

INTERNATIONAL SNP RADIOSENSITIVITY STUDY

**Predicting Individual Radiation Sensitivity:
Current and Evolving Technologies
March 17-18, 2007**

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HYPOTHESIS

People who are carriers of certain single nucleotide polymorphisms (SNPs) may more likely to develop adverse radiation effects compared with individuals who not possess these DNA markers.

If we can identify SNPs associated with radiosensitivity and develop a predictive assay, what can be done with this information?

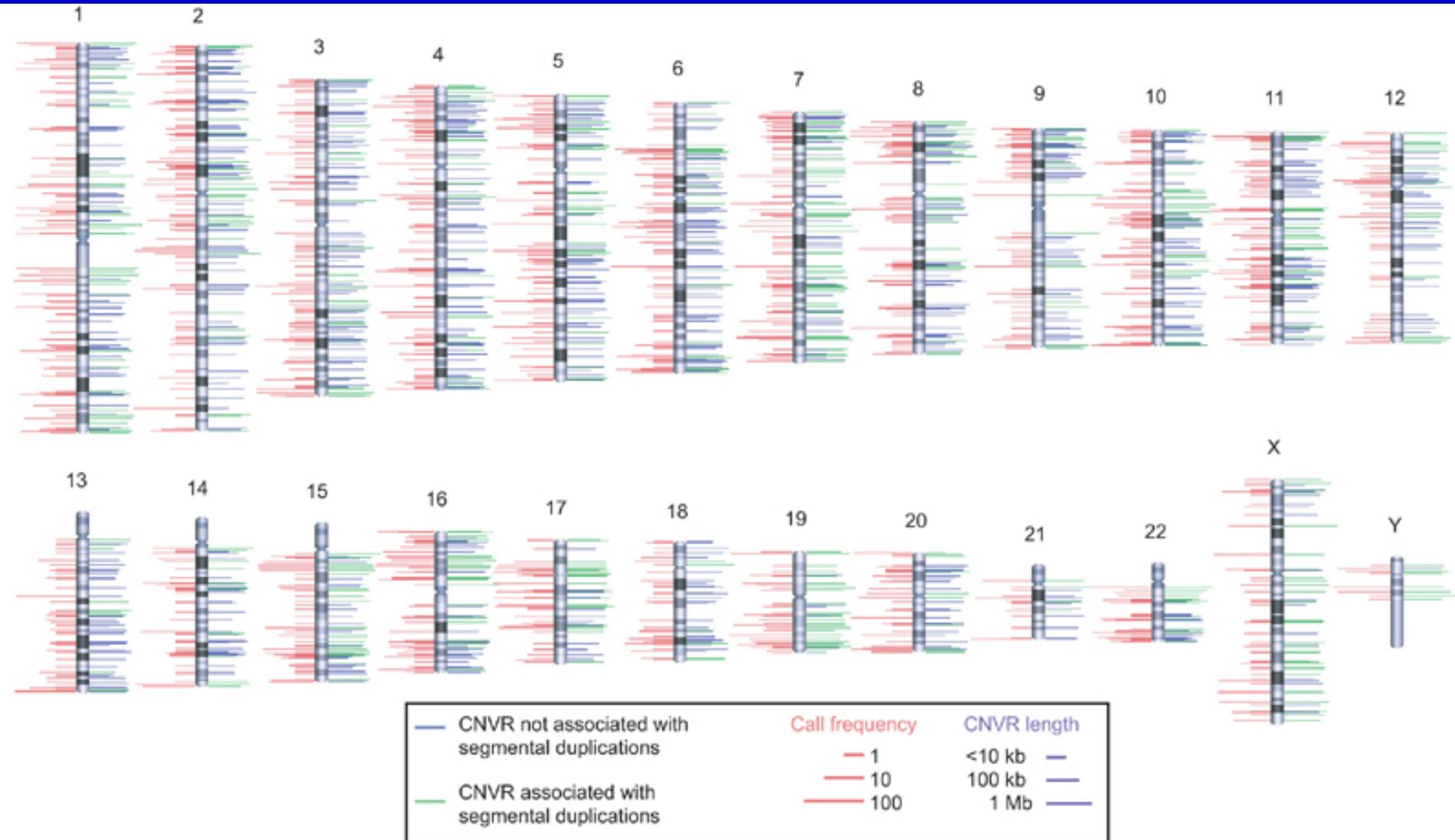
Victims of radiologic terrorism;

