"The best prevention, is Early Detection"

EDRN Today

March 2019

Early Detection Research Network (EDRN)
by Felicia Evans Long, MBA and Isabel Zaru-Roque, MPH

EDRN is on the MOVE!

From the 34th EDRN Steering Committee Meeting in Nashville, Tennessee we're looking forward to our Annual US Japan Workshop on Cancer Biomarkers Collaboration with NCI Early Detection Research Network. This meeting is very special because it is the joint meeting with Japan and US Biomarker researchers.

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. Richard Mazurchuk

Dr. Richard Mazurchuk, Program Director in the Cancer Biomarkers Research Group in the Division of Cancer Prevention at the National Cancer Institute.

After completing his academic training (BS in physics, MS and PhD in Molecular Biophysics) and Post Doc (Univ. NM, Center for Non-Invasive Diagnosis, his research primarily focused on the development of preclinical and clinical multi-modality imaging techniques, novel contrast (enhancing) agents and methods to assess the efficacy of various experimental therapeutics in cancer. "Maz" joined the faculty of SUNY Buffalo School of Medicine and Roswell Park Cancer Institute attaining the rank of Assoc Prof in the Departments of Diagnostic Imaging and Molecular and Cellular Biochemistry and Biophysics. For over 20 years he served as Scientific Director of Clinical MR Imaging and Director of Preclinical Imaging Resources. In 2010, he moved to NCI, joined DCP, and now focuses his efforts on improving methods for the Early Detection of Aggressive Cancer.

He enjoys family and traveling to his hometown of Buffalo, New York.

Early Detection Research Network

Investigator Spotlight, Dr. Arul Chinnaiyan, M.D., Ph.D.

The Landscape of Circular RNA in Cancer

A landmark paper from an EDRN Investigator, Dr. Arul Chinnaiyan and his colleagues at the University of Michigan, Ann Arbor MI, was published in the February 7th, 2019 in the Journal Cell. The team reported the creation of a comprehensive database of circular RNAs (circRNA) in multiple cancers and conducted initial research that suggests these molecules could serve as cancer markers in tissue blood and urine.

Circular RNA (or circRNA) are single-stranded covalently closed 3' and 5' ends of RNA molecules, which originated from pre-mRNA through a process known as backsplicing. circRNAs are predominantly found in the cytoplasm. However, circular intronic RNA (CiRNA) are distinct from circRNA, are predominantly located in the nucleus, and seem to be primarily involved in regulation of the expression of the parent genes. Interestingly, the number of circRNAs, derived from a particular locus could be much higher than the number of linear transcripts transcribed from the same locus (up to 10x). The circular structure is stable and quite resistant to exonuclease-mediated degradation. While most of the circRNA are known as noncoding RNA, more recently it was reported that some could code for proteins. This class of molecules was reported to participate in several different biological activities including binding of microRNA (miRNA) and proteins, and in epithelial-mesenchymal transition during cancer development.

In a recent paper in the journal Cell (Cell. 2019 Feb 7;176(4):869-881.e13. doi: 10.1016/j.cell.2018.12.021.) Dr. Arul Chinnaiyan's team developed an improved exome capture RNA-seq protocol for circRNA. They have applied this method to characterize circRNA molecules from 868 samples obtained from previously published datasets of clinical samples, cancer cell lines, and pooled normal tissues. The study resulted in the development of the most comprehensive catalog of cancer based circRNA – MiOncoCirc. New computational tools that were developed were used to detect a read-through circRNAs (rt-circRNA), a new class of circRNA that involve exons from different genes (fused circRNA). Differentially expressed circRNAs were detected in many cancers including prostate. Furthermore, such markers were also detected in urine of prostate cancer patients.

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 is joined by the investigators engaged in biomarker research and supported by AMED. This is the sixth joint meeting between the two funding agencies committed to prevention of cancer through biomarker research. The meeting is being held in Nashville, Tennessee and is being hosted by the an EDRN investigator, Dr. Pierre Massion of the Vanderbilt School of Medicine. The meeting being attended by more than a dozen investigators from Japan.

