



# NIBN REPORT

The National Institute for Biotechnology in the Negev November 2005

## Message from the President

*The National Institute for Biotechnology in the Negev (NIBN) is entering an exciting new phase in its development. With the publication of this report, our scientists at the NIBN have an opportunity to showcase the unique character of their research and the development of the Institute to friends and colleagues.*

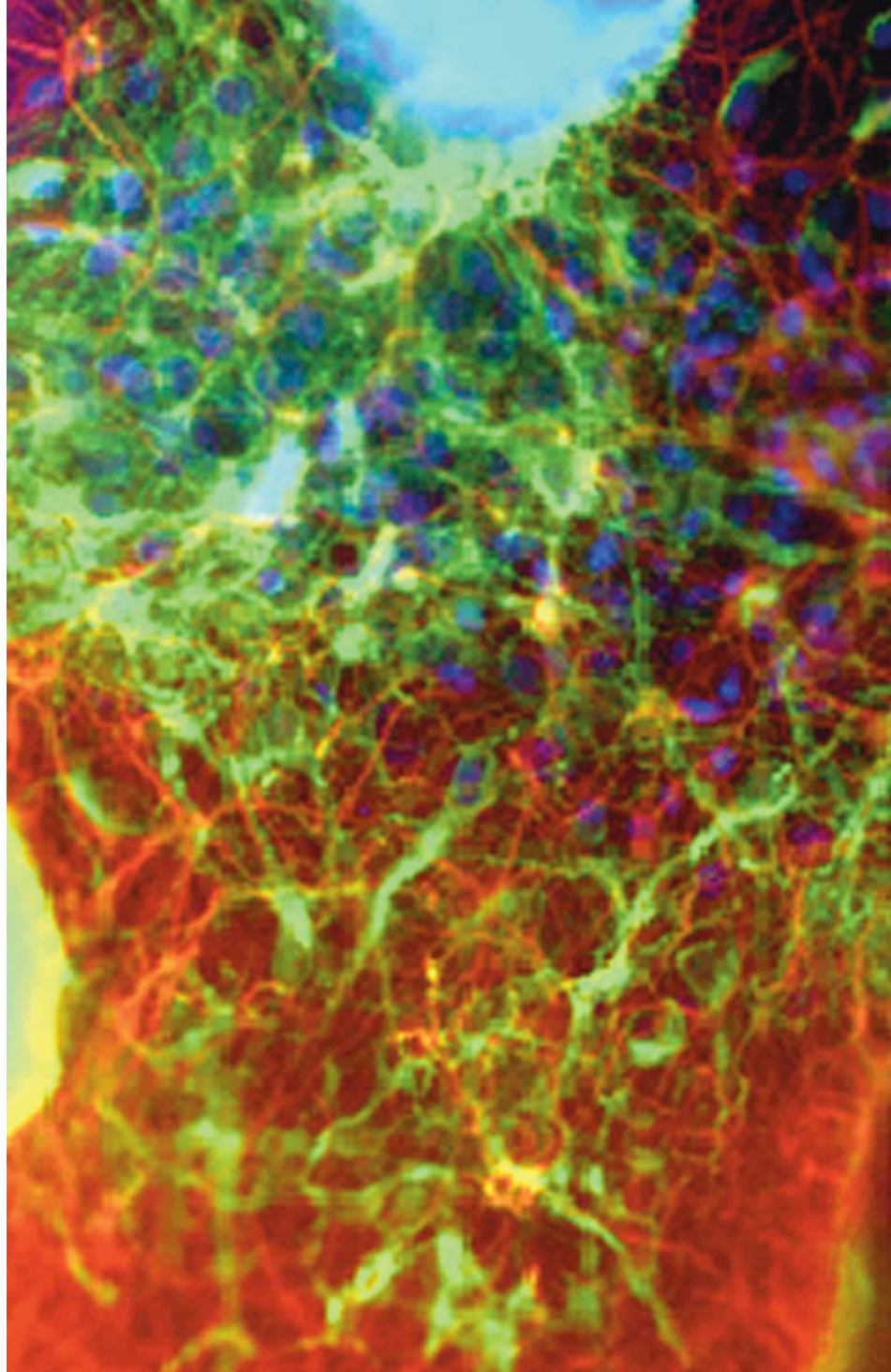
*It is my sincere hope that this report will expose NIBN activities to a wider audience. Our scientists and the leadership of the NIBN, including international luminaries who support its work, are inspirational individuals who have chosen to tackle the unique challenges of biotechnology from the Negev.*

*One man in particular – our dear friend Dr. h.c. Edgar de Picciotto of Switzerland – had the foresight to envision and establish the NIBN. We are thrilled to see the fruits of our labors and dreams come true, just as we mark the centennial anniversary of David Ben-Gurion's Aliya. It is due to the vision and magnanimous support of a number of great friends that the NIBN has come to fruition and will serve as a force for peace in the region.*

