משרד המדע,
הטכנולוגיה והחלל
Ministry of Science, Technology & Space

dkfz. GERMAN CANCER RESEARCH CENTER IN THE HELMHOLTZ ASSOCIATION

50 Years – Research for
A Life Without Cancer

1976 – 2016
German-Israeli Cooperation in Cancer Research
40th Anniversary

Among other bi-national collaborations between Germany and Israel, the DKFZ-MOST program in cancer research is undoubtedly unique. In the last 40 years it was shaped by many people with a strong commitment to contribute to both German-Israel scientific collaboration in cancer research and to foster faith and friendship.

It is the program's ambition to support outstanding projects in a broad spectrum of disciplines of comprehensive cancer research including cell and tumor biology, functional and structural genome research, tumor immunology, infection and cancer as well as translational cancer research. The joint scientific projects, each with a three-year duration, consist of an Israeli and a DKFZ subproject with a high degree of complementarity. The program serves to strengthen existing collaborations and to initiate new cooperations between the Israeli and German partners, with particular emphasis on the nurturing of young group leaders. In the early phase of an academic career, the program serves as an efficient promoter for the development of an independent research profile and realization of experimental groundwork for long-standing research cooperations that frequently also act as a starting point for larger transnational research partnerships.

Up to now, 171 tandem projects were funded as part of the DKFZ-MOST Cooperation of which 154 have been successfully completed. This anniversary brochure gives a brief look at the history of the program and all the projects are listed. The fruits of the hard work are very well seen. Almost 1.500 publications, demonstrating outstanding findings in cancer research and leading to breakthroughs in the understanding of cancer and in successful treatments were published. The participation in the program is part of not few successful careers leading to most prestigious national and international awards – Nobel Prize, Israel Prize, EMET Prize, German Cancer Prize and more, and benefits patients all over the world.

Building on the positive experience gained by the DKFZ-MOST program, yearly Winter Schools were established where junior scientists from the participating institutes meet to discuss with internationally recognized experts cutting-edge science on emerging fields of cancer research. All these are the program's achievements and the success of the many involved. Many thanks go to all principal investigators and PhD students, who have been part of the program. Their achievements and the personal contacts with their project partners have shaped the structure of the program.

The coordinators would like to thank BMBF, MOST and DKFZ for continuous and increased funding and constant support. To date, the yearly budget comprises of 1,3 million euros and the total funding of this program amounts to 32 million euros.

Finally, we like to highlight the past and present members of the joint scientific program committee to whom we all owe our gratitude; top-level scientists, who donate their valuable time, experience and knowledge to provide advice and keep the program's high scientific level. The success of this showcase of German-Israeli collaboration and friendship is an encouragement to us all to keep the wheel running and to improve and extend the program for the benefit of science in both countries and the entire world.

Prof. Dr. Peter Angel *Dr. Hagit Schwimmer*

National Coordinators
DKFZ-MOST Cooperation in Cancer Research

Prof. Dr. Johanna Wanka
Federal Minister
of Education and Research, Germany

Germany and Israel are linked by a unique relationship. Scientific contacts played a crucial role in the post-war rapprochement between the two countries. Through their bilateral cooperation, German and Israeli researchers paved the way for the establishment of diplomatic ties in 1965.
Government-level cooperation between Germany's and Israel's Research Ministries was forged in 1973. The bilateral cancer research cooperation program began to blaze a trail of success as early as 1976. It started off with three cooperative projects and was steadily expanded. Today, it can look back on 40 years of cooperation and draws on an annual funding volume of 1.5 million euros, which allows it to fund 18 tandem projects from the entire spectrum of modern cancer research.
The success of the cancer research cooperation program is reflected not only in the excellence of its research results and its high international profile but also in the many lasting research collaborations and friendships between the researchers involved. Exchanges of young scientists in particular are a major factor in keeping German-Israeli science and research cooperation as dynamic as it is.
I wish the program continued scientific success and hope it will continue to sow the seeds of ever more fruitful relations between German and Israeli researchers.

Johanna Wanka

Ofir Akunis, MK
Minister of Science, Technology and Space, Israel

While remaining ever mindful of the darkest period in mankind's history, Israelis and Germans were capable already in the second decade following the Holocaust of jointly envisioning a common future of understanding, collaboration and friendship. Back in 1964, scientists from the Weizmann Institute and the Max Planck Association signed their first cooperation agreement, paving the way for the establishment of diplomatic relations between Israel and Germany on May 12, 1965.
Since 1973, Israel and Germany have maintained an extensive program of research cooperation on an inter-ministerial level with the participation of both the Federal Ministry of Education and Research (BMBF) and what is known today as the Ministry of Science, Technology and Space (MOST). In November 1976, the Deutsches Krebsforschungszentrum (DKFZ) signed an Agreement on Cooperation in Cancer Research with MOST.
In the four decades since then, the cooperation in cancer research between MOST and the DKFZ has expanded and flourished into thriving ties connecting prominent scientists and renowned academic institutions. These channels of cooperation within the BMBF-MOST programs comprise joint projects and publications, conferences and seminars, mutual visits and schools for young scientists, on all levels and in continuous growing demand. These frameworks have become key instruments for the improvement of our bilateral relations, and are proof of the successful links between our countries.
I thank all the stakeholders who have dedicated their lives to promoting the German-Israeli collaboration in cancer research. I particularly appreciate the active involvement of the DKFZ management in this unique program. I firmly believe that light will defeat darkness, and that science and relations like ours play a paramount role in building a brighter future for all humanity.

Ofir Akunis

Prof. Dr. Dr. h.c. Otmar D. Wiestler
President of the Hemholtz Association
of German Research Centres, Germany

Over the past 40 years, the DKFZ-MOST program in cancer research has initiated an impressive number of scientific collaborations and friendships between DKFZ scientists and partners in Israel. Not only the work in the laboratories but also regular personal interactions invigorated longterm exchange. Every year, joint summer and winter schools on relevant topics of cancer research attract young talents from both countries to exchange with experts on their specific research interests .
The successful model of the DKFZ-MOST program finally paved the way for further fruitful bi-national initiatives such as a joint research school in cancer biology between the DKFZ and the Weizmann Institute in Rehovot. Graduate students benefit greatly from both mentoring offered by the two institutions and visits to the respective partner site.
Based on the long tradition of the German-Israeli cooperation in cancer research, the health-related Helmholtz Centers established a novel bi-national partnership in the emerging area of personalized medicine. A major goal is to unravel causes and mechanisms of major widespread diseases such as cancer, cardiovascular and metabolic disorders, neurodegenerative, and infectious or environmentally related diseases. Establishing new paradigms for personalized medicine is among the major challenges. Certainly, a significant impact on personalized approaches for diagnosis, treatment and prevention based on patient stratification will be achieved by this new joint initiative.
For the coming years, I wish the DKFZ-MOST program continuous great success with as many exciting research and personal activities as possible.

Otmar D. Wiestler

Peretz Vazan
Director General
Ministry of Science, Technology and Space,
Israel

In 2015 we marked 50 years of diplomatic relations between Germany and Israel. The scientific relations have always been one of the most important pillars of these relations, starting even before the official establishment of the diplomatic relations. It is therefore significant that we mark only a year later 40 years of the most fruitful cooperation program between the Israeli Ministry of Science, Technology and Space (MOST) and the German Cancer Research Center (DKFZ).
This program, which started in 1976, has included numerous scientists from both countries and yielded hundreds of published articles in prestigious professional journals. The outstanding success of this program over four decades motivated the two MOST and DKFZ to increase in 2015 the scope of the program, both in number of projects as well as in the budget allocated for it, to enable the strengthening and expansion of the cooperation in cancer research for the benefit of scientists and citizens in both Germany and Israel.
I salute the many talented and devoted scientists and administrators whose efforts made this program such a success. I am confident that this program will continue to thrive and its results will contribute to the development of effective measures for the prevention and cure of cancer, thus bringing improvement in health care to all mankind.

Peretz Vazan

Prof. Dr. Michael Boutros
Scientific Director (interim)
German Cancer Research Center (DKFZ),
Germany

The DKFZ-MOST program is a prominent example of a longlasting highly successful partnership beween scientists in Germany and Israel. Over the last 40 years more than 160 tandem projects between cancer researchers of the DKFZ and all scientific institutions in Israel could be supported through this program.
The shared long-term goal of all these efforts is unveiling the causes and mechanisms of cancer development and progression as well as the development of novel approaches to make tumor diagnosis more precise and treatment of cancer patients more successful. Over the years, the joint projects have generated an impressive high number of innovative scientific results, many of them were published in high ranking journals. But this program has also always been the basis of a growing network of personal contacts and friendships over many years.
Particular emphasis has been put on the training and support of young scientists. Exchange of scientific interests and technical know-how offers young talents a unique opportunity to receive training in an international setting, which prepares them for an internationally-competitive scientific career in cancer biology.
From my perspective, the collaboration between the participating research groups has provided significant added value for all partners and will hopefully do so in the coming years.

