0.94/0.051         0.98/0.02         0.         0.         0.93/0.07         0.98/0.02         0.         0.         0.86/0.14         0.82/0.18         0.83/0.17         0.84/0.16         0.87/0.13         0.93/0.07         0.73/0.27         0.52/0.48         0.81/0.19         0.84/0.16         0.87/0.13         0.51/0.44         0.83/0.37         0.86/0.14         0.         0.56/0.44         0.58/0.15											0.18/0.82	
umor Suppressor #4 tepair #7         A/S         G/T         0.93/0.07         0.93/0.07         0.96/0.02         0.93/0.07         0.96/0.04         0.84/0.16         0.84/0.16           tepair #7         R/H         G/A         0.82/0.18         0.86/0.12         0.85/0.15         0.83/0.17         0.94/0.06         0.44/0.16           hrom osome Seg.#4         S/L         C/T         0.86/0.14         0.86/0.12         0.85/0.15         0.83/0.17         0.94/0.06         0.44/0.06           umor Suppressor #5a         R/Q         G/A         0.82/0.18         0.86/0.14         0.86/0.14         0.86/0.14         0.86/0.12         0.87/0.13         0.99/0.07         0.94/0.06         0.47/0.13         0.47/0.53         0.51/0.49         0.56/0.44         0.86/0.42         0.47/0.53         0.51/0.49         0.56/0.44         0.82/0.18         0.86/0.14         0.56/0.44         0.82/0.18         0.86/0.14         0.56/0.44         0.82/0.18         0.83/0.07         0.96/0.04         0.81/0.19         0.67/0.33         0.66/0.34         0.87/0.13         0.86/0.14         0.56/0.14         0.56/0.14         0.56/0.14         0.56/0.14         0.56/0.15         0.74/0.28         0.87/0.13         0.86/0.14         0.56/0.15         0.74/0.28         0.87/0.22         0.87/0.13         0.86/0					0.00, 0.40						1.00/0	
tepair # 7         R/H         G/A         0.82/0.18         0.88/0.12         0.86/0.15         0.83/0.17         0.94/0.06         0.0           hhromosome Seg.#4         S/L         C/T         0.86/0.14         0.82/0.18         0.82/0.18         0.82/0.18         0.82/0.18         0.82/0.18         0.82/0.18         0.82/0.13         0.82/0.14         0.82/0.13         0.82/0.14         0.82/0.13         0.82/0.14         0.82/0.13         0.82/0.14         0.82/0.13         0.82/0.14         0.82/0.13         0.82/0.14         0.82/0.14         0.82/0.14         0.82/0.14         0.82/0.14         0.82/0.14         0.82/0.15         0.73/0.27         0.52/0.48         0.51/0.45         0.52/0.48         0.51/0.45         0.51/0.45         0.51/0.45         0.51/0.45         0.51/0.45         0.51/0.45         0.51/0.45         0.51/0.45         0.51/0.45	•										1.00/0	
hromosome Seg.#4         S/L         C/T         0.86/0.14         0.82/0.18         0.86/0.15         0.82/0.18         0.98/0.02         0.1           tetabolic #2         H/R         A/G         0.76/0.24         0.66/0.34         0.49/0.51         0.09/0.91         0/1.00         0.6           tetabolic #3         I/V         A/G         0.82/0.18         0.66/0.34         0.49/0.51         0.09/0.91         0/1.00         0.6           tetabolic #3         I/V         A/G         0.82/0.18         0.66/0.34         0.68/0.34         0.69/0.40         0.66/0.34         0.69/0.40         0.66/0.34         0.69/0.40         0.66/0.34         0.69/0.40         0.66/0.34         0.69/0.41         0.67/0.33         0.66/0.34         0.68/0.16         0.73/0.27         0.52/0.48         0.66/0.44         0.88/0.42         0.47/0.53         0.61/0.49         0.66/0.34         0.69/0.31         0.66/0.34         0.68/0.16         0.73/0.27         0.52/0.48         0.66/0.34         0.68/0.16         0.73/0.27         0.52/0.48         0.66/0.34         0.69/0.31         0.66/0.34         0.68/0.31         0.66/0.34         0.69/0.31         0.66/0.34         0.69/0.31         0.66/0.34         0.66/0.34         0.66/0.34         0.66/0.34         0.66/0.34         0.66/0.33         <											0.65/0.35	