*Ben-Gurion once said that, "In Israel, in order to be a realist you must believe in miracles." A miracle has indeed occurred in the Negev. Kol HaKavod to all of our partners in this tremendous effort and Yeshar Koach to the scientists of the NIBN!*

*In friendship and partnership,*

**Prof. Avishay Braverman**  
President



## Highlight on NIBN

**Prof. Varda Shoshan-Barmatz**  
Deputy Director

*The National Institute for Biotechnology in the Negev (NIBN) is proud to publish this NIBN REPORT.*

*The purpose of the NIBN REPORT is to summarize the progress and achievements of the NIBN, which is at the spearhead of the University's efforts to promote excellence in research. The NIBN, made possible through the magnanimous support and vision of Dr. h.c. Edgar de Picciotto of Switzerland, brings together scientists from different disciplines with medical personnel and professional consultants to create a front-line interdisciplinary institute focusing on biotechnology.*

*Revolutions come in stages, and we have now advanced from the first stages of adoption of new ideas, tools and methods.*

*We would like to express our thanks and appreciation to Prof. Sir Aaron Klug OM FRS, who served as Acting Executive Director of the NIBN, and members of the International Advisory Committee: Prof. Yehudit Birk, Prof. Aaron Ciechanover, Prof. Raymond Dwek FRS and Prof. Philip Needleman, all of whom represent a reservoir of experience, information and authority and have an important impact on the development and achievements of the NIBN.*

*The strong point of the NIBN has been its ability to recruit outstanding young scientists. These talented researchers are supported by NIBN's overall commitment to invest in the technical infrastructure for sophisticated state-of-the-art biotechnology laboratories. This combination has made the NIBN one of the most attractive research centers in Israel today and this REPORT contains a brief summary of some of their exciting and innovative achievements*

*This issue includes an article by NIBN's newly appointed director, Prof. Irun Cohen, who 30 years ago was a member of the team that founded BGU's Faculty of Health Sciences. The article, focusing on "Why Biotechnology and Why in the Negev" addresses very important questions and their answers in one line: this is the right time, the right place and the right decision.*

*We believe that NIBN will create a significant impact on the economic prosperity of the Negev region and throughout Israel. NIBN will fuel spin-off companies, incubator programs and accelerator corporations will be established to commercialize the novel ideas and technologies at the NIBN. The interaction and combination of academic merit with economic prosperity will attract scientific excellence and serve as a hub for research, development and teaching in the Negev.*

## Establishing NIBN

**Prof. Sir Aaron Klug, OM, FRS**  
Chair of the International Advisory Committee

*It is now five years since we first made the approach to the Government for funding a National Institute of Biotechnology in the Negev at BGU.*

*The basis was to be the Institute of Applied Biosciences which had been built and funded with the generous support of Dr. h.c. Edgar de Picciotto of Geneva.*

*It was his vision that this Institute could and would form the nucleus of a future National Center for Biotechnology.*

*Although there was a generally favourable recommendation from the Government departments and acceptance in principle, no money was forthcoming.*

*We nevertheless continued to plan that it would eventually happen, and were very fortunate to gain generous support from the Morris Kahn Humanitarian Fund, originally for a program in the Faculty of Health Sciences initiated by Professor Rivka Carmi on the genetic approach to human health. This was later expanded to recruit outstanding young researchers in cognate subjects and to provide new instrumentation.*

*Two years ago, these two funding initiatives came together, and, as Chair of the International Advisory Committee, I took up the position of Acting Executive Director while we searched for a Director of NIBN. We were able to attract*

*Professor Irun Cohen to that position, with his deputy, Professor Varda Shoshan-Barmatz, who throughout the years has worked indefatigably towards our aim.*

*I also wish to thank my fellow members of the International Advisory Committee, particularly Professors Raymond Dwek and Philip Needleman, who brought their wide ranging expertise to the project.*

*We look forward to the event this week which highlights NIBN and at which Dr. h.c. de Picciotto and Minister Ehud Olmert will formally announce long term funding for NIBN, enabling the Institute to enter a new phase of development.*

## Why the NIBN

**Prof. Irun R. Cohen, MD, Director**

Many have asked how Israel might succeed in achieving greater returns in intellectual property and biotechnology products for a given investment in basic research in the life sciences. Or to be more specific, why do I think the NIBN will be more effective than previous efforts in launching successful biotechnology. I shall answer that question by summarizing the problems inherent in the relationship between university research and biotechnology to clarify the rationale of the NIBN model and its implementation.