Michael Boutros

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HISTORY

Foundation – Treaty between National Council of Research and Development and DKFZ **1976**

10th Anniversary in Jerusalem **1986**

20th Anniversary at the DKFZ with honoring of 7 highlight projects **1996**

International Reviewing by Profs. Kleihues, Fleckenstein, Sachs **1997**

Brochure “Cooperation and Friendship” with Literature Appendix published **1999**

25th Anniversary Symposium in Berlin, Magnus-Haus **2003**

Nobel Prize in Chemistry for Aaron Ciechanover **2004**

DKFZ-MOST Project Ca 81 (running period 01.01.98 – 31.12.200):
Regulation of cell regulatory proteins by the ubiquitin-dependent proteolytic pathway

30th Anniversary Symposium in Tel Aviv **2006**

International Reviewing, again chaired by Prof. Kleihues **2007**

First German Israeli Cancer Research School in Pichl **2008**

Increase of funds for running projects **2014**

40th Anniversary Symposium at the Weizmann Institute **2016**

FORMER MEMBERS AND COORDINATORS OF THE JOINT SCIENTIFIC PROGRAM COMMITTEE FROM 1976 TO 2016

ISRAELI MEMBERS AND MOST-COORDINATORS

Prof. Dr. Jacob Bar-Tana
Department of Medical Biochemistry, the Hebrew University – Hadassah Medical School, Jerusalem:
1979 – 1980

Prof. Dr. Zvi Fuks
Department of Radiation and Clinical Oncology, Hadassah University Hospital, Jerusalem:
1978 – 1983

Prof. Dr. Nechama Haran-Ghera
Department of Chemical Immunology, the Weizmann Institute of Science, Rehovot:
1981 – 1987

Prof. Dr. Iafa Keydar
Department of Cell Research and Immunology, Faculty of Life Sciences, Tel-Aviv University:
1986 – 1993, 1996 – 1997

Prof. Dr. Michel Revel
Department of Molecular Genetics, the Weizmann Institute of Science, Rehovot:
1993 – 1998

Prof. Dr. Eliezer Robinson
Department of Oncology, Rambam Hospital and the Technion Faculty of Medicine, Haifa:
1978 – 2002

Prof. Dr. Michael Schlesinger
Department of Experimental Medicine and Cancer Research, the Hebrew University – Hadassah Medical School, Jerusalem:
1988 – 2011

Prof. Dr. Dov Sulitzeanu
Department of Immunology, the Hebrew University – Hadassah Medical School, Jerusalem:
1984 – 1987

Prof. Dr. Nathan Trainin
Department of Cell Biology, the Weizmann Institute of Science, Rehovot:
1978 – 1985

Prof. Dr. Ernest Winocour
Department of Molecular Genetics and Virology, the Weizmann Institute of Science, Rehovot:
1988 – 1992

Prof. Dr. Isaac P. Witz
Department of Cell Research and Immunology, Tel viv University, Tel Aviv:
1998 - 2014

Prof. Dr. Avraham Yaniv
Department of Human Microbiology, Tel Aviv University:
1994 – 1995

ISRAELI COORDINATORS

Dr. Yair Degani: 1983 – 2003
Dr. Shlomo Sarig; 2003 – 2011
Dr. Ahmi-Ben-Yehudah: 2011 – 2014

EUROPEAN MEMBERS *(incl. DKFZ-Coordinators):*

Prof. Dr. Max Burger
Director, Friedrich-Miescher-Institute, Basel, Switzerland:
1976 – 2011

Prof. Dr. Bernhard Fleckenstein
Director, Institut für Klinische und Molekulare Virologie, University Erlangen:
1984 – 1987

Prof. Dr. Dres. h.c. Harald zur Hausen
Chairman of the Management Board, DKFZ, Heidelberg:
1979 – 1983

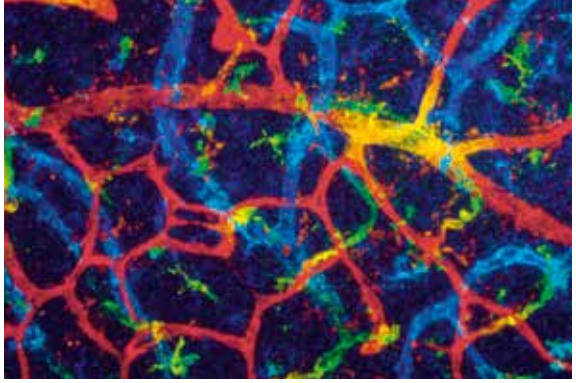
Prof. Dr. Rolf Knippers
Universität Konstanz, Fakultät für Biologie, Lehrstuhl für Molekulare Genetik:
1989 – 1997

Prof. Dr. Erwin Rüde
Director, Institut für Immunologie, University Mainz:
1976 – 1997

GERMAN COORDINATORS

Prof. Dr. Erich Hecker
Director em. at the DKFZ, DKFZ-Coordinator of the Cooperation Program:
1976 – 2003

Prof. Dr. Dr. Wolfhard Semmler
Prof. em. at the DKFZ
2003 – 2011



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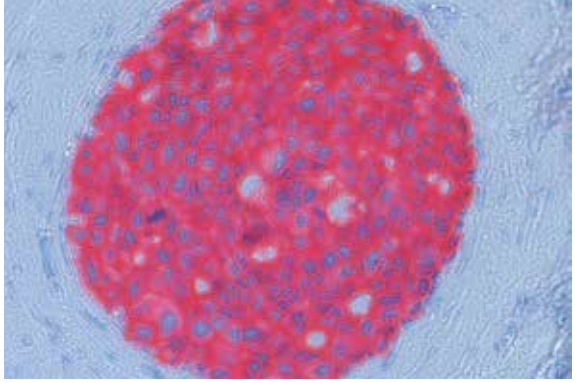


On the occasion of the 40th Anniversary Symposium at the Weizmann Institute in April 2016, a selection of seven investigators from Israel and Germany known for their outstanding achievements throughout the Cooperation Program summarized past and ongoing research and outlined future perspectives of the bilateral projects.

GREETINGS

Prof. Dr. Varda Rotter
Weizmann Institute of Science

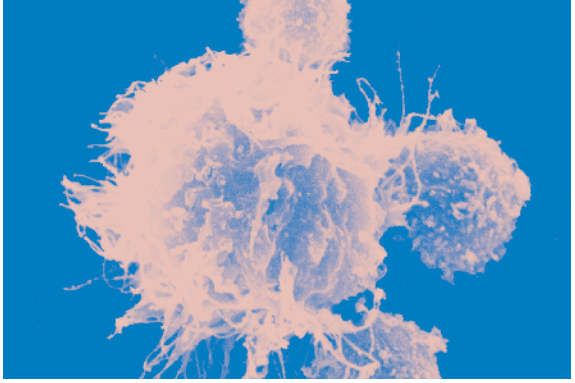
Science is best advanced upon collaboration between complementary research teams that share interest in similar scientific issues. This concept underlies the relationship between investigators of the DKFZ and Israel. The collaboration was initially triggered by awarding grants to excellent DKFZ and Israeli teams that suggested studying jointly cancer related issues. This exchange resulted in seminal and important publications and above all authentic long lasting friendship that yielded world leading excellent science.
This successful program inspired the establishment of the German Israeli Cancer Research School, that is celebrating its 8th round. It takes place at inspiring spots in Israel or Germany and brings together young students with leading cancer researches from DKFZ and Israel. The school serves as a platform for stimulating discussions, further enhances the active collaboration between students, post-docs and scientists of the two countries. Another recent example of bringing together German and Israeli scientists towards the mutual scientific endeavors aimed at facilitating precision cancer medicine.
In all, the long lasting collaboration between Germany and Israel is a dynamic program that is supporting the progress of cancer research. Already as a PhD student I was acquainted with the DKFZ as a leading institute in immunology. However, my first collaborations as a scientist, supported by the DKFZ-MOST grants, were with Prof. Schirrmacher and Prof. Richter, in which we focused on understanding the role of p53 in cancer development. During this time I repeatedly had the opportunity to visit the DKFZ and was exposed to the excellent ongoing research. In 2003, I was nominated member of the DKFZ-MOST Committee and since then I feel privileged to serve the program in any possible way.

ABSTRACTS

Prof. Dr. Peter H. Krammer
German Cancer Research Center

Death receptor and Annexin induced apoptosis and self tolerance

A soluble biological, CD95-Fc, for the treatment of patients in which cells use the CD95 system for pathological cell death or proliferation (e.g. cancer) has been developed.
Another way by which apoptosis interferes with the function of the entire organism is the Annexin checkpoint system.
Removal of excess cells by apoptosis maintains tissue homeostasis. To preclude the development of autoimmunity, dying cells are rapidly cleared by neighbouring phagocytes, such as dendritic cells (DC). The uptake of apoptotic cells usually does not lead to an autoimmune response, even though many self-antigens are presented by professional antigen presenting cells. Apoptotic cells play an active part in preventing autoimmunity by modulating DC activity, leading to the development of "tolerogenic" DC. To define signals on the surface of apoptotic cells involved in this process, we raised monoclonal antibodies against apoptotic cells and screened for their ability to differentiate between live and apoptotic cells. We identified the lipid binding protein Annexin A1 (Anx A1) on the surface of early apoptotic cells and not on live cells. Anx A1 suppressed pro-inflammatory cytokine secretion, upregulation of costimulatory surface molecules and T cell stimulatory capacity of DC. In mice, Anx A1 on apoptotic cells or on antigen coupled beads injected into the animals leads to non-activation of antigen-specific T cells. Our results indicate that Anx A1 acts as an endogenous anti-inflammatory signal, suppressing the immune response against self antigens. Thus, Anx A1 contributes to the induction of peripheral tolerance, and immune reactivity might be impaired by Anx A1 released from tumor cells killed by chemo- or radiotherapy.



Prof. Dr. Moshe Oren
Weizmann Institute of Science

Exploring the roles of p53 in cancer

The p53 tumor suppressor serves as a major barrier against cancer. It is believed that in almost all human cancer cases, p53 is either inactivated or at least altered in a way that prevents it from fulfilling its role as a key tumor suppressor. In about half of all cases, the p53 gene is directly inactivated by mutations, making p53 the most frequently mutated gene in cancer.
Over the years, we and others have been studying the molecular and biological mechanisms that underlie the activity of p53 as a potent tumor suppressor, as well as the consequences of its mutation in human tumors. These studies, performed in hundreds of labs throughout the world, have revealed that p53 is positioned centrally in a complex signaling network that serves to maintain genome integrity and cellular homeostasis, and can effectively eliminate cells that have undergone cancerous changes and are now endangering the body. The knowledge gained through those studies is currently being harnessed towards developing novel therapeutic approaches to treat cancer.