Interval       H/R       A/G       0.76/0.24       0.66/0.34       0.49/0.51       0.09/0.91       0/1.00       0         umor Suppressor #56       R/Q       G/A       0.82/0.18       0.62/0.38       0.66/0.34       0.66/0.34       0.82/0.18       0.66/0.34       0.80/0.40       0.66/0.34       0.87/0.13       0.3         ranscrip.Factor #1       R/G       C/G       0.57/0.43       0.87/0.13       0.36/0.42       0.47/0.53       0.51/0.49       0.3         umor Suppressor #56       Q/P       A/C       0.81/0.19       0.86/0.16       0.82/0.18       0.93/0.07       0.96/0.04       0.3         umor Suppressor #58       Q/P       A/C       0.81/0.19       0.67/0.33       0.66/0.44       0.82/0.18       0.93/0.07       0.96/0.04       0.3         umor Suppressor #8       S/P       T/C       0.85/0.15       0.76/0.24       0.63/0.37       0.63/0.31       0.86/0.14       0.30/0.70       0.96/0.04       0.3         informosome Seg.#5a       P/Q       C/A       0.78/0.22       0.77/0.24       0.63/0.37       0.63/0.37       0.63/0.37       0.83/0.17       0.22       0.67/0.33       0.3       0.63/0.37       0.63/0.37       0.63/0.37       0.63/0.37       0.63/0.37       0.63/0.37       0.63/	•										0.99/0.01	
Sumor Suppressor #5a         R/Q         G/A         0.82/0.18         0.82/0.18         0.62/0.38         0.60/0.40         0.66/0.34         0.87/0.13         0.73/0.27         0.52/0.48         0.73/0.27         0.52/0.48         0.73/0.27         0.52/0.48         0.73/0.27         0.52/0.48         0.73/0.27         0.52/0.48         0.73/0.27         0.52/0.48         0.73/0.27         0.52/0.48         0.73/0.27         0.52/0.48         0.73/0.27         0.52/0.48         0.73/0.27         0.52/0.48         0.73/0.27         0.52/0.48         0.73/0.27         0.52/0.48         0.73/0.27         0.52/0.48         0.73/0.27         0.52/0.48         0.73/0.27         0.52/0.48         0.73/0.27         0.52/0.48         0.73/0.27         0.56/0.44         0.83/0.37         0.86/0.14         0.74/0.26         0.84/0.16         0.70/0.30         0.74/0.22         0.74/0.26         0.84/0.16         0.70/0.30         0.74/0.22         0.76/0.24         0.72/0.33         0.86/0.13         0.86/0.14         0.73/0.27         0.85/0.15         0.73/0.37         0.81/0.15         0.83/0.37         0.81/0.13         0.83/0.37         0.81/0.13         0.81/0.13         0.81/0.13         0.81/0.13         0.81/0.13         0.81/0.13         0.81/0.13         0.81/0.13         0.81/0.13         0.81/0.13         0.81/0.13 <th< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>0/1.00</td><td></td></th<>											0/1.00	
Metabolic #3       I/V       A/G       0.95/0.05       0.87/0.13       0.93/0.07       0.73/0.27       0.52/0.48       0.3         ranscrip.Factor #1       R/G       C/G       0.57/0.43       0.56/0.44       0.56/0.44       0.56/0.42       0.47/0.53       0.51/0.49       0.47/0.28											0.77/0.23	
ranscrip.Factor # 1       R/G       C/G       0.57/0.43       0.56/0.44       0.58/0.42       0.47/0.53       0.51/0.49       0.51/0.49         lignaling # 1       S/L       C/T       0.78/0.22       0.84/0.16       0.84/0.16       0.83/0.17       0.93/0.07       0.96/0.04       0.51/0.49       0.31       0.86/0.14       0.93/0.07       0.96/0.04       0.51/0.49       0.51/0.49       0.84/0.16       0.84/0.16       0.83/0.17       0.93/0.07       0.96/0.04       0.51/0.49       0.56/0.44       0.84/0.16       0.83/0.17       0.93/0.07       0.96/0.04       0.51/0.49       0.56/0.44       0.84/0.16       0.83/0.31       0.86/0.14       0.56/0.44       0.84/0.16       0.70/0.30       0.74/0.26       0.74/0.26       0.84/0.16       0.70/0.30       0.74/0.26       0.74/0.26       0.84/0.16       0.70/0.30       0.74/0.26       0.74/0.26       0.83/0.37       0.85/0.15       0.76/0.22       0.77/0.33       0.74/0.26       0.83/0.37       0.83/0.17       0.74/0.26       0.83/0.37       0.83/0.37       0.83/0.33       0.83/0.37       0.83/0.33       0.83/0.37       0.83/0.33       0.83/0.33       0.83/0.33       0.83/0.33       0.83/0.33       0.83/0.33       0.83/0.33       0.83/0.33       0.83/0.33       0.83/0.33       0.83/0.33       0.83/0.33       0.83/0.33 </td <td></td> <td>0.94/0.06</td> <td></td>											0.94/0.06	
