"The best prevention, is Early Detection"

EDRN Today

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CANCER BIOMARKERS RESEARCH GROUP

Early Detection Research Network (EDRN)

by Felicia Evans Long, MBA and Isabel Zaru-Roque, MPH

The Cancer Biomarkers Research Group (CBRG) has expertly led the extramural biomarker research. As the result of continuing proactive initiatives and discussions the group has taken several steps to involve key stakeholders in further developing the field of biomarkers in cancer risk assessment and early detection.

CBRG is increasing its social media presence! Tweets and Instagram updates will be sent out weekly to the NCI pages. NCI Blog updates will be forwarded on a monthly basis. Please forward all topics or ideas to Isabel Zaru-Roque.

Program Director of the Month
Dr. Christos Patriotis

Dr. Patriotis obtained his M.Sc. in Biochemistry from the University of Sofia, Bulgaria and his Ph.D. in Molecular Biology from the Bulgarian Academy of Sciences. His postdoctoral training focused on signal transduction and tumor cell biology. He joined the faculty at Fox Chase Cancer Center in 1994 where his research was directed toward understanding the mechanisms of breast and ovarian cancer pathogenesis and the identification of biomarkers associated with the early stages of the two types of cancer. This work included the development and characterization of animal models of breast and ovarian cancers, as well as transcriptomic and mutational analyses of human and animal model specimens for biomarker discovery for the early detection of breast and ovarian cancers. He joined CBRG in March, 2007, where he actively undertook the management and coordination of several key activities of the group, including the management and coordination of the EDRN Breast/Gyn Cancers Collaborative Group, the MCL Consortium focused on understanding the biological underpinnings of overdiagnosis, and the NCI-NASA/JPL interagency agreement focused on the development of the EDRN and MCL Knowledge Environments and for providing informatics support to these and other programs managed by the CBRG.

Investigator Spotlight, Dr. James G. Herman

DREAMing Platform for Melt-analysis of Methylated DNA

The Herman lab in collaboration with Dr. Jeff Wang at Johns Hopkins University have engineered a complex microfluidic platform to carry out DREAMing for detection of rare methylated genes as will be required for a diagnostic test. The feasibility of using this device to successfully carry out melt analysis of PCR products produced from their methylation-on-bead (MOB) technique was accomplished in an IMAT R21 grant. This device is now being enhanced to enable analysis of a higher resolution dimensional melt chip array allowing greater dilution of the molecular PCR products where detection of the rare methylation events among an overabundance of normal DNA is feasible.

The goal of this engineering feat is to automate DNA extraction and MOB on the microfluidic platform, perform PCR, and then analyze the products by melt analysis. The time to complete all the steps from initial DNA extraction to qPCR is reduced from 7 hours to 4.5 hours with the added advantage that all manipulations are handled robotically and should thus be more reproducible than standard lab handling. A publication was just accepted in Science Advances journal describing the high resolution melt chip array. Joining the manipulation of samples from MOB with loading onto the melt chips should complete the goals of this engineering plan where analysis of epigenetic biomarkers by the Herman lab can begin using this innovative technology. The plan is that the Herman lab will have a duplicate platform at Pittsburgh so both labs can compare results for concordance. It is likely that other epigenetic EDRN labs may be interested in using this technology. Such a device may transform the manner in which epialleles are detected and analyzed.

Herman Lab

Little bacteria, BIG questions

JOHNS HOPKINS UNIVERSITY

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Table 2. Comparison of DREAMing against commonly employed methylation analysis platforms

Technology	AveragePrep Time	AverageAssay Time	Cost perSample	Native Sensitivity	Heterogeneous Methylation Detection	Multi-Epiallelic Discrimination	Directly Quantitative	Main application
MSP/MethyLight	<30 min	2–3 h	$10–$100	0.01–0.1%	No	No	No	Fully methylated detection
MS-HRM (biased primers)	<30 min	2–3 h	$10–$100	0.1%	Yes	No	No	Rough HM Epiallele detection
Pyrosequencing	~1 h	~6 h	$50–$100	5%	Yes	No	No	Abundant Methylation Detection
Bisulfite sequencing	days	0.5–9 days	$1K–$10K	0.1%–1%	Yes	Yes	No	Methylome Analysis
DREAMing	**<30 min**	**2–3 h**	**$50–$100**	**0.005%**	**Yes**	**Yes**	**Yes**	**Epiallelic Heterogeneity analysis**

HM: heterogeneously-methylated.

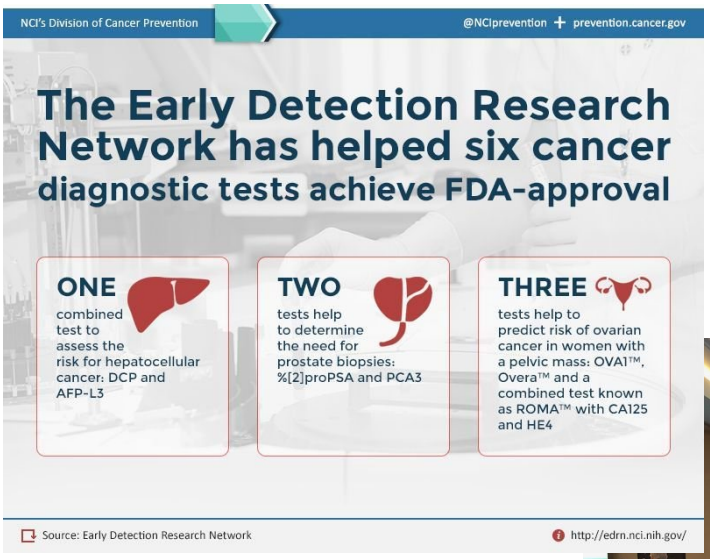
Pisanic, T. R., 2nd, Athamanolap, P., Poh, W., Chen, C., Hulbert, A., Brock, M. V., ... Wang, T. H. (2015). DREAMing: a simple and ultrasensitive method for assessing intratumor epigenetic heterogeneity directly from liquid biopsies. Nucleic acids research, 43(22), e154. doi:10.1093/nar/gkv795