### University and Biotechnology in Conflict of Interest

#### *The University*

Classically, universities have been designed to fulfill two primary functions: research and teaching. University research in its broadest sense extends beyond laboratory experimentation to include the convocation of scholars and the provisions they need to advance and disseminate collective knowledge and understanding in the humanities, arts and sciences. University teaching prepares coming generations of professional scholars and educates the non-professional members of society as well.

The pursuit of research and teaching has dictated the organization of universities into specific departments and faculties and has led to the prevalent operational machinery (department heads, deans, committees, senate, rector, and so forth) for academic decision-making regarding funding, appointments, evaluations, advancement, and tenure. This university structure oversees the responsibility of the staff for teaching, scholarly achievement and publishing.

#### *Biotechnology*

Biotechnology strives to fulfill a different agenda: Biotechnology focuses on the discovery and development of technologies, devices, and reagents that tend to the biological needs of humans for sustenance, health, and enlightened economic welfare. Biotechnology has little or no interest in university teaching or research – except for the specific research or teaching that is part of a defined product goal. Biotechnology is not interested in professorships, publications, or the operational machinery of university departments, deans, committees, senates, and rectors. Indeed, much of the university activities carried out by the researcher can interfere with his or her participation in the biotechnology

enterprise. But despite the conflict of interest, biotechnology still depends on university researchers and their ideas, expertise, technical staff and research to thrive. University researchers are the innovators of most successful biotechnology products. In short, biotechnology needs the university.

Universities too, until recently, have shown no interest in biotechnology, which is usually foreign to the pursuit of teaching and basic, disinterested research. Despite the conflict of interest, however, universities have discovered the economic value of intellectual property developed at the university; successful university biotechnology can provide funds much needed by the university to carry out its traditional agenda of education and scholarship. The university benefits from biotechnology.

### ***Interdisciplinary and converging technologies***

Not only is biotechnology at variance with the teaching and basic research missions of the university, biotechnology is inherently multidisciplinary and interdisciplinary, and so crosses the barriers of traditional academic subdivisions. The technological crossing of academic barriers has been called convergence. Convergence, or Converging Technology has been defined as the need for academically independent fields of science and technology to work together to create innovative ideas and products. To succeed in multidisciplinary problem solving, biotechnology needs an interdisciplinary organizational structure foreign to the department/faculty makeup of the present university model.

### **The NIBN Model**

The NIBN has been conceived as an innovative model to circumvent or resolve the traditional conflict of interest that estranges the university from interdisciplinary, converging biotechnology. The NIBN is structured as a collection of multidisciplinary task forces culled from all the different faculties at BGU, but yet the NIBN remains free of the need to concern itself with promotions, tenure, and other parochial academic concerns.

The NIBN operates through multidisciplinary channels of communication and collaboration, relatively free of departmental concerns. Indeed, membership in the NIBN, unlike tenured membership in a department, is subject to regular review and adjustment: staff earn membership and can have it withdrawn as judged by outside evaluation of the appropriateness of the research program and the excellence of the scientists'

performance. Affiliates outside the university are recruited to join the various NIBN groups as needed. Networks, local and international, are established to further the programs. The NIBN is situated within BGU and staffed by BGU scientists, but it is significantly independent of the traditional university department/faculty structure.

### ***NIBN Programs***

The biotechnology programs being developed at the NIBN embody the concept of multidisciplinary convergence. NIBN biotechnology, like converging technologies being developed in the USA, the European Union and elsewhere, cuts across academic boundaries. The NIBN staff is rich in multidisciplinary expertise:

The *Human Genetic Diseases* program mixes clinical and molecular technology to discover novel genes and generate gene products that promise to lead to therapies for several health problems;

The *Glycobiology* program is based on advanced carbohydrate chemistry and proteomics, and hosts the National Center for Glycobiology, providing a unique service to Israel industry along with its development of novel approaches to diagnosis;

The NIBN has established an electron microscopy tomography unit that exists in only three other locations worldwide. This advanced device adds front-line structural imaging technology to the development of health applications;

The *Microbial Biotechnology* program exploits molecular genetics along with its new technology for cultivating previously un-culturable bacteria as a means to obtain useful microbial products;

*Bio-materials and tissue engineering* have provided tissue scaffolds for the regeneration of heart muscle or bone in patients suffering from a loss of the tissue and its function. Nanotechnology directed to bio-sensors is part of the NIBN program in bio-materials.

*Immune biotechnology* mines information from the immune system to develop therapeutic approaches to Alzheimer's and other chronic diseases. IVRI, the Israel Vaccine Research Initiative, with affiliates abroad and throughout Israel, is closely connected to NIBN immune system biotechnology.

*Informatics* is essential to biotechnology; informatic tools are indispensable to integrating, manipulating and understanding the complexity of the living organism.