Bignaling # 1       S/L       C/T       0.78/0.22       0.84/0.16       0.82/0.18       0.93/0.07       0.96/0.04       0.2         umor Suppressor # 5b       Q/P       A/C       0.81/0.19       0.67/0.33       0.66/0.34       0.69/0.31       0.86/0.14       0.5         umor Suppressor # 8       S/P       T/C       0.85/0.15       0.74/0.26       0.84/0.16       0.70/0.30       0.66/0.34       0.69/0.31       0.86/0.14       0.5         ihrom osome Seg.# 5a       P/Q       C/A       0.78/0.22       0.76/0.24       0.62/0.38       0.83/0.37       0.81/0.19       0.5         ignaling # 2       S/T       G/C       0.79/0.21       0.73/0.27       0.85/0.15       0.78/0.22       0.67/0.33       0.63/0.37       0.63/0.37       0.63/0.37       0.63/0.37       0.63/0.37       0.63/0.37       0.63/0.37       0.63/0.37       0.5 <td></td> <td>0.89/0.11</td> <td></td>											0.89/0.11	
Jumor Suppressor # 5b         Q/P         A/C         0.81/0.19         0.87/0.33         0.66/0.34         0.69/0.31         0.86/0.14         0.5           umor Suppressor # 8         S/P         T/C         0.85/0.15         0.74/0.26         0.84/0.16         0.70/0.30         0.74/0.26         0.74/0.26         0.74/0.26         0.74/0.26         0.74/0.26         0.74/0.26         0.74/0.26         0.77/0.33         0.66/0.34         0.77/0.30         0.74/0.26         0.77/0.26         0.77/0.26         0.77/0.27         0.85/0.15         0.77/0.22         0.77/0.27         0.85/0.15         0.78/0.22         0.67/0.33         0.66/0.34         0.78/0.22         0.67/0.33         0.77/0.22         0.77/0.27         0.85/0.15         0.78/0.22         0.67/0.33         0.78/0.22         0.67/0.33         0.67/0.33         0.78/0.22         0.67/0.33         0.78/0.22         0.67/0.33         0.77/0.22         0.77/0.28         0.87/0.15         0.78/0.22         0.67/0.33         0.78/0.22         0.67/0.33         0.78/0.22         0.67/0.33         0.78/0.22         0.67/0.33         0.78/0.22         0.67/0.33         0.78/0.22         0.67/0.33         0.78/0.22         0.67/0.33         0.78/0.22         0.67/0.33         0.77/0.73         0.7         0.7         0.71/0.28         0.77/0.73 <td< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>0.99/0.01</td><td></td></td<>											0.99/0.01	
umor Suppressor #8       S/P       T/C       0.85/0.15       0.74/0.26       0.84/0.16       0.70/0.30       0.74/0.26       0.81/0.19       0.74/0.26       0.81/0.19       0.74/0.26       0.81/0.19       0.74/0.26       0.81/0.19       0.74/0.26       0.74/0.27       0.74/0.26       0.74/0.27       0.74/0.26       0.74/0.26       0.74/0.26       0.74/0.26       0.74/0.26       0.74/0.26       0.74/0.26       0.74/0.26 <th0.70< th="">       0.74/0.26       <th< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>0.92/0.08</td><td></td></th<></th0.70<>											0.92/0.08	
chromosome Seg.#5a       P/Q       C/A       0.78/0.22       0.78/0.22       0.76/0.24       0.62/0.38       0.63/0.37       0.81/0.19       0.73/0.21         hromosome Seg.#5b       P/A       C/G       0.79/0.21       0.73/0.27       0.86/0.15       0.78/0.22       0.67/0.33       0.3											0.73/0.27	