PD Dr. Adelheid Cerwenka
German Cancer Research Center

Harnessing innate immunity against cancer

Until recently, the concept that the immune system can actively prevent cancer has been controversial. Currently, however, the immunotherapy of cancer is an emerging field with many promising treatment options tested in clinical trials. The immune system consists of effector cells of the innate and adaptive immune system that work closely together orchestrating effective immune responses. So far, most approaches focus on harnessing adaptive immunity such as exploiting tumor-reactive T lymphocytes. Tumors, however, frequently escape from T cell mediated recognition. Thus, additional anti-tumor effector cells of the innate immune system such as Natural Killer cells have attracted increasing attention. Natural Killer (NK) cells use tumor recognition strategies that are distinct from T cells and can efficiently kill tumors that had escaped from CD8+ T cell attack. NK cells recognize their targets by an interaction of activating receptors and recognition structures present on cancer cells but mostly absent on healthy cells. Although NK cells can promote the elimination of tumors, their effector function is often modulated or suppressed by the tumor microenvironment. Our laboratory aims at defining mechanisms of NK cell recognition of cancer in particular focussing on the activating receptors NKG2D and NKp30. We dissect the interaction of these receptors with their tumor expressed ligands and define how this interaction is modulated by the tumor microenvironment. Moreover, strategies to sustain NK cell activity in the tumor microenvironment for long-term are currently developed. A better understanding of NK cell biology in the tumor microenvironment will help us to develop novel therapeutic strategies to further amplify immune responses towards cancer by additionally recruiting NK cells as potent effector cells into the anti-tumor immune response.

Prof. Dr. Sara Lavi
Tel Aviv University

PPM1A, the Janus of microenvironment, a friend or a foe in the combat against cancer

Tumor microenvironment has been gradually recognized as a key contributor to cancer progression. Using conditional PPM1A knockout mice created in our laboratory we identified PPM1A as a major regulator of the microenvironment. In the PPM1A ablated mice the wound healing process goes awry and culminates into uncontrolled inflammation and angiogenesis. These features are two of the hallmarks of cancer reflecting the microenvironment response to tumor cell growth. We investigated the role of PPM1A in cancer, using different mouse models. To our surprise, the absence of PPM1A could be either tumor promoting or tumor suppressive depending on the tumor initiating protocol. Fibroblasts are ubiquitous stromal cells which influence other cells through the secretion of cytokines and growth factors. Skin fibroblasts play critical roles in normal wound healing and in cancer. While fibroblasts can have a tumor suppressing activity, the phenotype of the fibroblast changes to a tumor promoting state as carcinogenesis progresses. Multipotent skin precursor cells (SKPs) capable to differentiate to fibroblasts were isolated from WT and KO mice and cultivated as 3D spheroids. PPM1A ablation led to major changes in gene expression and in functional characteristics of the SKPs. PPM1A was shown to be a major player in cellular ROS (reactive oxygen species) signaling. The absence of PPM1A led to altered expression of the immunomodulatory genes, and genes regulating cell death of immune cells and the recruitment of antigen presenting cells.
The role of PPM1A in immunomodulation and tumorigenesis will be discussed. Our studies might lead to the development of a new strategy in cancer treatment involving immunomodulation of the tumor microenvironment via the manipulation of PPM1A or its targets.

Prof. Dr. Hellmut Augustin
German Cancer Research Center

Stromal control of tumor progression and metastasis

Metastasis is the primary cause of tumor-associated mortality. Yet, metastasis is mechanistically the least well understood process of the tumor progression cascade. Clinically, therapies, which are almost entirely designed and clinically tested to treat primary tumors, disappointingly fail to work for metastatic disease.
One critical bottleneck of bench-to-bedside metastasis research is the limited availability of preclinical tumor models that truthfully mimic the pathogenesis and the course of human tumors as well as the response to therapy. Importantly, the reductionist nature of preclinical tumor models insufficiently reflects the complexity of the bi-directional tumor-host interactions that facilitate metastasis. The stromal response (vascular response, fibroblastic response, immune response) is on the one hand part of the host defense program. On the other hand, tumor-mediated stromal reprogramming plays essential and rate-limiting roles in tumor progression and particularly metastatic growth. The better mechanistic understanding of these pathophysiological processes holds great promise to pave the way towards the development of novel therapeutic strategies. This presentation will focus on bottlenecks of contemporary metastasis research and present proof-of-concept experiments aimed at preclinically validating novel stroma targeting combination therapies for metastatic disease.

Prof. Dr. Batsheva Kerem
Hebrew University

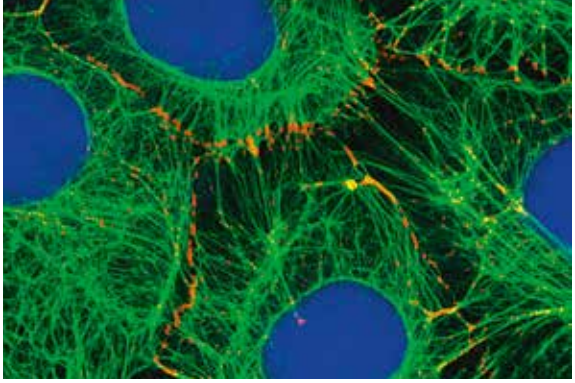
The different layers regulating genomic instability in cancer

Chromosomal instability is a hallmark driving tumorigenesis. We and others have found that oncogene expression generates genomic instability by inducing DNA replication stress, resulting in perturbed replication dynamics. We found that onco-gene-induced replication stress results from uncoordinated activation of factors regulating cell proliferation leading to insufficient nucleotides that fail to support normal replication and genome stability. Cancer development is driven by alterations in both genetic and environmental factors. In our recent DKFZ project we are studying whether replication stress can be modulated by both genetic and non-genetic factors and whether the extent of replication stress affects the probability of neoplastic transformation. To do so, we study the effect of folate, a micronutrient that is essential for nucleotide biosynthesis, on oncogene-induced tumorigenicity.
Recurrent genomic instability in cancer is attributed to positive selection and/or the sensitivity of specific genomic regions to breakage. Among these regions are fragile sites (FSs), genomic regions sensitive to replication stress conditions induced by the DNA polymerase inhibitor aphidicolin. However, the basis for the majority of cancer genomic instability hotspots remains unclear. We are studying the effect of aberrant oncogene expression on fragile sites induction. We mapped the cytogenetic locations of oncogene-induced fragile sites and show that in the same cells, each oncogene creates a unique fragility landscape that only partially overlaps with aphidicolin induced FSs. The characterization of the identified oncogene-induced FSs demonstrates that they share prominent features with aphidicolin-induced FSs. Our results highlight an additional level of complexity in the molecular basis for replication-induced recurrent fragility in cancer.

Prof. Dr. Yosef Yarden
Weizmann Institute of Science

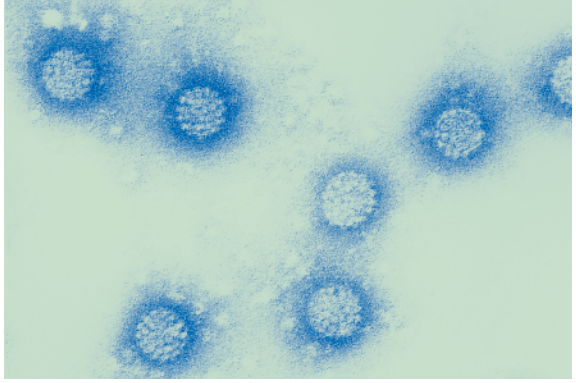
RNA-based feedback regulation of growth gactor signaling in cancer

Tumor-specific combinations of oncogenic mutations often free cancer cells from their reliance on growth factors. One important example comprises the epidermal growth factor receptor (EGFR) and its kin, HER2. In tumors, both EGFR and HER2 frequently display overexpression, internal deletions and point mutations. Accordingly, monoclonal antibodies and kinase inhibitors specific to these receptors have been approved for clinical application. My lecture introduces to our efforts to resolve the logic underlying gene expression programs activated by growth factors and relationships to tumor progression. Wave-like induction of defined groups of transcripts follows receptor activation, and a similar pattern is displayed by microRNAs. Interestingly, the earliest event we detect is a concerted down-regulation of microRNAs that collectively suppress the earliest wave of up-regulated genes, a group of transcription factors that includes FOS and JUN. Importantly, the waves of mRNAs and microRNAs are reflected in breast and other tumors, implying that feedback regulation of growth factors and their downstream signals play vital roles in tumor progression.
The focus of my lecture are two emerging features of gene expression programs, which are initiated by activated receptors for growth factors. The first feature is a seemingly pulsatile mode of signals that regulates cell cycle progression. Accordingly, commitment to S-phase entry depends on a fruitful second pulse of signaling, which removes inhibition by the wild type form of p53. The other feature relates to an apparent diurnal regulation of growth factor signaling. This requires signaling by steroid hormones and entails a crosstalk between nuclear receptors and receptor tyrosine kinases, such as EGFR. The implications of both pulsatile regulation of transcription and its diurnal control will be discussed in the context of tumor progression.

