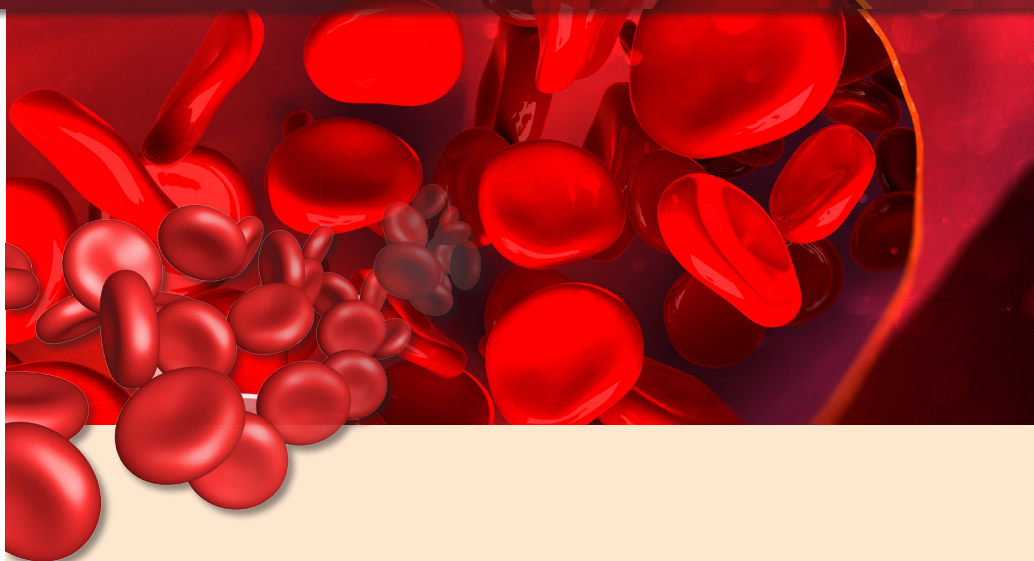


THE SECOND DOTAN INTERNATIONAL SYMPOSIUM

HEMATOLOGICAL MALIGNANCIES BRIDGING THE TRANSLATIONAL GAP



05 . 09 . 17

Beit Hatfutsot, Tel Aviv University

The Dotan Center for research in Hemato-Oncology



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Meeting Coordinator

Judith Ben-Porath

Greetings



Dear Colleagues,

Varda and Boaz Dotan have founded a unique center in Tel Aviv University. Their generous donation has fostered advanced research of hematological malignancies bringing together physicians and scientists in Tel Aviv University and in the affiliated university hospitals. The ultimate goal of this translational research is to harness biology for the cure of hematological malignancies.

The focus of the Second International Dotan Symposium on Hematological Malignancies is on bridging the translation gap between basic research discoveries and the clinical needs. The conference is designed in pairs of lectures given by esteemed international and Israeli physicians and scientists. A clinician lecture on the “translational gap” – describing the unmet needs for treatment of a specific hematological cancer is followed by research talks describing recent breakthroughs that could bring us closer to new approaches for treatment of hematological malignancies with the ultimate goal of cure.

Shai Izraeli, MD

Head, the Varda and Boaz Dotan Center for Hemato-Oncology Research
The Dora and Gregorio orgio Shapiro Professor of Hematological Malignancies
Tel Aviv University
Head, the Genes Development and Cancer Pediatric Research Institute
Edmond and Lily Safra Children’s Hospital

Conference Agenda

September 5th 2017

8.00–8.45 Registration and Reception

8.45–9.00 GREETINGS

Joseph Klafter, President, Tel Aviv University

Ehud Grossman, Dean, Sackler Faculty of Medicine, Tel Aviv University

Moshe Mittelman, Chair, Israel Society of Hematology and Blood Transfusion

Dan Peer, Chair “Cancer Biology Research Center” Tel Aviv University

Boaz Dotan

9:00–11:00 SESSION I

Chairs: **Drorit Merkel**, Sheba Medical Center, Tel Hashomer;
Tsila Zuckerman, Rambam Medical Center, Haifa