Chromosome Seg.#5b         P/A         C/G         0.79/0.21         0.73/0.27         0.85/0.15         0.78/0.22         0.67/0.33         0.73/0.37           bignaling #2         S/T         G/C         0.65/0.35         0.63/0.37         0.63/0.37         0.63/0.37         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.63/0.37         0.30/0.70         0.51/0.48         0.51/0.43         0.61/0.38         0.51/0.43         0.61/0.38         0.51/0.43         0.61/0.32         0.37/0.63         0.28/0.72         0.51/0.43         0.63/0.37         0.51/0.49         0.64/0.36         0.51/0.49         0.64/0.36         0.51/0.43         0.63/0.37         0.51/0.49         0.51/0.43         0.51/0.43         0.37/0.63         0.31/0.63         0.51/0.43	••										0.95/0.05	
Hignaling #2       S/T       G/C       0.65/0.35       0.63/0.37       0.55/0.45       0.30/0.70       0.63/0.37       0.5         tepair #8       H/D       C/G       0.54/0.46       0.86/0.64       0.28/0.64       0.29/0.71       0.27/0.73       0.4         Metabolic #4       I/V       A/G       0.86/0.14       0.86/0.14       0.83/0.17       0.76/0.24       0.29/0.71       0.27/0.73       0.4         Sell-Cell Inter.#1       P/R       C/G       0.71/0.29       0.83/0.17       0.76/0.24       0.72/0.28       0.61/0.39       0.4         ward Suppressor #9       W/L       A/T       0.64/0.36       0.87/0.13       0.80/0.20       0.74/0.26       0.95/0.05       0.5         ward Suppressor #9       V/M       G/A       0.64/0.36       0.52/0.48       0.51/0.49       0.64/0.36       0.28/0.72       0.4         ward Suppressor #9       Y/H       T/C       0.52/0.48       0.54/0.46       0.47/0.53       0.12/0.88       0.22/0.78       0.4         whrom some Seg.#7       R/Q       G/A       0.74/0.26       9       22       17       11       10         SUMMARY]       Similar       +13%       0       5       5       15       15       8											0.95/0.05	
Vepair #8         H/D         C/G         0.54/0.46         0.54/0.46         0.36/0.64         0.29/0.71         0.27/0.73         0.4           Aetabolic #4         1/V         A/G         0.86/0.14         0.83/0.17         0.76/0.24         0.72/0.28         0.61/0.39         0.4           Sell-Cell Inter.#1         P/R         C/G         0.71/0.29         0.64/0.36         0.87/0.13         0.80/0.20         0.74/0.26         0.95/0.05         0.4           iell-Cell Inter.#2         M/L         A/T         0.64/0.36         0.51/0.49         0.64/0.36         0.59/0.41         0.63/0.37         0.28/0.72         0.4           iumor Suppressor #9         V/M         G/A         0.64/0.36         0.51/0.49         0.64/0.36         0.59/0.41         0.63/0.37         0.4           ithromosome Seg.#7         R/Q         G/A         0.74/0.26         0.74/0.26         0.65/0.35         0.57/0.43         0.37/0.63         0.21/0.78         0.4           SUMMARY]         Identical         ±5%         42         15         9         22         17         11         10           similar         ±13%         0         5         5         15         8         9         9         2         17 <td></td> <td>0.27/0.73</td> <td></td>											0.27/0.73	
Metabolic #4       I/V       A/G       0.86/0.14       0.83/0.17       0.76/0.24       0.72/0.28       0.81/0.39       0.         bell-cell Inter.#1       P/R       C/G       0.71/0.29       0.87/0.13       0.80/0.20       0.74/0.26       0.95/0.05       0.         bell-cell Inter.#2       M/L       A/T       0.64/0.36       0.74/0.28       0.83/0.17       0.76/0.24       0.72/0.28       0.95/0.05       0.         sumor Suppressor #9       V/M       G/A       0.64/0.36       0.75/0.22       0.68/0.32       0.37/0.63       0.28/0.72       0.         sepair #10       Y/H       T/C       0.52/0.48       0.54/0.46       0.47/0.53       0.12/0.88       0.22/0.78       0.         Chromosome Seg.#7       R/Q       G/A       0.74/0.26       0.5       9       22       17       11       10         SUMMARY]       Similar       ±13%       0       5       5       15       8       9         Neutral       13 - 20%       0       1       0       4       6       7       5											0.54/0.46	