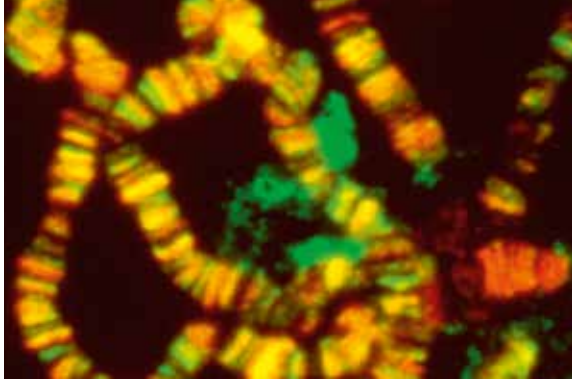


DKFZ-MOST COOPERATION IN CANCER RESEARCH – LIST OF ALL PROJECTS CA 01–CA 169 (*as per July 2015*)

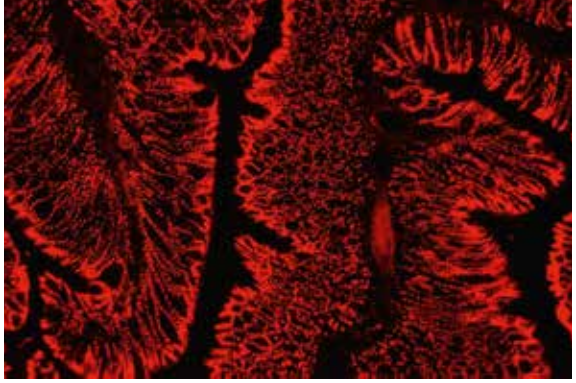
Ca-No.	Israeli Partner	German Partner	Joint Project Title
Project phase I – 01.01.1976 – 31.12.1979			
001	E. Winocour, Weizmann Institute of Science	G. Sauer, DKFZ	Integration of SV40 into the cellular genome
002	L. Sachs, Weizmann Institute of Science	W. Franke, DKFZ	Membrane organisation in leukemic cells – kinetics of formation and heterogeneity of surface membrane components and mosaics and its interference with membranotropic drugs
007	E. Shaaya	E. Sekeris, DKFZ	Regulation of synthesis of HnRNA in epidermis cells of insects and its posttranscriptional modification
Project phase II – 01.01.1977 – 31.12.1980			
003	M. Schlesinger, Hebrew University	W. Droege, DKFZ	Analysis of lymphocyte subpopulations with a combination of physical and serological techniques
004	R. Laskov, Hebrew University	K. Eichmann, DKFZ	Control mechanisms of immunoglobulin synthesis in myeloma cells
005	F. Doljanski, Hebrew University	V. Kinzel, DKFZ	Cell surface shedding in normal and neoplastic cells
Project phase III, group 1 – 01.07.1979 – 30.06.1982			
008	J. Haimovich, Tel Aviv University	P. Krammer, DKFZ	Differentiation of normal and malignant T and B lymphocytes
009	S. Lavi, W. Winocour, Weizmann Institute of Science	G. Sauer, DKFZ	Synergistic carcinogenic effects of viral and chemical agents and DNA mutagenesis in primates
010	J. Witz, Tel Aviv University	K. Munk, DKFZ	Systemic and *in situ* tumoral immunity in rats inoculated with herpes-simplex virus (HSV) transformed cells and bearing metastasising tumors
011	T. Mekori, E. Robinson, Technion	H. Kirchner, E. Storch, DKFZ	Mechanism of immunosuppression in cancer patients and experimental models. The role of adjuvant radio-chemo- and immunotherapy
012	D. Sulitzeanu, Hadassah Med. School	M. Zöller, S. Matzku, DKFZ	Identification and biological activity of antigens in immune complexes of patients with breast cancer
013	J. Treves, S. Biran, Hadassah Univ. Hospital	W. Dröge / V. Schirrmacher, DKFZ	Specific adoptive immunotherapy of human and experimental tumors by lymphocytes sensitized *in vitro* against autologous tumor cells



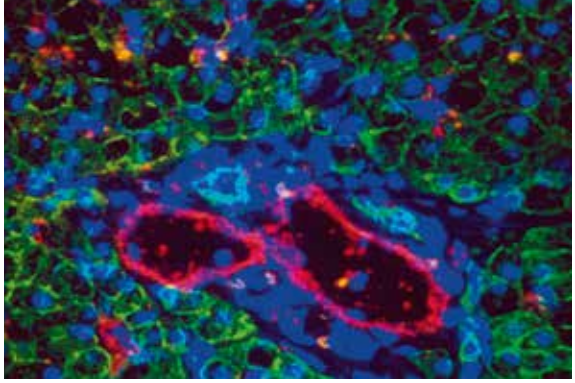
Ca-No.	Israeli Partner	German Partner	Joint Project Title
Project phase III, group 2 – 01.10.1979 – 30.09.1982			
014	E. Pick, Tel Aviv University	D. Gemsa, H. Kirchner, DKFZ	Macrophage activation induction and effects on cell cooperation
015	D. Givol, P. Lonai, Weizmann Institute of Science	K. Eichmann, DKFZ	Expression of immunoglobin variable region determinants on functionally defined T lymphocyte populations
016	R. Ben-Ishai, Technion	H. W. Thielmann, DKFZ	A study of the mechanism of environmental carcinogenesis
Projects phase III, group 3 – 01.07.1981 – 30.06.1984			
017	R. Simantov, Weizmann Institute of Science	F. Marks, DKFZ	Biochemical dissection of early promotion specific and pleiotropic effects evoked by phorbol ester tumor promoters and related compounds
018	S. Segal, E. Gorelik, Ben-Gurion University	G. Haemmerling / V. Schirrmacher, DKFZ	The immunobiology of tumor metastases
Project phase IV, group 1 – 01.07.1982 – 30.06.1985			
019	E. Canaani, Weizmann Institute of Science	T. Graf, DKFZ	Virus-mediated genetic rearrangements
020	M. Herzberg, Tel Aviv University	D. Werner, K. Munk, DKFZ	Nucleic acid binding activities and nucleolytic activities associated to the nuclear matrix in mammalian cells
021	J. Kapitulnik, R. Koren, Hebrew University	F. Kolar / N. Fusenig, DKFZ	Alteration of growth regulation in chemical carcinogenesis
Project phase IV, group 2 – 01.01.1983 – 31.12.1985			
022	B. Geiger, Weizmann Institute of Science	W. Franke, DKFZ	Biochemical and immunochemical characterization of type-specific intermediate filaments and their attachment sites in normal and in transformed cells
023	U.Z. Linttauer, I. Ginzburg, Weizmann Institute of Science	H. Ponstingl, DKFZ	Cytostatic binding sites in normal and corresponding tumor cells
024	I. Vlodavsky, Hadassah University Hospital	V. Schirrmacher, DKFZ	Interaction of metastasizing and non-metastasizing tumors with cultured vascular endothelial cells and their underlying lamina
025	S. Shaltiel, Weizmann Institute of Science	V. Kinzel, M. Gagelmann, DKFZ	Structure of cAMP-dependent kinases as bioregulatory enzymes



Ca-No.	Israeli Partner	German Partner	Joint Project Title
Project phase IV, group 3 – 01.07.1984 – 30.06.1987			
026	A. Panet, Hebrew University	H. Kirchner, H. Jacobsen, DKFZ	Inhibition by interferon of herpes simplex virus or regulation of other viruses in murine cells
027	M. Bar-Eli, Ben Gurion University	G. Haemmerling, DKFZ	The molecular genetics of tumor growth
028	R. Kaempfer, Hebrew University	P. Krammer, DKFZ	Lymphokine receptors on murine B- and T-cell tumors
029	A. Raz, A. Ben-Ze'ev, Weizmann Institute of Science	M. Zoeller, DKFZ	Escape mechanisms of metastatic tumor variants
Project phase V, group 1– 01.01.1986 – 31.12.1988			
030	V. Rotter, Weizmann Institute of Science	V. Schirrmacher, DKFZ	P53 expression in tumor cells of different metastatic capacity
031	S. Mitrani-Rosenbaum, Hebrew University	L. Gissmann, DKFZ	Detection and characterization of human papilloma viruses in genital lesions from Israelian patients
032	S. Lavi, Tel Aviv University	J. Schlehofer, DKFZ	The role of DNA-amplification in tumor initiation
033	Y. Milner, Hebrew University	M. Hergenhahn, DKFZ	The role of plasma membrane physical organization in control of growth and differentiation of human epidermal cells
034	J. Schlessinger, Weizmann Institute of Science	V. Kinzel, F. Marks, DKFZ	The role of polypeptide growth factors in multistage tumorigenesis
035	H. Manor, Technion	M. Pawlita, DKFZ	Carcinogen induced replication and recombination of polyoma and lymphotropic papovavirus DNA
Project phase V, group 2 – 01.07.1987 – 30.06.1990			
036	B. Czernobilsky, Kaplan Hospital	W. Franke, DKFZ	Intermediate filaments in germ cell tumors
037	I. Friedberg, Tel Aviv University	D. Kübler, W. Pyerin, DKFZ	Role of cell surface-mediated utilization of extracellular nucleotides in normal and transformed cells
038	Y. Kaufmann, Chaim Sheba Medical Center	W. Falk, P. Krammer, DKFZ	Induction of cytolytic lymphocytes by cytokines
039	M. Revel, Weizmann Institute of Science	R. Zawatzky, H. Kirchner, DKFZ	Agents controlling the growth and differentiation of primitive blood lymhomyeloid/erythroid stem cells