- Treat more aggressively to prevent or mitigate radiation injury**
- Follow more closely to detect radiation-induced cancers at an early stage**

Cancer patients;

- Receive a strictly surgical treatment, if feasible**
- Receive more of a conformal treatment (i.e. IMRT, protons, partial breast irradiation etc.)**
- Could be ideal RT candidates as their cancers may be radiosensitive; standard treatment overdoses**

Copy Number Polymorphisms/Variants (CNP/CNVs)



RADIOGENOMICS

**Predicting the radiation
response of people based
upon genetic profiles**

CANDIDATE GENE STUDIES

2000-2008

But, clearly we need to screen a much greater spectrum of genes and SNPs in order to develop a useful predictive assay that is characterized by a high level of sensitivity and specificity.

**THE PROBLEMS
WITH
CANDIDATE GENE STUDIES**

1. Although a number of studies have detected correlations between possession of a minor SNP allele with an increased incidence of radiation toxicity, the results of early studies have not always been validated in subsequent work.

2. There is relative ignorance of the full spectrum of genes and proteins that are associated with the development of radiation injury and/or radiation-induced cancers.

3. Even if all of the important genes that encode the essential protein products associated with radiation toxicity were included in candidate gene studies, it is not certain whether any of these genes would possess SNPs that would both alter protein function and be present at a high enough frequency in the population to be of importance.

4. Critical SNPs associated with radiosensitivity may not even be located within genes, but in regulatory portions of the DNA.

**Genome Wide Studies For
Identification of SNPs and CNPs
Associated with the Development of
Radiation Injury
and
Radiation-Induced Cancers**

International HapMap Project



SNP/CNP (Genotyping) Arrays



Affymetrix



Illumina

Cost of SNP Genotyping

1998 - \$1 per SNP

2008 - \$0.0004 per SNP

~2,500-fold decrease in the cost of SNP genotyping in the past decade!!!

The

RaPiD

International Consortium

**Radiotherapy Patient
Biorepository and Databank**

Satellite Meeting
Creation of an International Consortium to Establish a Radiotherapy Patient Biorepository/Databank

<u>Presenter</u>	<u>Institution</u>	<u>RT Populations that may be Contributed to the Biorepository/Databank</u>
David Azria	CRLC Val d'Aurelle, Montpellier, France	Breast and prostate cancer patients treated in CO-HO-RT, PHRC and BONBIS European cooperative trials
Yuhchyou Chen	University of Rochester Medical Center, Rochester, NY	Patients treated by investigators who are members of CURED (Cancer Survivorship Research and Education)
Karen Drumea	Rambam Medical Center, Haifa, Israel	Breast, prostate, head&neck and cervical cancer patients treated at the Rambam
Silvia Formenti	NYU Medical Center, New York, NY	Breast cancer patients treated under NYU protocols
Debra Friedman	Fred Hutchinson Cancer Research Center, Seattle, WA	Patients treated with total body irradiation at the Fred Hutchinson Cancer Center
Bruce Haffty	UMDNJ-New Brunswick, NJ	Breast cancer patients treated at UMDNJ, Yale and Korea
Germaine Heeren	ESTRO, Brussels, Belgium	Patients enrolled in the GENEPI Biorepository
Alice Ho	Memorial Sloan-Kettering Cancer Center, New York	Breast cancer patients treated at MSKCC
Mayumi Iwakawa	National Institute of Radiological Sciences, Chiba, Japan	Breast, prostate, head&neck and cervical cancer patients enrolled in the RadGenomics Biorepository
Shannon MacDonald	Massachusetts General Hospital Boston, MA	Breast and pediatric cancer patients treated at MGH
Thomas Merchant	St. Jude Children's Research Hospital, Memphis, TN	Pediatric patients treated at St. Jude
Mahmut Ozsahin	Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland	Cancer patients treated under EORTC protocols
Matthew Parliament	Cross Cancer Institute/University of Alberta, Edmonton, Canada	Prostate, breast and head&neck cancer patients treated at the Cross Cancer Institute
Barry Rosenstein	Mount Sinai and NYU Schools of Medicine, New York, NY	Patients enrolled in the Gene-PARE biorepository, the U.K. Start trial and RTOG