Thus the NIBN is already on the way towards fulfilling the promise of convergent biotechnology. Its multidisciplinary activities and its multi-faculty organizational structure place the NIBN in a uniquely

advanced position. The key issue is implementation.

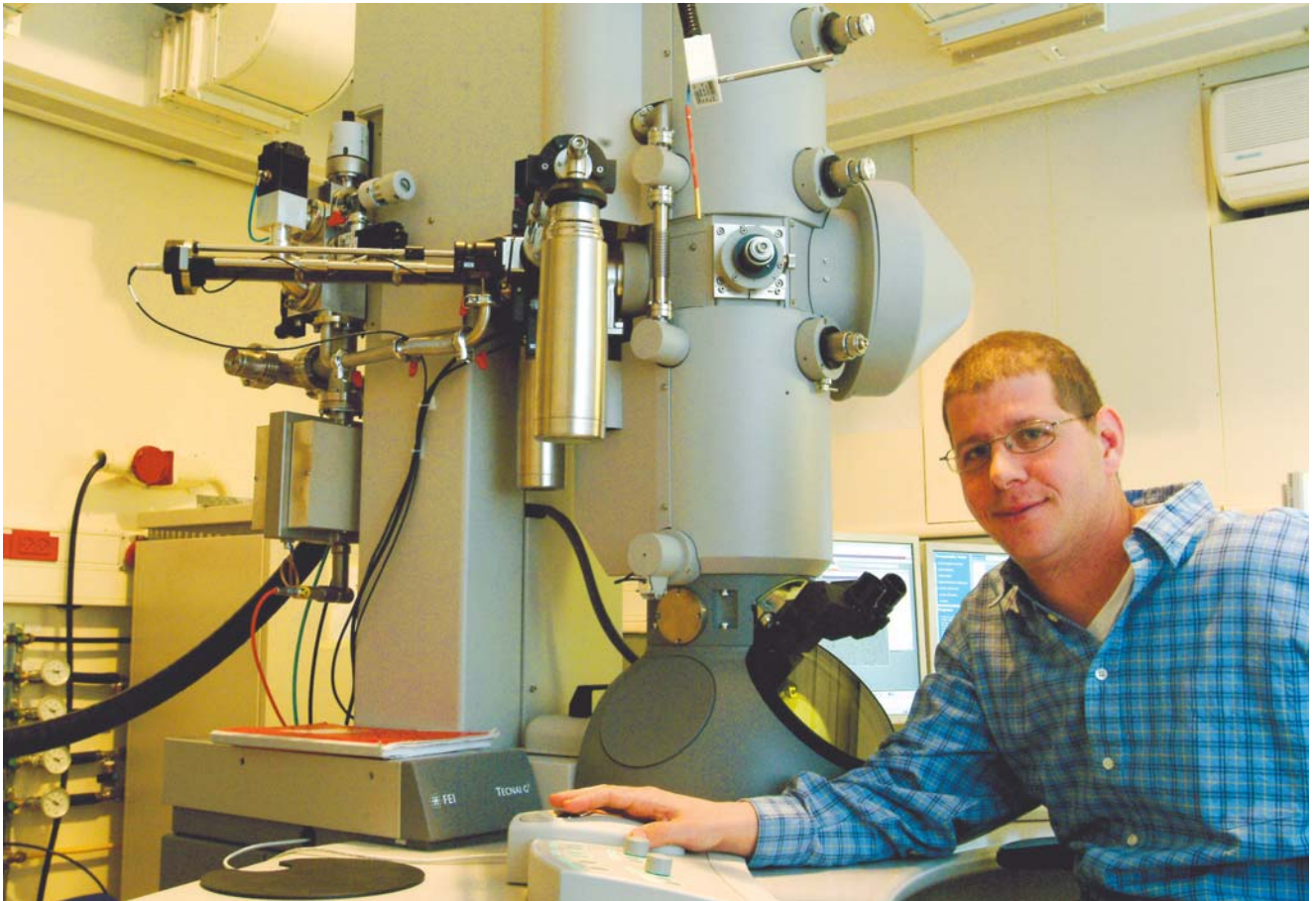
### ***Implementation***

The success of the NIBN model will depend on three factors: excellence, collaboration and resources.

**Excellence.** The success of the NIBN depends greatly – perhaps entirely – on the continuing recruitment of outstanding scientists from among the talented young Israelis returning from advanced training abroad. The NIBN will continue to attract such talent only if it can compete with other institutions in Israel and abroad in providing opportunity, and not only in offering a challenge. It is especially gratifying to note that the NIBN has succeeded in recruiting talented young Israelis who have been offered staff positions abroad at frontline institutions. These scientists share an appreciation for the importance of the NIBN model. Indeed, in the past month, the NIBN has been joined by an Israeli scientist returning from two years as the head of a central systems biology unit at Harvard.