9:00–9:15 *THE TRANSLATIONAL GAP: STEM CELL TRANSPLANTATION*

Avichai Shimoni, Sheba Medical Center, Tel Hashomer

9:15–9:40 WHERE IT ALL BEGINS: THE BONE MARROW MICROENVIRONMENT

Tsvee Lapidot, Weizmann Institute of Science, Rehovot

9:40–9:55 *THE TRANSLATIONAL GAP: AML*

Yishai Ofran, Faculty of Medicine, Technion, Haifa

9:55–10:20 AML: THE Evil SIDE OF GENE REGULATION

Ruud Delwel, Department of Hematology, Erasmus MC

10:20–10:35 *THE TRANSLATIONAL GAP: MDS*

Ofir Wolach, Rabin Medical Center, Petah Tikva

10:35–11:00 MDS – FROM GENOMICS TO PERSONALIZED THERAPIES

Joop Jansen, Radboud University, Nijmegen Medical Centre

11:00–11:30 Coffee Break

11:30–13:15 **SESSION II**

Chairs: **Adrian Duek**, Sheba Medical Center, Tel Hashomer;
Pia Raanani, Rabin Medical Center, Petah Tikva

11:30–11:45 *THE TRANSLATIONAL GAP: MYELOPROLIFERATIVE NEOPLASMS*
Maya Michowitz-Koren, Assaf Harofeh Medical Center, Tzrifin

11:45–12:10 MYELOPROLIFERATIVE NEOPLASMS – FROM BIOLOGY TO THERAPY
Radek C. Skoda, Department of Biomedicine, University Hospital Basel

12:10–12:35 NOVEL DIFFERENTIATION THERAPY OF MYELOFIBROSIS
John Crispino, Feinberg School of Medicine, Northwestern University

12:35–12:50 *THE TRANSLATIONAL GAP: MYELOMA*
Irit Avivi, Sourasky Medical Center, Tel Aviv

12:50–13:15 WHAT WE HAVE LEARNED FROM THALIDOMIDE IN DRUG DEVELOPMENT
FOR MYELOMA AND OTHER HAEMATOLOGICAL CANCERS
Raj Chopra, Institute of Cancer Research London.

13:15–14:15 Lunch Break

14:15–16:00 **SESSION III**

Chairs: **Ninette Amariglio**, Sheba Medical Center;
Dan Peer, Faculty of Life Sciences, Tel Aviv University

14:15–14:30 *THE TRANSLATIONAL GAP: NON-HODGKIN LYMPHOMA*
Abraham Avigdor, Sheba Medical Center, Tel-Hashomer

14:30–14:55 PRE-CLINICAL MODELS FOR DRUG DEVELOPMENT FOR NHL
David Weinstock, Harvard Medical School

14:55–15:20 THE POTENTIAL ROLE OF **LIVIN**, INHIBITOR OF APOPTOSIS, IN
LYMPHOMA THERAPY
Dina Ben-Yehuda, Hadassa Medical Center, Jerusalem

15:20–15:35 *THE TRANSLATIONAL GAP: ACUTE LYMPHOBLASTIC LEUKEMIA*
Shai Izraeli, Sheba Medical Center, Tel Hashomer

15:35–16:00 ALL: WHY DO WE ROUTINELY CURE CHILDREN AND RARELY CURE
OLDER ADULTS?
Adele Fielding, University College London



Dr. Abraham Avigdor

Dr. Abraham Avigdor is the director of the Institute of Hematology at Sheba Medical Center. He is also the founder and the chairman of The Israeli Lymphoma Study Group since 2011. He was trained in Internal Medicine and Hematology at Sheba Medical Center, and did his post-doctoral fellowship at Tsvee Lapidot's Lab at the Weizmann Institute

of Science, studying normal and leukemic hematopoietic stem cell development and migration. Dr. Avigdor is a medical Hemato-oncologist who focuses on the care of patients with lymphoma, and has clinical expertise in all types of lymphomas. His current clinical research focuses on the integration of PET/CT into the modern management of Hodgkin and non-Hodgkin lymphomas and the development of new therapy regimens, integrating biological and immunological agents in lymphomas. He has international collaborations with many research groups, including the LYSA (Lymphoma Study Association in France), EMCL (European Mantle Cell Lymphoma Network) and the International Study Group on PET in Lymphoma and Myeloma.



Dr. Irit Avivi

Dr. Irit Avivi serves as the Director of Hematology division at Sourasky Tel Aviv Medical Center.

She was trained in adult Hemato-Oncology at Rambam Medical Center and completed a fellowship in lymphoma and myeloma at London University College Hospitals.

She served as the Head of the Israeli Myeloma group between 2013-2017.

Her major research and clinical expertise are in prognostication and treatment of myeloma, including the use of immune- modulating strategies, and in managing hematological cancers during pregnancy.

She has over 100 scientific publications, has been a frequently invited speaker and has won several awards for her immune- translational research in myeloma.

She is running an extensive educational program in Hematology at Tel Aviv Medical Center and has trained more than 20 graduate and postgraduate students over the last decade.

She has extensive international collaborations with multiple groups in Europe and USA and is highly involved in many pivotal, phase 1-4 clinical studies in myeloma and lymphoma.