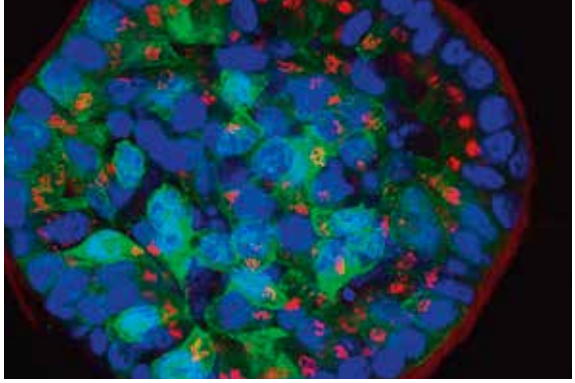


Ca-No.	Israeli Partner	German Partner	Joint Project Title
Project phase V, group 3 – 01.01.1989 – 31.12.1991			
040	J. Kark, Hebrew University	J. Wahrendorf, DKFZ	Biochemical predictors of 20 years cancer incidence in the Israeli Civil Servant Cohort
041	D. Wallach, Weizmann Institute of Science	D. Maennel, DKFZ, H. Holtmann, Univ. Hannover	Mechanisms controlling the response to tumor necrosis factor
042	G. Berke, Weizmann Institute of Science	W. Droege, DKFZ	Immunotherapy by tumor infiltration lymphocytes (TIL) activated by IL-2: The development of large granular cytolytic T lymphocytes (LGCTL) and the function of lytic granules and perforins(s) in inducing tumor regression
043	E. Kedar, Hebrew University	V. Schirrmacher, DKFZ	Application of human cytokine and effector cells for immunotherapy of human tumors in nude mice
044	R. N. Apte, Ben Gurion University	M. Zoeller, DKFZ	Cytokine secretion of tumor cells influence on tumor initiation, progression and interaction with the immune system
045	P. Rozen, Ichilov Hospital	H. Boeing, DKFZ	Dietary factors in the recurrence and progression of colorectal adenomas; A calcium intervention study
Project phase VI, group 1 – 01.07.1990 – 30.06.1993			
046	A. Ben-Ze'ev, Weizmann Institute of Science	J. Kartenbeck, W. Franke, DKFZ	Regulation of synthesis of intermediate filament and desmosomal proteins in attached and unattached states of normal and transformed cells
047	Y. Shiloh, Tel Aviv University	A. Weith, M. Schwab, DKFZ	Amplification in human solid tumors: search for new oncogenes
048	J. Tal, Ben Gurion University	J. Schlehofer, DKFZ	Involvement of the NS genes in the antitumor activity of parvoviruses
049	B. Geiger, Weizmann Institute of Science	W. Franke, DKFZ	Structure-function relationships in adhering cell junctions of normal and transformed cells
Project phase VI, group 2 – 01.01.1992 – 31.12.1994			
050	M. Aboud, Ben Gurion University	R. Flügel, M. Löchelt, DKFZ	Tumorigenic cooperation between human retroviruses, oncogenes and other carcinogens
051	M. Oren, Weizmann Institute of Science	M. Schwab, DKFZ	Analysis of tumor suppressor genes in human cancers
052	H. Degani, Y. Salomon, Weizmann Institute of Science	W. Lehmann, W.E. Hull, DKFZ	Development of NMR and mass spectroscopic techniques and their application in the investigation of fatty acid and phospholipid metabolism and alterations involved in cellular transduction and malignant growth



Ca-No.	Israeli Partner	German Partner	Joint Project Title
053	S.A. Lamprecht, Ben Gurion University	G. Fürstenberger, F. Marks, DKFZ	Transforming growth factor-beta in epithelial growth control, differentiation and neoplasia
054	M. Liscovitch, Weizmann Inst. of Science	V. Kinzel, DKFZ	Role of phospholipase C and D in cell signaling and growth control
055	J. Bar-Tana, Hebrew University	D. Keppler, DKFZ	Cell signaling and growth control induced by amphipathic carboxylates – an unifying theory
Project phase VI, group 3 – 01.07.1993 – 30.06.1996			
056	I. Ginzburg, Weizmann Institute of Science	H. Ponstingl, DKFZ	Arrest of cell division in tumor cells by inducing expression of control proteins: (A) Cytoskeletal Tau MAP (Israel), (B) Mitotic Control Proteins (Germany)
057	G. Neufeld, Technion	R. Schwartz-Albiez (div. V. Schirrmacher), DKFZ	Growth factor regulated interaction between leukemias/lymphomas and endothelium
058	E. Keshet, Hebrew University	E. Spiess (div. W. Franke), DKFZ	Regulation of proteases and their respective inhibitors mediating cell invasiveness during angiogenesis and metastasis
059	A. Kimchi, Weizmann Institute of Science	N. E. Fusenig, DKFZ	Negative regulating growth factors and the significance of their abrogation in carcinogenesis
060	S. Lavi, Tel Aviv University	R. Heilbronn, MPI f. Biochemie / J. Kleinschmidt, DKFZ	Onco suppression by adeno-associated viruses
061	V. Rotter, Weizmann Institute of Science	K.H. Richter (div. F. Marks), DKFZ	The involvement of tumor suppressor p53 in differentiation
062	B. Shilo, Weizmann Institute of Science	B. Mechler, DKFZ	Signaling pathways of *Drosophila* receptors and tumor suppressor gene products
Project phase VII, group 1 – 01.01.1995 – 31.12.1997			
063	D. Canaani, Tel Aviv University	M. Schwab, DKFZ	Phosphorylation of proteins encoded by oncogenes and tumor suppressor genes as a determinant for protein association and tumorigenesis
064	S. Segal, Ben Gurion University	F. Momburg (div. G. Haemmerling), DKFZ	The influence of TAP peptide transporters on tumorgenisity
065	Z. Zor, Weizmann Institute of Science	G. Fuerstenberger (div. F. Marks), DKFZ	Regulation of gene expression in tumor growth: over expression of phospholipase A2 and prostaglandin H synthase isoenzymes as potential markers for epithelial tumors
066	R. Apte, Ben Gurion University	D. Schnabel, M. Zoeller, DKFZ	Induction of immune response against T cell lymphomas by IL-1alpha and anti-CD44v monoclonal antibodies

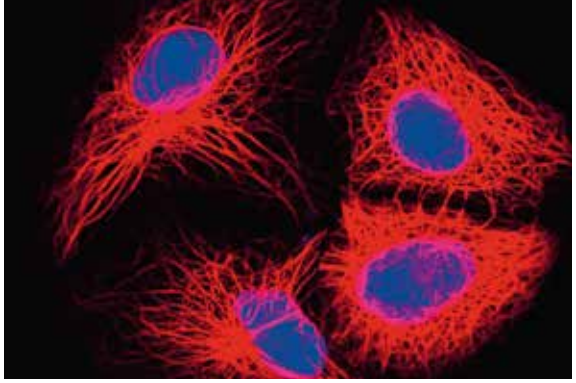
Ca-No.	Israeli Partner	German Partner	Joint Project Title
067	G. Berke, Weizmann Institute of Science	P. Krammer, DKFZ	Induction on tumor cell apoptosis by killer cells
068	L. Eisenbach, Weizmann Institute of Science	M. Zoeller, DKFZ	Treatment of metastasis by activation of immune effector cells via a combination of active and passive vaccination protocols including genetic manipulation of tumor cells and lymphocytes
069	I. Witz, Tel Aviv University	V. Schirrmacher, DKFZ	Activation antigens: role in anti-tumor immune response and potential targets for therapy
Project phase VII, group 2 – 01.07.1996 – 30.06.1999			
070	Y. Ben-Neriah, Hebrew University	W. Droege, DKFZ	Identifying signaling intermediates of the T-cell costimulatory receptor CD28
071	Z. Fishelson, Tel Aviv University	M. Kirschfink, University of Heidelberg	Molecular basis of the resistance of tumor cells to complement-mediated lysis
072	Y. Shaul, Weizmann Institute of Science	C. Schröder, DKFZ	Functional interaction of pX of HBV with the tumor suppressor p53
073	L. Sherman, Sackler School of Medicine	M. Dürst (div. A. Alonso), DKFZ	Human papillomavirus (HPV) transformation: The role of HPV16 E6 in the induction of resistance to serum/Ca2+ mediated differentiation
074	Z. Eshhar, Weizmann Institute of Science	M. Little, DKFZ	Redirecting effector lymphocytes to Hodgkin's disease/lymphoma using chimeric receptors with antibody specificity
075	Y. Groner, Weizmann Institute of Science	M. Schwab, DKFZ	Possible role of AML2 and other genes on distal chromosome 1p for human cancers
076	A. Hochberg, Hebrew University	D. Komitowski, DKFZ	Imprinted genes in human cancer, biology, diagnosis and therapy
Project phase VII, group 3 – 01.01.1998 – 31.12.2000			
077	N. Arber, Tel Aviv University	W. Pyerin, DKFZ	The importance of cyclin D1, RB, K-ras and cyclin-like CENP-C in cell cycle control and progression
078	R. Bar-Shavit, Hadassah Med. School – Hospital	P. Altevogt (div. V. Schirrmacher), DKFZ	The role of avb3 integrin and protease activated receptor in tumor metastasis: involvement of thrombin-receptor (ThR) and L1 adhesion molecule
079	A. Ben Ze'ev, Weizmann Institute of Science	W. Franke, DKFZ	Extrajunctional function of plaque proteins in growth control, tumorigenesis and differentiation
080	E. Canaani, Weizmann Institute of Science	R. Paro, ZMBH Heidelberg	Mechanism of action of *Drosophila* trithorax-group and polycomb-group proteins and their mammalian homologues