**Collaboration.** Not only must the NIBN attract excellent staff scientists, the NIBN must provide the physical and intellectual environment needed to bring this talent to work together. To this end, the NIBN research leaders hold weekly meetings with NIBN management aimed at fostering mutual participation and collaboration. Monthly research seminars are held for all the students, technicians and associates as well as for the scientists. The NIBN provides competitive grants for selected interdisciplinary projects. These and other measures are undertaken to promote convergence and interdisciplinary problem solving.

**Resources.** To attract and maintain an outstanding staff, the NIBN must be able to deploy its own sources of funding to enable it to purchase frontline equipment, support technicians, students and fellows for advanced research, and provide suitable space for a critical mass of multidisciplinary researchers. Intellectual property generated by NIBN science will return in part to the scientist inventors and to the NIBN, as well as to the university. A successful NIBN will ultimately generate much of its own funding. A substantial endowment, however, is needed now to sow the seeds for commercial enterprises. Moreover, a building suited to the interdisciplinary needs of a converging biotechnology needs to be built to house the NIBN; a well-designed building will itself attract excellent researchers and provide the NIBN with a competitive advantage in performance.



## Exploring the Inner-space of Cells at the NIBN

*Ohad Medalia, Ph.D*

Visualization of the three-dimensional (3D) organization of a eukaryotic cell, with its dynamic internal structure and distinct protein complexes in their native context, requires a non-invasive imaging technique of high resolution combined with a means for arresting cellular elements in their momentary state of function. Electron tomography (ET) is such a method, possessing, in addition, a unique potential for 3D visualization of large pleiomorphic structures such as intact cells and appears likely to revolutionize the way cells are viewed.

After three years of post-doctoral training at the Max-Planck institute of Biochemistry, where I focused on cryo-ET of eukaryotic cells, I had to decide on my next scientific step. The possibilities were to accept an academic position at: 1. The European Molecular Biology Laboratories (EMBL), Heidelberg. 2. The Weizmann Institute of Science. 3. The Hebrew University 4. The Ben-Gurion University and the NIBN. I joined the BGU and the NIBN in March 2005, because it is the most dynamic and the only academic institution in Israel that is developing with an eye to the future.

The challenge I faced was to establish an electron microscopy facility that can compete with the best electron microscopy laboratories in the world.

At a cost of \$2.8 million dollars, BGU acquired the 300kV electron microscope which is housed in the NIBN. This facility is unique to Israel and one of seven worldwide. It will be used to gain new insights into the lesions of Alzheimer's Disease and other chronic conditions.

Recently, we were able to generate the first cell reconstructions that gave us our first 3-dimensional glimpse into the photosynthetic system in bacteria.

In my laboratory, we apply cryo-electron tomography to intact cells, focusing on two main goals: 1. Reconstructing the eukaryotic cytoskeleton in 3D- Cell motility relies on fast and regulated polymerization/depolymerization of actin filaments that push the plasma membrane. Using live cell imaging techniques, many of the factors contributing to this dynamic process have been revealed. Nevertheless, due to the dimensions of actin filaments and the density of the filamentous network, important aspects of this important mechanism have remained unsolved, in part,

because of a lack of resolving power. Indeed, while traditional 2-D electron microscopy has been applied to the study of the actin content in cellular protrusions, only ET with its 3D view of this network in an unperturbed state possesses the potential to reveal the secrets of cell motility. A major project in my lab, therefore, is to elucidate the 3D structure of the adhesion machinery of cells.

2. Structural analysis of the nuclear periphery, the nuclear pore complex and the nuclear lamina. The cell nucleus is an extremely complex compartment that is responsible for many processes in a living cell. However, its organization, at the nanometer scale, is still uncharted territory. While much has been learned, in recent years about the movement of soluble transport factors across the nuclear pore complex (NPC), high resolution structure of these large macromolecular assemblies is still not available. Since a clear picture of the molecular organization and dynamics of the NPC is one of the basic elements required to resolve the mechanism of transport within cells, a major emphasis in my lab is to produce a high resolution map of these complexes.

# The Bioinformatics Support Unit

*Vered Caspi, Ph.D*

During the last decade and with accelerating speed, biological sciences are undergoing a transformation, whereby extremely large datasets are being generated experimentally, stored in international databases and being integrated for a wide variety of uses. The emergence of bioinformatics has thus evolved; a multi-disciplinary field integrating a blend of biological, mathematical and computer sciences, providing the opportunity to accelerate the discovery process for the biological, biotechnological and biomedical sciences. Israel is an internationally recognized center of excellence in bioinformatics. Even so, there remains a great par that separates the knowledge-base of most Israeli biologists and the emerging bioinformatics applications relevant to particular biological fields. With this in mind, the Bioinformatics Support Unit was established at BGU with the major role of helping university biologists to become acquainted with bioinformatics tools, and to keep the more informed scientists updated with recent developments in bioinformatics technologies, in order to advance research efforts.