Prof. Dina Ben-Yehuda

Prof. Dina Ben-Yehuda received her medical degree from the Ben-Gurion University Medical School, she then continued her medical training as an intern and resident at Hadassah University Hospital specializing in Hematology. Her training in basic research started at the Hebrew University Medical School at the Lautenberg Center for Immunology followed by fellowship at Sloan Kettering Institute for Cancer Research in New York. In April 2000, Professor Ben-Yehuda was appointed to be the Director of the Hematology Department in Hadassah University Hospital.

Dina is extensively involved in clinical work as well as research and teaching. This year she was awarded the prize for outstanding physicians – Healing with Heart-The Danielle Foundation and the price for outstanding teacher of the Faculty of Medicine, the Hebrew university.

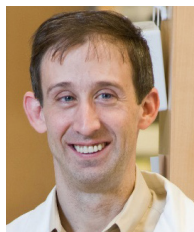
She received many competitive international grants which allow her to pursue both clinical and research work. Among her known research achievements are her discovery on de novo methylation on the ABL promoter in late stage CML, the DNA repair deficiency in patients with therapy related leukemia and more recently the characterization of LIVIN with its dual action as anti and pro-apoptotic protein.

Recently Prof. Ben Yehuda was nominated Dean of the Faculty of Medicine of the Hebrew University.



Prof. Raj Chopra

Prof. Raj Chopra is Director of the Cancer Research UK Cancer Therapeutics Unit and Head of the Division of Cancer Therapeutic at the Institute of Cancer Research in London. He has had experience of working both in academia and industry having been Director of Hematological Oncology, Christie Hospital in Manchester and subsequently in the Oncology Therapeutic area at AstraZeneca. From 2009-2016, he was leader of the Executive R&D Team and Corporate Vice President of Translational and Early Drug Development at Celgene Corporation, Summit, NJ, where he led a team of over 100 scientists in San Diego, San Francisco and Seville. There he was involved in a large number of drug discovery and development projects and part of a team that helped to define the mechanism of action of Thalidomide and its analogues. In addition Raj was also involved in the New Drug Applications for pomalidomide (a second generation IMiD agent) and apremilast (a PDE4 inhibitor). Both drugs were approved in 2013 and 2014 respectively.



Dr. John Crispino

John Crispino, PhD is the Robert I. Lurie, MD and Lora S. Lurie Professor of Medicine at Northwestern University. He received his PhD from the Massachusetts Institute of Technology for research on the mechanisms of RNA splicing performed in the laboratory of Dr. Phillip Sharp. He then performed post-doctoral hematology research at Harvard Medical School with Dr. Stuart Orkin before moving to Chicago in 2000. Over the past 17 years, Dr. Crispino and members of his laboratory have made many important contributions to improve our understanding of the mechanisms of normal and malignant blood development. Currently, his research is focused on the biology of red blood cells and megakaryocytes, the characterization of genetic changes that lead to Myeloproliferative Neoplasms and Acute Myeloid Leukemia, and the development of novel, targeted therapies for patients with these malignancies.



Prof. Ruud Delwel

Ruud Delwel PhD, is Professor of Molecular Leukemogenesis at the Erasmus University Medical Center in Rotterdam. 1983, Degree in Biology at the Leiden University in The Netherlands. 1990, PhD (Cum Laude) at the Erasmus University Rotterdam. 1991-1992, Postdoctoral Fellowship at the St. Jude's Children's Research Hospital; His work is dedicated to the understanding of the molecular and epigenetic alterations that are at the basis of acute myeloid leukemia (AML) development in humans. Using functional genomics, the molecular defects in particular AML subtypes were unraveled by his research team. A major breakthrough was the 2004 NEJM gene expression profiling study, by Drs. Delwel, Valk and Lowenberg, demonstrating that the distinct AML subtypes could be distinguished by specific gene expression profiles. The work of Professor Delwel's group and his collaborators has been published in international journals, including Blood, Cancer Cell and Cell. Dr. Delwel is EHA member and international ASH member, and he is member of the Scientific Program Committee of the EHA.



Prof. Joop Jansen

Joop Jansen was trained as a molecular biologist at the Utrecht and Leiden Universities in the Netherlands. After his PhD, he worked for four years as a post-doctoral fellow in Harvard, Boston and at the Institut Pasteur in Paris. Currently he is head of the laboratory of Hematology and holds the Chair of Experimental Hematology at the Radboud University Medical Center in Nijmegen, The Netherlands. He is principal investigator of the Radboud Center for Molecular Life Sciences and leader of the research theme Cancer development and Immune Defense. Research addresses the molecular basis of myeloid leukemia, myelodysplastic syndromes and other myeloproliferative neoplasms. Projects focus on the identification and biological significance of aberrant transcription factors and epigenetic regulators, including TET2 and EZH2, and on clonal evolution patterns in MDS and AML.