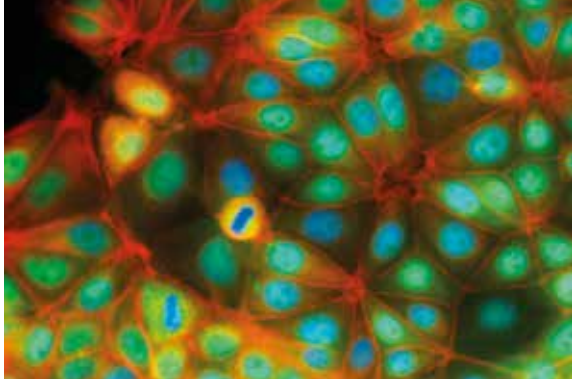
Ca-No.	Israeli Partner	German Partner	Joint Project Title
081	A. Ciechanover, Technion	M. Scheffner (div. E. M. de Villiers), DKFZ	Regulation of cell regulatory proteins by the ubiquitin-dependent proteolytic pathway
082	I. Friedberg, Tel Aviv University	D. Kübler (div. V. Kinzel), DKFZ	Selective growth inhibition of malignant cells by a phosphoprotein inhibitor
083	A. Levitzky, Hebrew University	F. Roesl, DKFZ	The role of EGF/IGF signal transduction in HPV 16/18-linked pathogenesis of cervical cancer
084	A. Eldor, Tel Aviv Sourasky Med. Center	K.-M. Debatin, DKFZ	Studies on the envelope glycoprotein of the avian hemangio-sarcoma retrovirus (AVH) which induces either apoptosis or proliferation in different cell types
Project phase VIII, group 1 – 01.07.1999 – 30.06.2002			
085	A. Kimchi, Weizmann Institute of Science	M. Schwab, DKFZ	Cell death associated proteins: Gene identification by functional approach and analysis of their apoptotic and tumor suppressor functions
086	M. Oren, Weizmann Institute of Science	P. Krammer, DKFZ	The role of p53 in drug-induced apoptosis
087	E. Razin, Hebrew University	P. Angel, DKFZ	Identification of cellular pathways mediating cell death in response to radiation and genotoxic agents
088	G. Golomb, Hebrew University	M. Berger, DKFZ	Development and evaluation of non-viral antisense oligonucleotide and gene controlled delivery systems for the treatment of mammary carcinoma and bone osteolysis
089	E. Keshet, Hebrew University	N. E. Fusenig, DKFZ	Role of PDGF and VEGF in blood vessel formation, maturation and regression: New targets for tumor therapy
090	I. Vlodavsky, Hadassah Univ. Hospital	V. Schirrmacher, DKFZ	Novel inhibitors of tumor metastasis and angiogenesis
091	Z. Fishelson, Sackler School of Medicine	M. Kirschfink, University of Heidelberg	Sensitization of human tumor cells to complement-mediated lysis
Project phase VIII, group 2 – 01.01.2001 – 31.12.2003			
092	O. Mandelboim, Hebrew University	F. Momburg (div. G. Haemmerling), DKFZ	Identification of NKp46 ligand: A ligand which is involved in the lysis of tumor cells and virally infected cells by natural killer cells
093	J. Bar-Tana, R. Hertz, Hebrew University	G. Schuetz, DKFZ	A biochemical and molecular genetic approach to study the role of hepatocyte nuclear factor 4 (HNF4) and suppression of tumor development by fatty acids

Ca-No.	Israeli Partner	German Partner	Joint Project Title
094	D. Ron, Technion	N. E. Fusenig, DKFZ	Modulation of the interaction of KGF with its receptor in normal and tumor cells
095	T. Tennenbaum, Bar-Ilan University	D. Breitkreutz (div. N. E. Fusenig), DKFZ	The functional relevance of alterations in integrin alpha6beta4 and protein kinase C regulation in human and mouse skin carcinogenesis
096	R. Apte, Ben Gurion University	M. Zoeller, DKFZ	Novel anti-cancer vaccines based on oral application of recombinant Salmonella typhimurium bacteria
097	V. Deutsch, A. Naparstek, Tel Aviv Med. Center	B. Fehse, A.R. Zander, Univ. Hospital Eppendorf	Expansion of human hematopoietic stem cells and megakaryocyte progenitors for transplantation in cancer patients
098	M. Liscovitch, Weizmann Institute of Science	D. Keppler, DKFZ	Phenotypic reversal in multidrug resistant cancer cells
Project phase VIII, group 3 – 01.07.2002 – 30.06.2005			
099	(P. Fishman, Tel Aviv University)	R. Koesters (div. M. v. Knebel Doeberitz), DKFZ	Targeting the adenosine A3 receptor for the treatment and prevention of colon carcinoma: molecular mechanisms and preclinical evaluation
100	G. Berke, Weizmann Institute of Science	P. Krammer, DKFZ	The CD95 (APO-1/Fas) death system in tumor progression
101	Y. Haupt, Hebrew University	F. Roesl, DKFZ	Involvement of c-Abl in HPV-induced carcinogenesis
102	G. Neufeld, Technion	M. Mueller, DKFZ	Tyrosine kinase VEGF receptors and neuropilins and the role of their VEGF and semaphoring ligands in tumor development and progression
103	L. Sherman, Sackler School of Medicine	L. Gissmann, DKFZ	Human papillomavirus type 16 in cervical cancer: the potential role of E6 natural variants in regression of progression of viral-induced disease
104	E. Wertheimer, Tel Aviv University	D. Breitkreutz, DKFZ	Functional significance of insulin signaling in skin and skin tumorigenesis
105	S. Lavi, Tel Aviv University	P. Peschke (div. P. Huber), DKFZ	Macromolecular polymers as a novel platform for the tumor directed delivery of drugs targeting molecular processes of apoptosis and radiation

Ca-No.	Israeli Partner	German Partner	Joint Project Title
Phase IX, group 1 – 01.01.2004 – 31.12.2006			
106	A. Fainsod, Hebrew University	C. Niehrs, DKFZ	Identification of the genetic network controlled by the caudal transcriptional regulator
107	Y. Gruenbaum, Hebrew University	H. Herrmann-Lerdon, DKFZ	The role of nuclear lamina proteins in organizing nuclear architecture in normal and transformed cells
108	D. Melamed, Technion	R. Arnold (div. P. Krammer)	Influence of antigen receptor mediated signaling in apoptosis and survival during the selection of lymphocytes
109	H. Werner, Tel Aviv University	D. Mayer, DKFZ	Functional and physical analysis of the IGF-I receptor gene in progression to advanced breast cancer
110	B. Kerem, Hebrew University	M. Schwab, DKFZ	Chromosomal fragile sites and cancer
111	M. Aboud, M. Huleihel, Ben Gurion Univ.	P. Krammer, M. Li-Weber, DKFZ	Oncogenic activity of HTLV-I Tax and its prevention
112	S. Segal, D. Fishman, Ben-Gurion Univ.	R. Ganss, G. Haemmerling, DKFZ	Tumor-associated blood vessel endothelium as a barrier to infiltration of effector immunocytes
01.07.2004 – 31.12.2005			
113	D. Rund, Hadasssah Univ. Hospital	A. Risch (div. of M. Bartsch), DKFZ	Genotypes of drug transporting and metabolising genes as potential modifiers of cancer risk and chemotherapy-sensitivity
Phase IX, group 2 – 01.07.2005 – 30.06.2008			
114	G. Golomb, Hebrew University	M. Berger, DKFZ	New strategies in the treatment of osteolytic bone metastasis of mammary carcinoma
115	R. Apte, Ben-Gurion Uniersity	M. Zoeller, DKFZ	The impact of host and tumor derived IL-1 on tumor growth and host defense
116	M. Baniyash, Hebrew University	V. Umansky (div. of D. Schadendorf), DKFZ	Melanoma growth, anti-tumor immune response and inflammation: a critical three-lateral interrelationship for successful immunotherapy
117	Y. Ben-Neriah, Hebrew University	P. Angel, DKFZ	Molecular mechanisms driving HCC development in mouse model of hepatitis-associated cancer
118	A. Porgador, Ben-Gurion University	A. Cerwenka, DKFZ	Evaluation of function for ligands of activating natural killer cells receptors in anti-tumor immunity
119	G. Ast, Tel Aviv University	A. Hotz-Wagenblatt, S. Suhai, DKFZ	Analysis of Alu exonization and alternative splicing in cancer genes

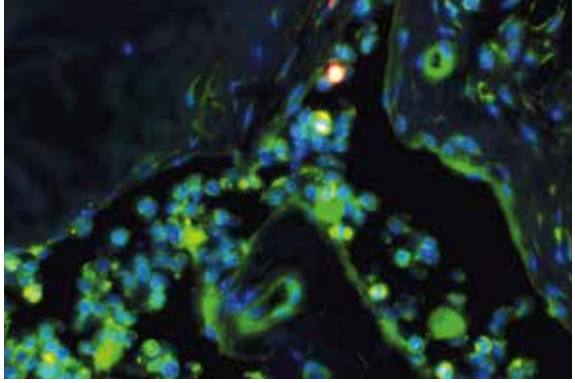


Ca-No.	Israeli Partner	German Partner	Joint Project Title
120	Y. Shiloh, Tel Aviv University	W. Lehmann (div. of W.E. Hull), DKFZ	Identification and functional analysis of protein phosphorylation and dephosphorylation in the ATM-mediated DNA damage response
Phase IX, group 3 – 01.01.2007 – 31.12.2009			
121	A. Eden, Hebrew University	F. Lyko, DKFZ	Hypomethylation-induced genetic instability as a factor in tumor formation
122	M. Kupiec, Tel Aviv University	I. Grummt, DKFZ	Epigenetic mechanisms regulating transcriptions and genome stability in cancer cells
123	E. Flescher, Tel Aviv University	M. Berger, DKFZ	Contribution of endoplasmic reticulum (ER) stress and mitochondrial perturbation in the death of breast and colon cancer cells induced by plant cytotoxic agents
124	A. Gross, Weizmann Institute of Science	H. Walczak, DKFZ	The role of DNA damage-mediated BID phosphorylation for TRAIL-induced apoptosis
125	S. Lev, Weizmann Institute of Science	I. Hoffmann, DKFZ	Identification and characterization of cytokinetic targets in cancer therapy
126	M. Neeman, Weizmann Institute of Science	F. Kiessling (div. of W. Semmler), DKFZ	High resolution assessment of antiogenesis and normalization of tumor vessel phenotype under therapy using implanted MR-coils and functional and molecular MR-imaging methods
127	I. Vlodavsky, Cancer and Vascular Biology Res. Center	P. Beckhove (div. of V. Schirrmacher), DKFZ	Human heparanase – a promising target for the development of therapeutic strategies in cancer
Phase X, group 1 – 01.07.2008 – 30.06.2011			
128	M. Baniyasch, Hebrew University	V. Umansky (div. of D. Schadendorf), DKFZ	Inflammation-dependent immunosuppressive tumor microenvironment: Its neutralization for successful tumor immunotherapy
129	D. Melamed, Technion	R. Arnold, P. Krammer, DKFZ	Intracellular signalling pathways controlling cell fate decisions of lymphocytes during differentiation and tumorigenesis
130	E. Pikarsky, Y. Ben-Neriah, Hebrew University	P. Angel, DKFZ	Molecular mechanisms of inflammation induced liver cancer
131	A. Kimchi, Weizmann Institute of Science	P. Krammer, R. Arnold, DKFZ	Molecular pathways underlying apoptotic and non apoptotic cell death and their implication in cancer development
132	E. Keshet, Hebrew University	H. Augustin, DKFZ	Interplay between VEGF and angiopoietins in the vascular tumor microenvironment