The Bioinformatics Support Unit was founded on September 2003 by Dr. Vered Caspi, who was recruited from the Weizmann Institute where she was one of the founders of the GeneCards database for human genes. More recently, the Unit was expanded with the recruitment of Dr. Daniel Harari, an experienced bioinformatician and molecular biologist from both academia and industry, Mr. Raphael Cohen, a third year Bioinformatics student at BGU who works as a system administrator and programmer, as well as a number of under-graduate teaching assistants and project students.

The Unit activities include:

- ▶ Conducting weekly workshops on practical usage of bioinformatics tools.
  - ▶ Teaching 3 academic semester courses to both undergraduate & graduate students.
  - ▶ One-on-one research consultation and support to scientists and students.
  - ▶ Research collaborations on large-scale analyses of entire genomes.
  - ▶ Development of automated software for functional genome analysis.
- ▶ Statistical analyses of microarray experiments run at the NIBN microarray facility and elsewhere.
  - ▶ Maintenance of a computer server containing cutting edge bioinformatics software and databases for the use of the BGU community.



These activities are crucial for enhancing the biotechnological potential of the NIBN and the larger BGU.

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## A Year in the NIBN

*Alon Monsonego, Ph.D*

My scientific career was initiated at the Weizmann Institute where I studied mechanisms of wound healing of the central nervous system as part of my Ph.D. thesis. Toward the end of this educational stage, I began appreciating the significant importance of our immune system to deal with diseases of non-infectious origin such as cancer, neurodegeneration, and autoimmunity. I then moved to Harvard to obtain the state-of-the-art knowledge and technologies required for basic understanding of autoimmunity and the dialog the immune system holds with the brain. I spent 5 years at Harvard (2 years as post doctoral fellow and then 3 years as a faculty member), during which I investigated novel immune mechanisms of Alzheimer's disease and became one of the leaders in the design of vaccination approaches to this disease.

It was then clear to me that the next step in my scientific carrier should be in Israel. The NIBN opened a unique and very challenging opportunity to reach my goals. It first allows one to function in a multidisciplinary unit which forms new directions of research. Second, it generates the ultimate combination between basic and applied research.

During the first year at the NIBN, I established an almost fully equipped laboratory based on generous funds from the NIBN and several national and international scientific grants. As part of our research program, our group established colonies of mouse models for Alzheimer's disease and multiple sclerosis and hopefully these will enter an essential new facility soon. Being exposed to the other groups at the institute, we have already initiated new collaborations with 3 groups at the NIBN



which otherwise would not have occurred.

In summary, we now wish to enter the second phase at the NIBN towards gaining novel aspects of autoimmune mechanisms in general and neurodegenerative diseases in particular and thus designing new approaches for therapy.

## From Harvard to NIBN

*Eitan Rubin, Ph.D*

System biology holds great promise for medical and agricultural research. Monitoring the components of life (genes and their products, cells and tissues) is not sufficient to predict the behavior of biological systems. As a result, we still cannot predict a patient's reaction to a new drug, or the nutritional properties of a new crop. Life is complex, and understanding how it reacts to perturbations requires understanding the dynamic interaction of many different molecules, cells, tissues and organs. Such an understanding is essential both for the progress of biotechnology from a trial-and-error science into a true rational field.

Scientists throughout the world are developing the experimental, computational and conceptual breakthroughs required for the systemic study of life. First, they measure in completeness the state of systems over time – collecting millions, billions and even trillions of data points in a single experiment. Harvard is a hub for such experiments: with an investment of \$100 million (shared with MIT), the Broad Institute was established specifically for this purpose. NIH provides multi million dollars a year grants to the Broad Institute, the Bauer Center for Genomics Research and to other groups throughout Harvard to perform such large experiments. These funds are being used to develop new technologies that would allow the measurement of all aspects of a system simultaneously at a reasonable price, to use existing technologies (at unreasonable prices) to obtain such data for the first time, and to utilize these data to establish the computational and conceptual frameworks required for its analysis.

Israel has a major role in allowing this field to flourish, especially in developing the computational techniques it requires. At the Bauer Center for Genomics Research,

nearly one third of all group leaders came from Israel. The root cause of this success is not fully clear to me, but it probably has to do with the Israeli culture of collaboration, our flexibility in acquiring new skills, and the ability of the nation (and friends) to quickly re-allocate resources. Finally, it can also do with the large proportion of computationally savvy scientists who enter universities in Israel: there are currently four degree programs in bioinformatics in Israel, which combine biology and computer life sciences training.