Prof. Adele Fielding

Adele Fielding is Professor of Hematology at UCL. She carried out undergraduate and postgraduate medical and hematology training in London and undertook her PhD in Cambridge, UK. Her first faculty position was at Mayo Clinic College of Medicine, Rochester MN, USA. She returned to UCL in 2003. She chairs the UK National Cancer Research Institute Adult ALL group and is Chief Investigator of the UK's frontline randomised trial for adult ALL, UKALL14. Her lab is the central lab for UKALL14 and other trials in Adult ALL. Her lab works on a number of translational projects in ALL as well as some projects which investigate the role of oncolytic measles virus as a therapy for ALL. The overall goal of her work is to improve the outcome for adults with ALL.



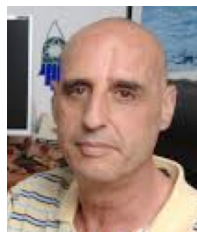
Prof. Shai Izraeli

Prof. Shai Izraeli, the Chair of the Boaz and Varda Dotan Center for Research of Hematological Malignancies and the Gregorio and Dora Shapiro Chair of Hematological Malignancies at Tel Aviv University. Trained in Pediatric Hemato-Oncology in the National Institutes of Health, he has been in Sheba Medical Center in Tel-Hashomer Israel where he is the founding chair of the Genes Development and Environment Research Institute at Edmond and Lily Safra Children Hospital. His major research and clinical expertise is in high-risk childhood leukemia. He has over 150 scientific publications, has been frequent invited speaker and has won several international awards for his research on childhood leukemias. During the last decade he has trained more than 30 graduate and postgraduate students. He has extensive international collaborations with multiple research groups in Europe, Canada, USA, China and Australia. He is an elected Board member and the past chair of the Scientific Program Committee of the European Hematology Association.



Dr. Maya Koren-Michowitz

Dr. Maya Koren-Michowitz is currently Head of Hematology and the Translational Hemato-Oncology Laboratory at Assaf Harofeh Medical Center in Israel. She received her MD from the Sackler School of Medicine at TAU, and completed a 3 year post-doctoral research fellowship at Prof. Phil Koeffler's laboratory in Cedars Sinai Medical Center in LA, studying molecular pathogenesis of myeloid hematological malignancies. Her major interest is in understanding the molecular pathogenesis of disease progression in chronic myeloid diseases, in particular the myeloproliferative neoplasms, and in the mechanism underlying resistance to therapy in these disorders. Dr. Koren-Michowitz is an active member of the Israeli MPN study group with major collaborations in clinical and translational research in the field of MPN both in Israel and internationally



Prof. Tsvee Lapidot

Tsvee Lapidot during his Post Doc. with John Dick developed functional preclinical models for identification and characterization of normal blood forming (Science 1992) and leukemia initiating (Nature 1994) human stem cells in transplanted immune deficient mice. Regulation of stem cell migration and development and the mechanism of clinical bone marrow transplantation are not fully understood. Over the years Tsvee's laboratory at the Weizmann Institute of Science made several key findings concerning regulation of human and murine hematopoietic stem cell homing and engraftment by the CXCR4/CXCL12 axis (Science 1999). Clinical stem cell mobilization (Nature Immunology 2002). Bone turnover and osteoclasts, (Nature Medicine 2006). The nervous system (Nature Immunology 2007). Connexin- 43 gap junction CXCL12 expression (Nature Immunology 2011). COX-2 macrophages (Nature Immunology 2012). Metabolic regulation by coagulation factors of stem cell BM retention, protection from chemotherapy, mobilization and homing by control of nitric oxide generation (Nature Medicine 2015) and stem cell ROS regulation by the blood-BM-barrier (Nature 2016).



Dr. Yishai Ofran

Yishai Ofran, MD, is a clinical assistant professor of hematology in the faculty of medicine, Technion Israel. He received his medical degree at the Hadassah Medical School, Jerusalem Israel, and had his medical training at Hadassah and Rambam medical centers in Israel. Between 2007 and 2009, he worked as a research fellow at Dana Farber Cancer Institute, Harvard medical school Boston USA, researching immune response in leukemia patients after allogeneic stem cell transplantation. After returning to Haifa, he established a clinical leukemia service that soon became the largest in Israel. Dr. Ofran is the chair of the Israeli leukemia working group and a member of the leukemia core committee of the eastern cooperative oncology group (ECOG) in USA. Dr. Ofran is also leading a translational research team and at his lab, the first hematological bio-bank was established. His main research interest is to review the effect of tumor heterogeneity and immune response against early response to chemotherapy and leukemogenesis.