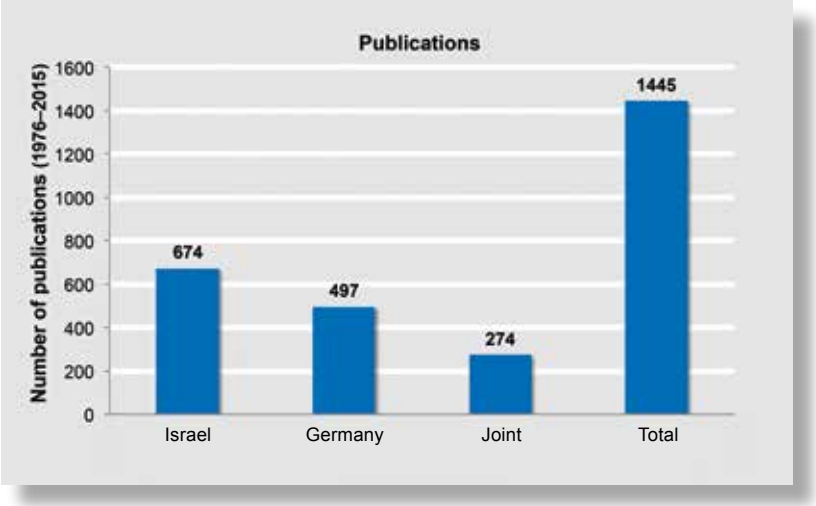
Ca-No.	Israeli Partner	German Partner	Joint Project Title
133	E. Razin, Hebrew University	M. Boutros, DKFZ	Exploring the network of STAT3 and MITF in melanoma using RNAi libraries
134	A. Levitzki, Hebrew University	F. Roesl, DKFZ	The Cellular pathways leading to cancer
Phase X, group 2 – 01.07.2009 – 30.06.2012			
135	O. Mandelboim, Hebrew University	S. Diederichs, DKFZ	Regulation and function of viral and cellular microRNAs controlling the immune response
136	N. Arber, Tel Aviv Sourasky Medical Center	P. Altevogt, DKFZ	Monochlonal antibodies targeting CD24 in the treatment of pancreatic cancer
137	Y. Shaul, Weizmann Institute of Science	T. Hofmann, DKFZ	Regulation of p53 family tumor suppressors under DNA damage stress
138	G. Neufeld, Technion	A. Fischer, DKFZ	The complex interactions of semaphorins and the delta-notch pathway in tumor angiogenesis
139	G. Ast, Tel Aviv University	A. Hotz-Wagenblatt, DKFZ	Defining control and function of alternative splicing during tumorigenesis
Phase X, group 3 – 01.07.2010 – 30.06.2013			
140	M. Fainzilber, Weizmann Institute of Science	N. Brady, DKFZ	RTK-dependent cell death in pediatric tumors of neural origin
141	S. Izraeli, Sheba Medical Center	A. Kraemer, DKFZ	The roles of SIL(STIL) in centrosome biology – relevance to cancer and developmental disorders
142	A. Porgador, Ben-Gurion University	A. Cerwenka, DKFZ	Characterization and regulation of NCR and NKG2D ligands in cancer
143	R. Apte, Ben-Gurion University	M. Mueller, DKFZ	Interactions between cancer associated fibroblasts (CAFs) and myeloid-derived inflammatory cells in the dynamic phenotype of the microenvironment during tumor progression; basic mechanisms and preclinical applications of novel intervention strategies
144	I. Vlodavsky, Technion	P. Beckhove, DKFZ	Heparanase: a promising target and tumor antigen for therapeutic strategies in cancer
Phase XI, group 1 – 01.07.2011 – 30.06.2014			
145	M. Kupiec, Tel Aviv Univ.	R. Eils, R. Koenig, DKFZ	A systems-level dissection of Telomere biology
146	E. Meshorer, Hebrew University	K. Rippe, DKFZ	Identifying features of chromatin organization and epigenetic modifications associated with pluripotency and self-renewal in stem cells and tumor initiating cells

Ca-No.	Israeli Partner	German Partner	Joint Project Title
147	E. Pikarsky, Hebrew University	P. Angel, DKFZ	Cross species inflammatory oncogenomics to identify therapeutic targets for liver cancer
148	G. Shakar, T. Feferman, Weizmann Institute	G. Haemmerling, DKFZ	Control of CTL-mediated tumor rejection by regulatory T cells: Imaging and molecular mechanisms
149	Y. Ben-Neriah, Hebrew University	H. Allgayer, DKFZ	microRNA control of tissue invasion and intestinal cancer
Phase XI, group 2 – 01.07.2012 – 30.06.2015			
150	Y. Bergman, Hebrew University	F. Lyko, DKFZ	The DNA methylation program in inflammation cancer
151	J. Abramson, Weizmann Institute of Science	M. Feuerer, DKFZ	Modulation of regulatory T cell function by novel T_{reg}-specific monoclonal antibodies
152	N. Erez, Tel Aviv University	K. Mueller-Decker, DKFZ	Characterizing the role of the microenvironment in facilitating melanoma brain metastasis
153	A. Ben-Baruch, Tel Aviv University	S. Wiemann, DKFZ	microRNA control of MSC and CAF in breast cancer: A proangiogenic switch and cell-remodeling
154	V. Krizhanovsky, Weizmann Institute of Science	J. Hess, DKFZ	Impact of the pro-inflammatory microenvironment on cellular programs of oncogene induced senescence during carcinogenesis
Phase XI, group 3 – 01.07.2013 – 30.06.2016			
155	B. Kerem, Hebrew University	F. Roesl, DKFZ	Folate deficiency and human papilloma virus-induced carcinogenesis.
156	D. Sprinzak, Tel Aviv University	A. Fischer, DKFZ	Quantitative analysis of Delta-Notch membrane distributions and its regulation during angiogenesis and metastasis
157	N. Karin, Technion	V. Umansky, DKFZ	The role of CCR5 in the recruitment of myeloid-derived suppressor cells (MDSC) from the bone marrow to support melanoma progression
158	R. Seger, Weizmann Institute of Science	E. Burgermeister, University of Heidelberg, Sponsor: H. Augustin	Function of the lipid phospatase MTMR7 in anti-EGFR therapy resistance of colorectal cancer (CRC)
159	C. Levy, Tel Aviv University	J. Hoheisel, DKFZ	Exploring microRNA transfer and melanoma progression: novel concept of cell-cell communication in the tumor microenvironment