34th EDRN Steering Committee Meeting and Sixth Annual US Japan Workshop on Cancer Biomarkers

The 34th Steering Committee Meeting of the NCI Early Detection Research Network was joined by the investigators engaged in biomarker research and supported by the Agency for Medical Research and Development (AMED). This was the sixth joint meeting between the two funding agencies committed to prevention of cancer through biomarker research. The meeting was held in Nashville, Tennessee and was hosted by the EDRN investigator, Dr. Pierre Massion of the Vanderbilt School of Medicine. The meeting was attended by more than a dozen investigators from Japan. Researchers discussed the challenges in early detection research, precision medicine, big data analysis, and on the nuances of biomarker discovery and validation.

For example, Dr. Chinnaiyan discussed CircRNA, a non coding RNA, as potential Biomarkers in early detection of prostate cancer. CircRNA is stable and resistant to exonucleases and can be assayed in urine.

A high-level Japanese delegation led by Dr. Tetsuo Noda, an eminent Japanese cancer researcher, was accompanied by the officials from Japans' AMED. AMED participated in the US Early Detection Research Network biannual meeting and discussed the potential collaboration on specimen and data sharing on pancreatic, prostate and GI cancers.



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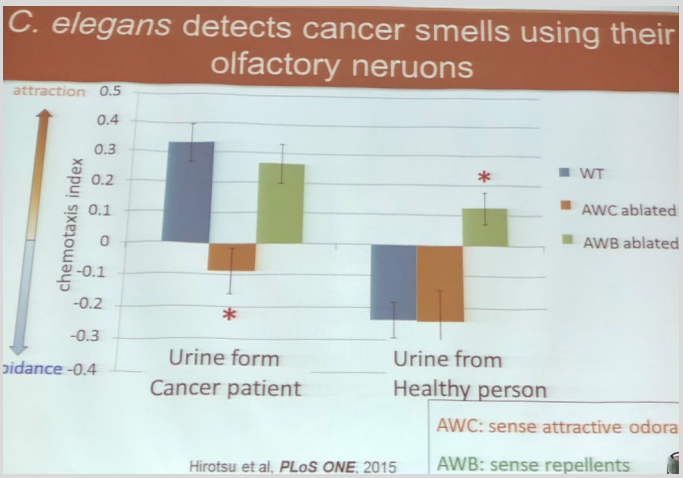
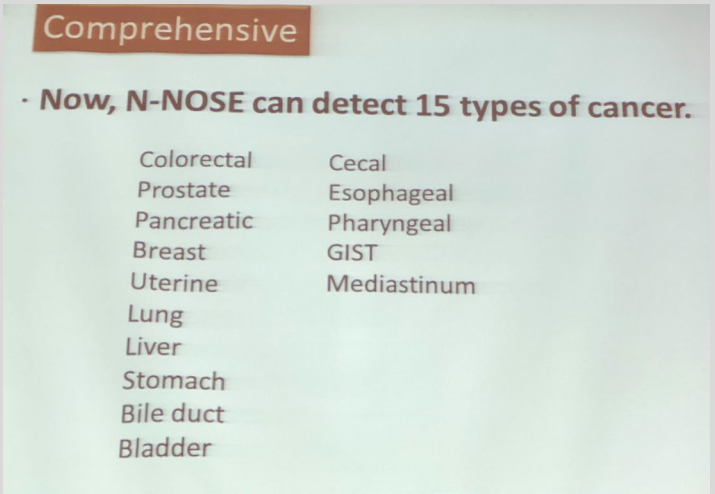
Dr. Yohei Matsunaga of Japan of Hirotsu Bio. Science, Inc. also spoke at the EDRN AMED joint meeting discussing his work with *C. elegans*. "Worms can detect early cancer by sensing odor emanating from cancer" The worm *C. elegans* can be grown and harvested rapidly on agar plate and can be used to detect cancer in urine with high sensitivity and specificity. The assay is named N-NOSE. Benefits of this organism include that it is a small model organism (1mm), free living, and that it has olfactory responses that can easily be measured by locomotion in small field (approximately 9 cm dishes). Handling and culture are performed easily in comparison to other formerly tested organisms.





NCI –Sponsored AACR Session on Liquid Biopsy Draws a Big Crowd!

The American Association for Cancer Research (AACR) Annual Meeting occurred March 29th to April 3rd at the Georgia World Congress Center in Atlanta, GA. The meeting program boasted a robust number of speakers covering "the latest discoveries across the spectrum of cancer research—from population science and prevention; to cancer biology, translational, and clinical studies; to survivorship and advocacy" according to the website. Meeting notes from the annual meeting can be found in this link. The conference room was filled to capacity requiring an overflow room for viewing.

The event was a success for the Cancer Biomarkers Research Group as noted in a story that CNN did on Liquid Biopsy, including quotes from Dr. Papadopoulos, a grantee in the Liquid Biopsy Consortium. The Liquid Biopsy Consortium is overseen by Chief of the Division, Dr. Sudhir Srivastava, and Program Director, Dr. Lynn Sorbara. Using blood, saliva, and urine are depicted as the "holy grail" of cancer detection, with the Consortium hard at work to make these kinds of tests a reality. The abstract can be found in this link.

Brain Break

Can you solve this months riddle? Answers will be given out in next months newsletter. The first one to solve the riddle correctly may email Ms. Felicia Evans Long (felicia.evanslong@nih.gov) for the correct answer.