This meeting covers topics ranging from challenges in early detection research, precision medicine through precision detection, big data analysis on biomarkers promoting crowd sourcing, and several panel discussions on the nuances of biomarker discovery and validation. There will be several case studies from US and Japanese investigators using a specific cancer type to share each other's experiences and tackling challenges in developing better diagnostic markers. It is also noteworthy that in addition to supporting Japanese investigators, this year AMED is supporting a young scientist to spend some time in the laboratory of Dr. Anirban Maitra of the MD Cancer Research Center. This is a remarkable event in the history of the US EDRN and Japan AMED collaboration.

The goal of the 34th EDRN SC meeting and the 6th US Japan Workshop is to further advance the development and validation of cancer biomarkers and imaging modalities for earlier detection, risk assessment, diagnosis and early prognosis. Investigators will also discuss the optimization of biomarkers panels to unique cohorts such as Japanese, African Americans and Caucasians. The meeting intends to foster close collaboration between EDRN-NCI and Japan Agency for Medical Research and Development (AMED) funded investigators. Topics for discussion will include but are not limited to:

- Progress on Biomarkers for Selected cancers
- Personalized Medicine in Companion Diagnostics
- Application of NextGen Sequencing for discovery of genomic and phenotypic markers
- Integration of multi-omics and clinical paraments for Earlier Detection
- Application of innovative technologies for discovery and high throughput testing of biomarkers for early detection
- Machine-learning assisted studies for earlier detection of aggressive cancer
- Progress reports from individual Laboratories
- Biospecimens: Collection Availability and Accessibility
- Reports on Network's Verification and Validation Studies
- Organ specific collaborative group's meetings and discussions

Women in Science

The Cancer Biomarkers Research Group is proud to applaud the success of their women in science during International Women's Day on February 11th , 2019. From farthest left to right, Dr. Lynn Sorbara, Dr. Sharmistha Ghosh-Janjigian, Dr. Natalie Abrams, Dr. Jo Ann Rinaudo, Dr. Wendy Wang, . The breadth of experience that these scientists have encompasses a large portion of the work contributed to the Cancer Biomarkers Research Group portfolio.

- Dr. Rinaudo leads ongoing work with pancreatic and liver cancer research while supporting EDRN activities.
- Dr. Wang contributes to EDRN activities and leads the adductomics and adducts cancer research.
- Dr. Abrams contributes to ongoing work with the Cancer Biomarker Data Aggregator and leads its adjoining grant work.
- Dr. Ghosh-Janjigian leads and manages the Pancreatic Cancer Detection Consortium and contributes to the trans-NCI Human Tumor Atlas Network.
- Dr. Sorbara leads the Liquid Biopsy Consortium and contributed to the management of EDRN in various capacities.

The Cancer Biomarkers Research Group is deeply indebted to these scientists for their contributions in research, leadership, and novel concepts. Thank you for your hard work and continued efforts at NCI.

"I was taught that the way of progress was neither swift nor easy."
- Marie Curie

"Don't be afraid of hard work. Nothing worthwhile comes easily. Don't let others discourage you or tell you that you can't do it. In my day I was told women didn't go into chemistry. I saw no reason why we couldn't." -Gertrude Elion

In Memorial of Dr. Adi Gazdar

Dr. Srivastava was invited to give a memorial lecture in remembrance of Dr. Adi Gazdar who passed away on December 29th, 2018. The memorial lecture was organized by Dr. John Minna and Dr. Ignacio Ivan Wistuba.

"This was one of the most memorable events for me when hearing about Adi's life achievements, discoveries and contributions he made to lung cancer research. Many speakers shared their personal experiences with Adi and appreciated his indelible contributions in furtherance of their professional careers. One of the incidents that has left me in awe of his dedication to lung cancer research occurred a night before he passed away. He contacted a colleague to discuss the data on his research and indicated the urgency in light of his deteriorating health. He even predicted that he may not be around on this earth very long and wished that he could complete the data analysis. When my turn came to speak about Adi, I was about to break down, but composed myself quickly to celebrate his life of achievements.