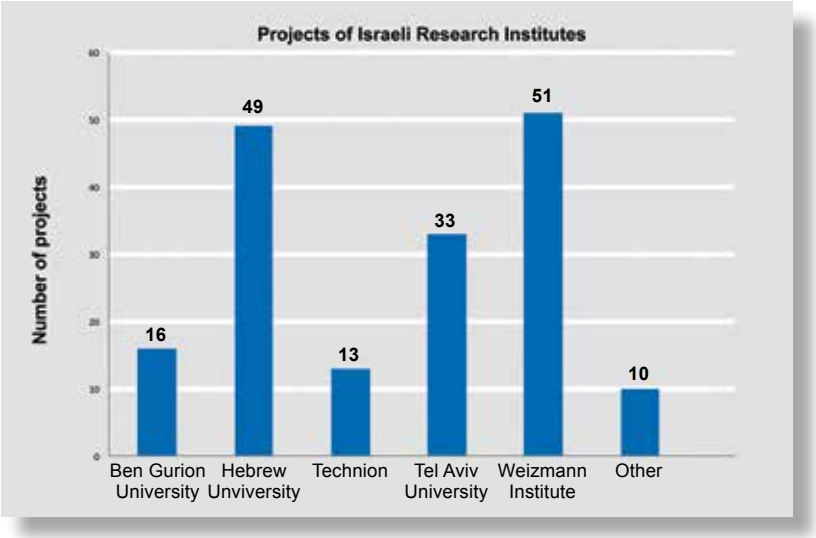


Ca-No.	Israeli Partner	German Partner	Joint Project Title
Phase XII, group 1 – 01.07.2014 – 30.06.2017			
160	R. Beck-Barkai, Tel Aviv University; B. Geiger, Weizmann Inst.	E. Gladilin, DKFZ	Dissecting the contribution of vimentin intermediate filaments to mechanical and structural properties of cancer cells, using advanced physical approaches
161	I. Ben-Porath, Hebrew University	T. Hofmann, DKFZ	Molecular regulation of cellular fate by p53: the choice between apoptosis and senescence
162	M. Berger, Hebrew University	A. Kraemer, DKFZ	The role of the quiescence inducer Slfn2, in T-ALL development
163	E.Galun, Hadassah Med. Organization	L. Zender, DKFZ	Tumor suppressive mechanisms of micro RNA 122*
164	M. Lotem, Hadassah Med. Organization	P. Beckhove, DKFZ	Identification of anticancer immune checkpoint molecules expressed by tumor cells or lymphocytes using high-throughput RNAi screening
2495	N. Papo, Ben-Gurion Univ.	A. Miller, DKFZ	Developing dual PAR1/KLK6 inhibitors based on bi-specific APPI peptide-small molecule conjugates for clinical translation as therapeutic anticancer agents
2511	A. Smadar, Schneider Children's Medical Center	H. Witt, DKFZ	Unraveling driver mutations and epigenetic alterations in pediatric solid tumors
Phase XII, group 2 – 01.07.2015 – 30.06.2018			
2526	A.Admon, Technion	M. Platten, DKFZ	Exploiting the immunopeptidome of experimental glioma
165	D. Friedmann-Morvinski, Tel Aviv Univ.	J. Gronych, D. Jones, DKFZ	Understanding the functional impact of genetic alterations in brain tumors
166	I. Shachar, Weizmann Institute of Science	M. Seiffert, DKFZ	Functional characterization of pathogenic changes in the microenvironment of chronic lymphocytic leukemia, with a focus on immunomodulatory SLAM receptors
167	L. Gilboa, Weizmann Institute of Science	M. Boutros, DKFZ	A comprehensive functional analysis of niche-stem cell interactions
168	T. Lapidot, Weizmann Institute of Science	H. Augustin, DKFZ	Regulation of normal and leukemic human stem cells by the endothelial blood-bone marrow barrier
169	D. Ginsberg, Bar-Ilan University	I. Grummt, DKFZ	A novel mode of non-coding RNA in gene regulation: An E2F1-dependent antisense RNA activates expression of the proto-oncogene *SPHK*

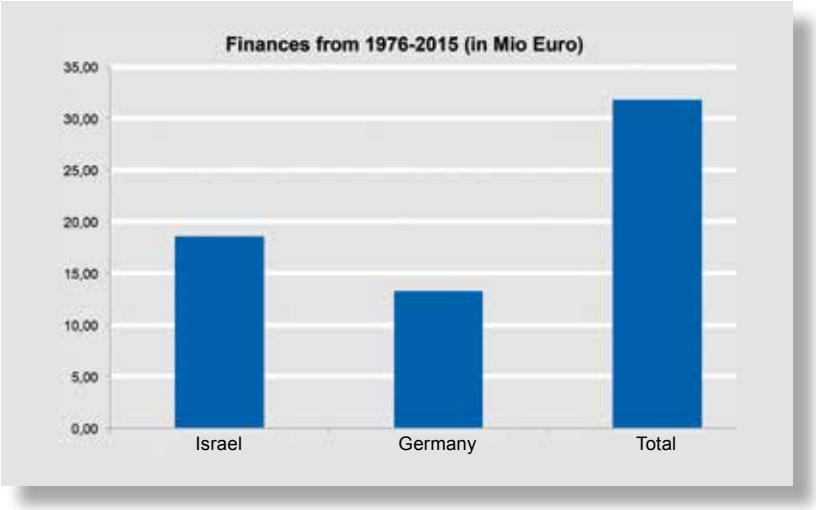
STATISTICS ON THE COOPERATIONAL PROGRAM



The scientific output of the cooperation program is illustrated by almost 1500 peer-reviewed publications in international well-renowned journals.



Distribution of all 171 joint DKFZ-MOST research projects 1976-2015 among the Israeli institutions.



To date, the total funding of the program amounts to 32 million Euro. Starting with three projects in 1976 over the years funding has grown constantly. On the basis of the most recent increase in 2014 the yearly budget comprises of 1,3 million Euro allowing the funding of 18 running projects.

GERMAN-ISRAELI WINTER-/SUMMER SCHOOLS


Pichl

In 2006, during the 30th Anniversary of the Cooperation, the idea of a "German Israeli Cancer Research School" was born to serve the students of the cooperation program. The aim was to bring together young scientists of cancer research from both countries in a friendly and casual atmosphere where the exchange of knowledge and ideas could take place. Lectures by well-renowned scientists from both countries give the opportunity to discuss the most recent scientific methods and achievements in exciting and emerging areas of cancer research. In the present brochure a summary of the past School held in the Negev Desert in Israel is given to highlight the style and peculiarity of this measure of German-Israeli Interaction.


Ein Gedi/Dead Sea

1st School of Cancer Research — **2008**
Winter School; Pich, Austria, March, 4th-7th

2nd School of Cancer Research — **2009**
Summer School; Ein Gedi/Dead Sea, Israel, November, 23rd - 26th


Garmisch-Partenkirchen

3rd School of Cancer Research — **2010**
Winter School; Pichl, Austria, Feb. 28th – March 5th
Topic: Cancer Immunology (G. Hämmerling and L. Eisenbach

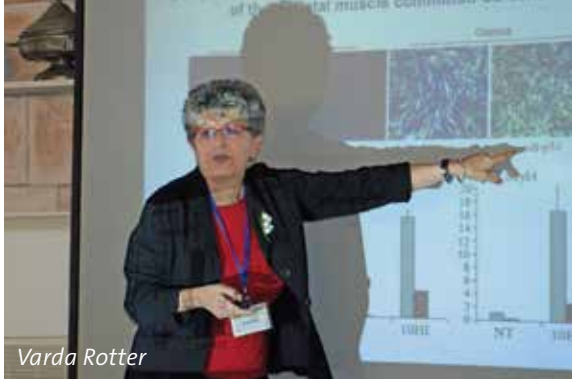
4th School of Cancer Research — **2011**
Summer School; Kibutz at Kfar Geladi, Israel, November, 13th – 15th
Topic: Genetics and Epigenetics (P. Lichter and H. Cedar)


Mitzpe Ramon, Negev Desert

5th School of Cancer Research — **2012**
Winter School; Pichl, Austria, December, 9th -13th
Topic: Metabolism and Cancer (S. Herzig and A. Elson)

6th School of Cancer Research — **2013**
Summer School; Negev Desert, Israel, November, 9th -13th
Topic: Mouse Models of Human Cancer (H. Augustin and E. Pikarsky)

7th School of Cancer Research — **2015**
Winter School; Garmisch-Partenkirchen, Germany, February, 8th-12th
Topic: Systems Medicine (T. Höfer, R. Eils and E. Galun)


Varda Rotter

GERMAN ISRAELI CANCER RESEARCH SCHOOL

The 6th German Israeli Cancer Research School on Mouse Models of Human Cancer focused on the most critical bottleneck in the advancement of basic tumor biology and translational research: the availability of suitable preclinical animal tumor models that better mimic the human pathology of cancer. The German-Israeli Cooperation fosters scientific cooperations between DKFZ scientists and Israeli cancer researchers. A winter school in 2014was jointly organized by Hellmut Augustin (DKFZ, Heidelberg) and Eli Pikarsky (Hebrew University, Jerusalem).

Eight speakers from Israel, six speakers from Germany, which are all members of the Helmholtz Alliance Preclinical Comprehensive Cancer Center (PCCC) and 26 young scientists (students and junior postdocs) met at Mitzpe Ramon in the middle of the Negev Desert for three intense and stimulating days of scientific exchange and development of new ideas. The participants highly appreciated that Otmar Wiestler, then Chairman and Scientific Director of the German Cancer Research Center, had joined the meeting for two days to engage in discussions about the latest developments in this rapidly moving field of ongoing cancer research. He emphasized the importance and success of the GermanIsraeli Cooperation, which promotes intense scientific cooperation and friendship between cancer researchers of both countries.


Klaus Rajewsky

The event provided the young scientists with the unique opportunity to meet some of the key opinion leaders in the field in the informal setting of a small workshop. Among others, the list of speakers included PCCC member Klaus Rajewsky, whose group has as early as 1994 established the feasibility and power of the Cre-lox recombination system for conditional gene targeting *in vivo* (Gu et al., Science). This technique has revolutionized preclinical mouse models and is nowadays used by hundreds of laboratories around the world.

The scientific program of the Cancer Research School focused on three tumor entities: gastrointestinal cancers, brain tumors and hematological malignancies and covered the cutting-edge research topics in the field. Tumors are now widely recognized not just as a clump of tumor cells, but as a neoplastically growing organ, consisting of tumor cells, host-derived stroma and recruited immune cells. This was reflected by the number of contributions covering the topic tumor microenvironment. Likewise, advanced models for deciphering the role of cancer stem cells and longevity in tumorigenesis were presented. Last, but not least a plethora of preclinical mouse models for various therapy approaches were discussed.


Uri Alon

A further highlight was the keynote lecture by Uri Alon, who is not only known as a very successful systems biologist, but also as an outstanding entertainer. Using simple flip chart lectures and his guitar, he spread his ideas about empathy in science to the upper echelons of scientific institutions around the world (see also "*Sunday in the Lab" http://www.youtube.com/watch?v=yhncg6GXYq8*).

The organization of the winter school incorporated two novel program points: Student speakers selected by the organizing team presented research short talks. A second novelty was a "grant writing competition". Students could choose between different topics which

were proposed by the invited speakers. With support of their mentor, the students presented their proposal in a 10 min talk which was discussed and evaluated by a panel of reviewers. This educative game was not only a great challenge but also a lot of fun for all participants. The students and postdocs were extremely curious, open to new ideas and the meeting was a great think tank for scientific exchange.

Besides the intense scientific program, there was ample time to enjoy the social activities. The walk for the sunrise at the Makhtesh Ramon crater rim was as impressive as the trip through the crater, where the group enjoyed an incredible sunset. The winter school in Mitzpe Ramon is a great example that such events are more than worthwhile. The organizers got an overwhelming feedback from junior and the senior participants. Notably, the selection of talks and the grant writing competition have been highly appreciated. The participants surely returned with a lot of new ideas and plenty of impressions from this exceptional winter school.

IMPRINT

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GERMAN
CANCER RESEARCH CENTER
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50 Years – Research for
A Life Without Cancer