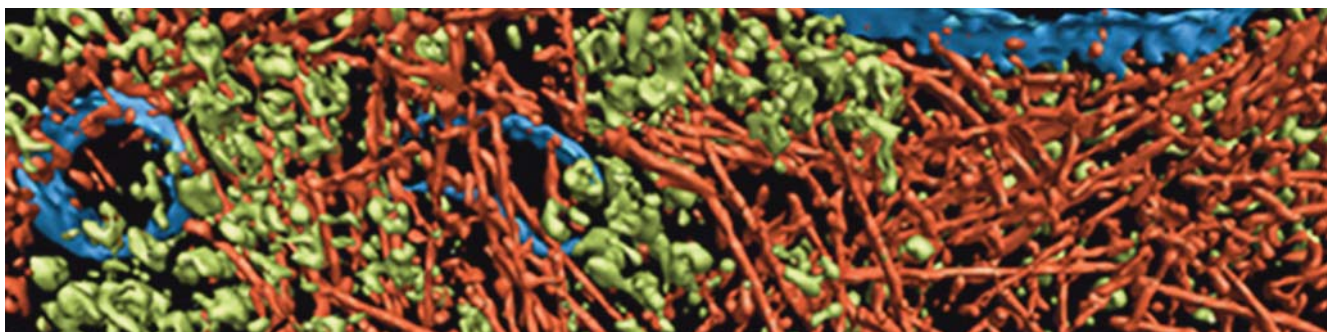
Here at NIBN, my lab is marrying systems biology with another emerging field, medical informatics. We are utilizing electronic clinical records as a source of information for systems biology research, specifically the Soroka Clinical Repository, which gives us information about how peoples' health change over time, how they respond (or not) to treatment, etc. We use these data as a substitute to experiments in which the phenotype (i.e. the observed state of the system) is scored in completeness for a large number of individuals. With some 600,000 individuals, we hope these data will allow developing more detailed and structured description of many diseases. We are using these data to study how a subset of disease causing genes, about 12% of all human genes, can lead to disease regardless of environment or other genes, while other genes don't. We are also working to develop new disease sub-classification schemes (a process known as disease stratification) which may prove crucial for clinical trials, identify new disease causing genes in silico., and help facilitate experimental gene identification through computational tools that predict which genes are more likely to be related to a given disease.

Others at NIBN are also working on projects which target crucial aspects of



systems biology. For example, Glycomics research, spearheaded by the “Sugers group” and Yoram Tekoa, is going to prove a limiting factor in systems biology; mitochondria, as studied by the Dan Mishmar group, is a peculiar subsystem which has immense impact on the ability of cells and tissues to perform their functions. But most importantly, we are currently working to join forces between researchers in the center and outside, in other parts of BGU, to harness the Israeli spirit together with the Ben Gurion family spirit, and create a non-traditional interdisciplinary network including faculty from departments which traditionally do not collaborate with biologists. For example, we found immense enthusiasm in the department of Industrial Engineering and Management.

To conclude, the move from Harvard to NIBN requires adapting to the relative lack of resources. I am convinced that by properly relying on our competitive advantage as Israelis and in BGU, and with help from funding agencies and donors, we will be able to be leaders in this field, and to reap its fruits in facilitating biotechnology development in NIBN. We should and can be equal competitors to Harvard by the improved utilization of resources we can secure for this purpose, most importantly the wonderful and unique human resources that Israel provides.



## From University of California, Irvine to NIBN, Beer-Sheva

*Dan Mishmar, Ph.D*

During my PhD studies at the Department of Genetics, Hebrew University, I was intrigued by mechanisms of genome instability, that underlie not only chromosomal breakage in cancer and several inherited disorders but also the formation of new chromosomal arrangements during speciation events in evolution. Studying variants that may either cause genetic disorders or drive the evolution of species led me to Prof. Douglas Wallace' laboratory in the University of California, Irvine, USA, the world's authority on human mitochondrial genetics and diseases who identified the first human mitochondrial DNA (mtDNA) mutation underlying mitochondrial inherited diseases. After almost four years of postdoctoral training, I shaped and focused my research on the role of mitochondrial genetic diversity in disease and evolution. Having visited all the major Universities in Israel, with offers of tenure-track positions at Bar-Ilan and at the Hebrew University, I chose to join the Department of Life Sciences and the NIBN at BGU. Now, after almost a year in BGU, I am grateful for the opportunity provided to me to establish my lab in outstanding conditions. Moreover, the recruitment of several new excellent scientists has created a supportive collegial environment leading to creativity and fruitful interactions.

