

The second Cancer Prevention Initiative (CPI) Research Meeting was held on January 18<sup>th</sup>, 2023. Following the success of the first meeting in 2021, this event was again held virtually and was moderated by Dr. Larry Brody, Director of the Division of Genomics at the National Human Genome Research Institute at the National Institutes of Health. He is a strong advocate for cancer prevention and has made pioneering discoveries of the genetic basis of breast cancer and the roles of the breast cancer genes BRCA1 and BRCA2.

CPI President and Chief Scientific Officer Dr. Theo Ross opened the meeting by welcoming the attendees and thanking Dr. Brody for moderating the event again this year. She reiterated the mission and the strategy of CPI, to accelerate the discovery and development of new medicines that prevent cancer by supporting research on the prevention of inherited cancers. She shared the good news that in addition to the progresses made in the scientific research front, CPI has successfully raised substantial funds to continue support of current projects as well to start additional projects this year. She also spoke of new funding opportunities in the external cancer prevention front: concept proposals by the National Cancer Institute's Division for Cancer Prevention in support of research related to immunoprevention and the discovery of natural compounds that may prevent cancer. This is a welcome change, as prevention research has historically received weak support from funding agencies. Even today, only a small fraction of the funding is devoted to prevention, and treatment remains the main focus. These new efforts, though small, may herald a rising interest in prevention by funding agencies.

This year's CPI research meeting featured a lineup of CPI-funded researchers who presented updates on their research projects. The first session of the meeting was dedicated to research projects on immunoprevention of cancer, harnessing the abilities of the immune system to stop precancerous lesions from developing into cancer. Dr. Peter Lee of the City of Hope Comprehensive Cancer Center discussed his project related to repurposing an FDA-approved antiparasitic drug that they showed could kill nascent tumor cells in a way that activates the immune surveillance system to prevent future cancer initiation.

The next presenter, Cleveland Clinic's Dr. Charis Eng, started her presentation with a historical imperative for prevention from the ancient Chinese medical text Huang Dee Nai-Chang: "Superior doctors prevent the disease, mediocre doctors treat the disease before evident, and inferior doctors treat the full-blown disease". This philosophy resonates with the mission and vision of CPI to shift the approach to cancer from treatment to prevention. Dr. Eng and her team are working on developing a vaccine that would specifically target BRCA1 mutated cells before they can proliferate into harmful tumors and can be given to BRCA1 mutation carriers to reduce their chance of developing cancer. Along the way, they have generated the first gene expression data comparing tumor and normal mammary tissue of BRCA1 mutation carriers. These data are an invaluable resource for all researchers studying breast cancer.

The second session was dedicated to projects exploring the earliest events that drive cancer initiation and understanding the mechanisms underlying these events. BRCA1 mutation carriers have only one "good" copy of BRCA1 instead of the normal two. It is well known that precancerous cells develop when the "good" copy of the BRCA1 gene is lost. Dr. Maria Jasin and her team at Memorial Sloan Kettering

Cancer Center have generated a very elegant cell-based assay to identify compounds and signaling pathways that contribute to BRCA1 gene loss. Their work can lead to finding ways to intercept this early step necessary for transformation.

CPI-funded researchers at the Women's College Research Center at University of Toronto, Drs. Joanne Kotsopoulos and Leonardo Salmena, and Ph.D. candidate Erin Sellars, attempt to prevent cancer development in BRCA1 mutation carriers by restoring BRCA1 expression levels to normal levels. They used a high-throughput screen they developed to identify drugs that increased BRCA1 expression, and they have hit upon some promising targets.

The CPI Research Meeting was an opportunity for CPI scientists to share their newest data and get productive feedback from fellow scientists. It was also an opportunity for cancer scientists with a shared interest in prevention to come together and have a larger conversation on the challenges of carrying out cancer prevention research - from limited funding and lack of enthusiasm from the medical community to restrictions posed by regulatory agencies. These are some of the challenges CPI attempts to address through its goals.

The meeting ended with closing remarks by Dr. Ross.

The meeting was supported by generous funding from Lyda Hill Philanthropies.

### Meeting Participants

Moderator:

Lawrence Brody, Ph.D.  
Director, Division of Genomics  
National Human Genome Research Institute  
National Institutes of Health

Participants:

Charis Eng, M.D., Ph.D. Presenter  
Professor, Sondra J. and Stephen R. Hardis Endowed Chair in Cancer Genomic  
Medicine  
Lerner Research Institute, Cleveland Clinic  
"Transcriptome guided vaccine for BRCA1/2 germline mutation carriers"

Maria Jasin, Ph.D. Presenter  
Professor, Lab Head  
Memorial Sloan Kettering Cancer Center  
"Preventing LOH in BRCA mutation carriers"

Joanne Kotsopoulos, Ph.D.  
Scientist, Familial Breast Cancer Research Unit, Women's College Research  
Institute  
Associate Professor, Department of Pharmacology & Toxicology, University of  
Toronto  
"Screening for modifiers of BRCA1 expression"

Peter P. Lee, M.D. Presenter  
Chair, Department of Immuno-Oncology  
Professor, Department of Hematology & Hematopoietic Cell Transplantation  
City of Hope Comprehensive Cancer Center  
“Chemo-immunoprevention for cancer via repurposing a low-cost, safe, anti-parasitic drug”

Steven Narod M.D., FRCPC, FRSC  
Tier 1 Canada Research Chair in Breast Cancer, Women’s College Research  
Institute  
Professor, Dalla Lana School of Public Health, University of Toronto

Ying Ni, Ph.D.  
Assistant Professor, Cleveland Clinic Center for Immunotherapy and Precision  
Immuno-oncology  
“Transcriptome guided vaccine for BRCA1/2 germline mutation carriers”

Leonardo Salmena, Ph.D.  
Associate Professor, Department of Pharmacology and Toxicology, University of  
Toronto  
Affiliate Scientist, Princess Margaret Cancer Centre  
Canada Research Chair, Tier 2  
“Screening for modifiers of BRCA1 expression”

Erin Sellars, M.Sc. Presenter  
Ph.D. Candidate, Salmena Lab  
Department of Pharmacology & Toxicology, University of Toronto  
“Screening for modifiers of BRCA1 expression”

CPI team participants:

Doug Hager, Ph.D.  
CPI Sr. Vice President, Project Management and Operations

Theo Ross, MD, Ph.D.  
CPI President and Chief Scientific Officer

Marion Stewart-Thomas, M.S.  
CPI Operations Manager

Angelique Whitehurst, PhD.  
CPI Sr. Scientist and Advisor

Ranjula Wijayatunge, Ph.D.  
CPI Project Manager