Dr. Avichai Shimoni

Avichai Shimoni, MD. Medical specialist in internal medicine and Hematology. Completed medical education in Hadassah Medical School in Jerusalem in 1988. Had clinical fellowship in bone marrow transplantation in MD Anderson Cancer Center, Houston, Texas, between the years 1998-2000. Currently, the director of the department of Bone

Marrow Transplantation at the Chaim Sheba Medical Center, Tel-Hashomer. Associate Professor of Hematology and Chairman, Department of Hematology, Sackler Faculty of Medicine at Tel Aviv University. Also serves as the Chairman of Hematology board examination committee, in the Israeli Medical Association.



Prof. Radek C. Skoda

Radek C. Skoda is Professor of Molecular Medicine in the Department of Biomedicine of the University of Basel and the University Hospital Basel. His research group “Experimental Hematology” studies the molecular pathogenesis of myeloproliferative neoplasms (MPN) that represent clonal stem cell disorders with a tendency towards leukemic

transformation. MPN are characterized by aberrant proliferation of precursors of the myeloid, erythroid and megakaryocytic lineages resulting in elevated blood counts for red cell, platelet and neutrophil granulocytes. Oncogenic driver mutations in the genes for Janus kinase 2 (JAK2), Calreticulin (CALR) or the thrombopoietin receptor (MPL) can be found in >90% of MPN patients, but additional mutations in genes encoding epigenetic regulators or signaling proteins are detectable in some of the patients. His group uses blood samples from MPN patients and mouse models of MPN to investigate how these mutations alter stem cell properties and interact in disease initiation and progression. This work involves functional and molecular analyses of single hematopoietic stem cells.

Radek Skoda is the principal investigator of the StemSysMed project supported by SystemX. His group has collaborations with groups in Basel as well as with the group of Markus Manz in Zurich and Simon Mendez-Ferrer in Cambridge, UK.



Dr. David Weinstock

David Weinstock completed fellowship training in Medical Oncology and Infectious Diseases at Memorial Sloan-Kettering Cancer Center. His postdoctoral research was performed in the laboratory of Dr. Maria Jasin at the Sloan-Kettering Institute and focused on identifying mechanisms that mediate leukemogenic rearrangements induced by site-specific DNA double-strand breaks and V(D)J recombination. His laboratory at Dana-Farber Cancer Institute utilizes agnostic approaches to identify therapeutic targets in lymphoid malignancies and interrogate pathways of aberrant DNA repair. Major findings include the phenotypes of double-strand break repair in human embryonic stem cells, the identification of CRLF2 as an oncoprotein in B-cell leukemias, the description of GNB1 mutations across a range of malignancies, and the triplication of HMGN1 as a driver of lymphoid leukemia linked to Down Syndrome. Dr. Weinstock leads the effort at Dana-Farber, Brigham and Women's Hospital, and Boston Children's Hospital to establish patient-derived xenografts of leukemias and lymphomas. He has utilized these models to perform pre-clinical phase II-like trials completely in mice and shared the models with laboratories across the world through an open-source repository (Public Repository of Xenografts; www.PRoXe.org). He also leads a multi-institutional Specialized Center of Research focused on targeting Peripheral T-cell Lymphomas and efforts to establish point-of-care lymphoma diagnostics in Latin America.



Dr. Ofir Wolach

Ofir Wolach is a senior hematologist and is currently in charge of the Leukemia inpatient unit at the Davidoff Cancer Center, Rabin Medical Center and leads the field of acute leukemia and myelodysplastic syndromes at the Davidoff Cancer Center.

Dr. Wolach graduated from the Sackler Faculty of Medicine at Tel Aviv University. He completed his Internal Medicine residency and Hematology fellowship at Rabin Medical Center, Petah-Tikva, Israel.

Dr. Wolach completed an advanced fellowship at Dana-Farber Cancer Institute in Boston, MA in the field of leukemia, myelodysplastic syndromes, myeloproliferative neoplasms and related disorders under the mentorship of Dr. Richard Stone, a leading figure in the field of myeloid malignancies.

He has specific interest in the genomics of myeloid malignancies and studied the effects of clonal hematopoiesis on disease phenotype and immune functions as a post-doc in the Ebert lab at Brigham and Women's Hospital in Boston, MA.

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המרכז לחקר המטואונקולוגי
על שם ורדה ובעז דותן