Scell-Cell Inter.#1         P/R         C/G         0.71/0.29         0.87/0.13         0.80/0.20         0.74/0.26         0.95/0.05         0.           vell-Cell Inter.#2         M/L         A/T         0.64/0.36         0.78/0.22         0.86/0.32         0.37/0.63         0.28/0.72         0.           'umor Suppressor #9         V/M         G/A         0.64/0.36         0.51/0.49         0.64/0.36         0.59/0.41         0.63/0.37         0.           'sepair #10         Y/H         T/C         0.52/0.48         0.54/0.46         0.47/0.53         0.12/0.88         0.22/0.76         0.           'chromosome Seg.#7         R/Q         G/A         0.74/0.26         0.74/0.26         0.37/0.63         0.22/0.76         0.           SUMMARY]         Similar         +13%         0         5         9         22         17         11         10           Neutral         13 - 20%         0         1         0         4         6         7         5											0.63/0.37	
Cell-Cell Inter.#2         M/L         A/T         0.64/0.36         0.78/0.22         0.68/0.32         0.37/0.63         0.28/0.72         0.78/0.22           Suppressor #9         V/M         G/A         0.64/0.36         0.64/0.36         0.51/0.49         0.68/0.32         0.37/0.63         0.28/0.72         0.71/0.25         0.71/0.49         0.68/0.32         0.59/0.41         0.63/0.37         0.71/0.25         0.71/0.49         0.64/0.36         0.59/0.41         0.63/0.37         0.71/0.25         0.71/0.49         0.64/0.36         0.59/0.41         0.63/0.37         0.71/0.25         0.71/0.49         0.66/0.14         0.65/0.35         0.12/0.88         0.22/0.78         0.71/0.63         0.71/0.63         0.71/0.63         0.71/0.63         0.71/0.63         0.71/0.63         0.71/0.63         0.71/0.63         0.71/0.63         0.71/0.63         0.71/0.63         0.71/0.70         0.71/0.63											0.85/0.15	
Summary         V/M         G/A         0.64/0.36         0.64/0.36         0.69/0.41         0.63/0.37 <td></td> <td>0.47/0.53</td> <td></td>											0.47/0.53	
Repair # 10         Y/H         T/C         0.52/0.48         0.54/0.46         0.47/0.53         0.12/0.88         0.22/0.78         0           Chromosome Seg.# 7         R/Q         G/A         0.74/0.26         0.86/0.14         0.65/0.35         0.12/0.88         0.22/0.78         0         0           SUMMARY]         Identical ±5%         42         15         9         22         17         11         10           SUMMARY]         Similar ±13%         0         5         5         15         8         9												
Chromosome Seg.#7         R/Q         G/A         0.74/0.26         0.86/0.14         0.65/0.35         0.57/0.43         0.37/0.63         0.5           SUMMARY]         Identical         ±5%         42         15         9         22         17         11         10           SUMMARY]         Similar         ±13%         0         5         5         15         15         8         9           Neutral         13 - 20%         0         1         0         4         6         7         5	••										0.65/0.35	
Identical         ± 5%         42         15         9         22         17         11         10           SUMMARY]         Similar         ± 13%         0         5         5         15         15         8         9           Neutral         13 - 20%         0         1         0         4         6         7         5												
SUMMARY]         Similar         +13%         0         5         5         15         8         9           Neutral         13 - 20%         0         1         0         4         6         7         5	iromosome seg.# /	<u> </u>	G/A	0.74/0.26			0.86/0.14	0.05/0.35	0.57/0.43	0.3770.63	0.94/0.06	
Neutral 13-20% 0 1 0 4 6 7 5		Identical		42	15	9	22	17	11	10	6	
	SUMMARY]	Similar	<u>+</u> 13%	0	5	5	15	15	8	9	5	
		Neutral	13 - 20%	0	1	0	4	6	7	5	7	
		Distinct	> 20%	0	0	0	1	4	16	18	24	
% Similarity 100 92 93 91 87 73 73							0.4				66	