Adi was wonderful colleague, friend and a gentleman. He visited my house several times when he was visiting NCI. During my ups and down with the EDRN program, he always encouraged me to be steadfast and determined to move forward with the program. He said the scientific accomplishment of the EDRN speaks for itself and I need not worry about. I really admired his support, mentorship and kind words that has come a long way to shape me up what I am today. Good Bye to my dear friend and may God bless his soul."
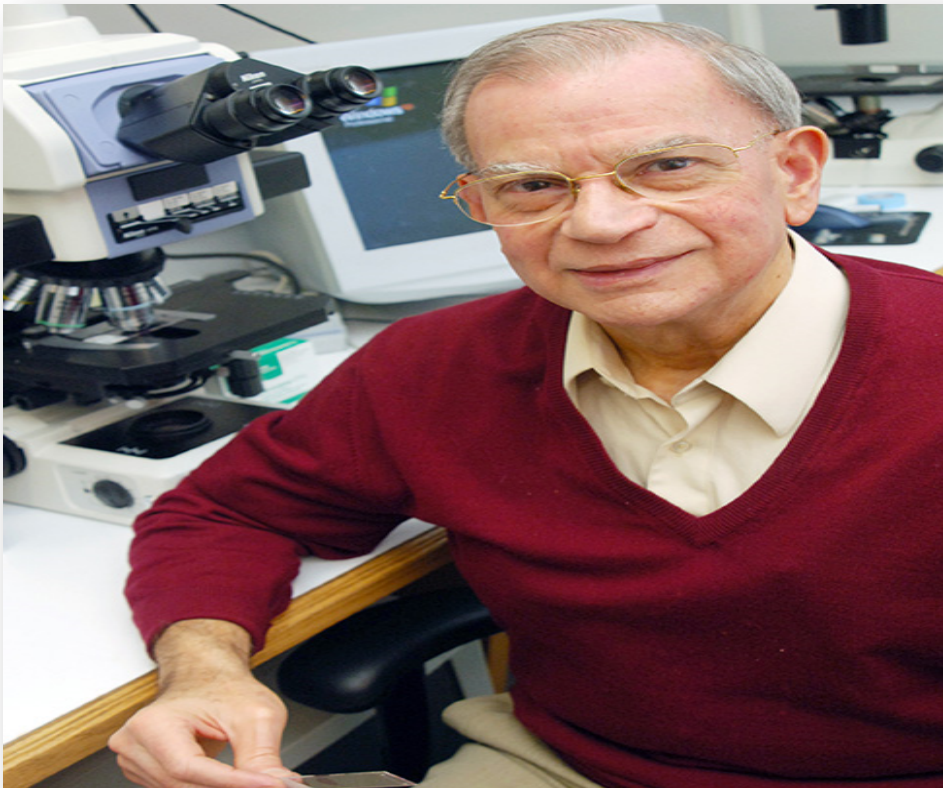
1st Translational Liver Cancer Consortium

The First Inaugural Translational Liver Cancer Consortium was held this past February to coordinate and focus their efforts on advancement of translational research focused on early detection of liver cancer. The consortium goals are to conduct studies to improve the surveillance of liver cancer in high-risk populations, increase the fraction of liver cancer detected at an early stage, and better stratify patients at risk of developing liver cancer.

Worldwide, liver cancer is the second most common cause of cancer-related death and it is a rising cause of cancer-related deaths in the United States. The etiological/risk factors for liver cancer include viral hepatitis (Hepatitis B virus and Hepatitis C virus),non-alcoholic steatohepatitis (NASH), and alcoholic liver disease (ALD). Approximately 80-90% of HCC occurs in patients with underlying liver cirrhosis. Patients with advanced cirrhosis represent a high-risk group for liver cancer.

This Consortium consists of five Translational Research Centers and one Data Management and Coordinating Center. These multidisciplinary teams address the following areas:

- Improving the surveillance for liver cancers in patients with cirrhosis;
- Increasing the detectability of liver cancers at early stages; and/or
- Approaches to better stratify patients with cirrhosis, who are at risk of developing liver cancer.

To achieve these goals, the consortium consists of clinical researchers with multi-disciplinary expertise in such areas as early cancer detection, biomarkers, surveillance, imaging, and biospecimen science.