#### Ethnic Variation in Allele Frequency of 42 ms-SNP of Cancer-related Genes

Criteria: Compared to Japanese data,

Green: identical

**Light blue:** Similar

Yellow: Intermediate

Red: Distinct

Data of Caucasians and Africans are from NCBI database

Genetic background of Japanese is similar to Korean, Chinese and Malay

	Population (Controls/ Cases			Population (Controls/ Cases)					Population (Controls/ Cases)					
	Japai	n	(474/2	10) a*	Mainland	China	u (114/150) b*			Singapore	(16	(164/103) c*		
Gene	Risk allele	Ref	OR	Age	Risk allele	Ref	OR	Age	Repl.	Risk allele	Ref	OR	Age	Repl
Repair # 2	ММ	R+	1.44	All	ММ	RR	5.91	× 71	ОК					
Repair # 3b	RR	M+	0.38	< 70	Н	мм	2.06			н	AO	1.43	AII	
TSG # 2	RR	MM	2.11	< 70	R+	ММ	1.65	< 71		RR	мм	2.52	AII	ОК
Metablic # 1	н	MM	2.48	> 70	R+	мм	2.07	< 71	OK?	н	мм	2.33		ОК
Repair # 4	RR	M+	2.83	> 70	RR	M	1.65	AII		RR	M+	1.56	AII	
Cell-Cycle # 1	ММ	R+	2.10	> 70	мм	н	1.67	< 71						
Chrom.Seg.#3	ММ	R+	1.49	AII	мм	R+ 🖌	2.58	71	OK?					
Chrom. Seg. #2	н	AO	1.53	AII	/н /	AO	1.39	AII						
TSG #3	н	AO	0.59	< 70	<b>R</b> R	AO	0.26	AII	OK?	н	MM	0.76	_	
TSG # 7	ММ	R+	1.68	> 70	ND				?	ММ	R+ (	2.85	AII	ОК
Signaling # 1	R+	MM	1.45	AIJ	ND				?	ND				?
TSG # 8	RR	н	0.50	> 70	ND				?	ND				?
TSG #6b	ММ	R+	1.60		ND				?	ND				?
Арор # 1			Not Sig.		RR	ММ	5.17	AII	х	ММ	R+	2.70	AII	Х
Repair # 5			Not Sig.		ММ	R+	1.70	AII	x	ММ	R+	1.81	AII	х
Chrom.Seg.#1			Not Sig.		Н	AO	0.45	< 71	х	RR	ММ	3.45	AII	х
Repair # 1			Not Sig.							RR	M+	0.34	AII	х

Comparison of Gene Repertoire Associated with Prostate Cancer Risk between Japan and Chinese Males

Risk SNPs comparison (Japanese vs. Chinese): 4were identical, 4 similar and 3 Chinese specific

#### Medical innovations

## Creation of advanced medical technology and global standard for TR

Established research seeds

Immune Gene Therapy
Analysis of Genetic
Predisposition for Cancer





47.

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Advisory board by outside experts

① Global standard

- 2 Ethics, Personal info.
- ③ Intellectual properties

Birth of Medical innovation

Academia network based on Okayama University's long-lasting international partnership

KAYAMA