One of my research subjects focuses on

the association of human mtDNA variation with type II diabetes mellitus (DM). Recently we have shown that linked sets of common mitochondrial DNA (mtDNA) variants (haplotypes, haplogroups) are subjected to positive selection, possibly driven by climate. Some of these variants were previously associated with age-related disorders (such as Parkinson and Alzheimer's diseases) and others with successful prolonged aging. Thus we hypothesized that common mtDNA variants affect mitochondrial energy metabolism and, in turn, alter the tendency to adapt to changing environmental conditions, yet also affect susceptibility to develop age-related disorders.

Several lines of evidence implicate the involvement of mitochondrial dysfunction and mitochondrial genetics in the mechanism underlying DM and its complications. By focusing on the association of mtDNA genetic variation with complications in type II DM, both epidemiological data and a careful medical assessment of the disorder in the affected subjects are fundamental. We believe that this research will shed light on the involvement of mtDNA common variants in aging and on the genetic inheritance of type II DM. Such information will assist in the design of preventive treatment of the population at risk against mitochondrial Reactive Oxygen Species



(ROS) production using antioxidants and vitamins.

The second line of research in my lab focuses on elucidating the structural and functional enigma of the first and largest protein complex of the mitochondrial oxidative phosphorylation, Complex I. Most inborn errors affecting oxidative phosphorylation function result in complex I dysfunction. Nevertheless, only meager information exists for complex I structure and function. Hence in this study, we set forth to analyze the function as well as possible tissue specificity of mitochondrial complex I subunit activity. Our study will shed light on the structure and function of complex I and on the mechanism by which it is involved in human mitochondrial disorders. Moreover our study might open a path towards understanding the molecular basis of tissue specificity in OXPHOS disorders. Such an investigation may assist in the design of therapeutic approaches for combatting this disease.

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## Fighting Human Diseases with Flies

*Uri Abdu, Ph.D*

After completing a PhD at the Department of Life Sciences at BGU and a post-doctoral training in developmental genetics in the Princeton University, I joined the Department of Life Sciences and the Unit of Genetics at NIBN. NIBN clearly provided me with an excellent starting point to perform my research in a competitive and effective manner, to build my scientific career and nurture the next generation of scientists. Moreover, NIBN recruited outstanding scientists from different disciplines which creates a unique stimulating scientific environment.

Model organisms provide an opportunity to examine the most highly conserved

aspects of a signaling pathway in normal development. Having impressive similarity to the human genome (60% homology in genes involved in human disorders), the fruit fly *Drosophila* has become a most popular model organism for studying human disease. Indeed, my research involves the use of *Drosophila* as a model system for studying human diseases including the leading causes of infertility and cancer. In my studies, I focus on defining the role of the DNA damage checkpoint proteins in mitotic cell division, a research directly related to cancer biology. This research is supported by the Israel Cancer Research Foundation (ICRF).

In a collaborative project with Dr. Ohad Birk, we are investigating the molecular mechanism underlying the polycystic ovary syndrome (PCOS), affecting 5-10% of women of fertile age and the leading cause



of female infertility. Utilizing the fruit fly allows investigating the function of specific candidate genes that we have found to be involved in the molecular basis PCOS. Understanding such functions will lead, in turn, to the development of therapeutic approaches targeting such genes.



## Genetics at NIBN

*Ohad Birk, MD, Ph.D*

The Genetics section of NIBN is focused on the identification and characterization of genes associated with human diseases.

The research is of importance in three venues:

- ▶ **Medicine:** provision of molecular diagnosis of hereditary human diseases, enabling carrier detection and prenatal diagnosis.
- ▶ **Science:** discovery of the molecular basis for human diseases, and of normal molecular developmental pathways.
- ▶ **Biotechnology:** discovery of novel drug targets for the treatment of those disorders. Such genes are of potential interest to big pharma companies as a basis for the design of novel drugs.

The studies are carried out through:

1. Linkage analysis of large inbred families, mostly of the Bedouin community of southern Israel.
2. Molecular analysis of chromosomal aberrations associated with specific human disorders.
3. Studies of mitochondrial function and mitochondrial molecular genetics associated with specific human disorders.
4. Microarray analysis of diseased vs normal tissues.
5. Functional genomic analysis (in-vitro and in-vivo) of disease-associated genes unraveled in 1-3 above.

Once disease-associated genes are identified, studies of these genes are carried out – from structural analysis of the encoded proteins and biochemical analyses, to cellular studies of mutated cells, to the generation and analysis of animal models of the diseases.

Some of our findings of the past year include:

1. A novel gene associated with seborrheic dermatitis and psoriasis.
2. A novel gene associated with symmetric growth retardation.
3. A novel gene associated with male infertility (azoospermia).
4. A novel gene associated with meconium ileus (congenital intestinal obstruction) - relevant to Cystic Fibrosis, and possibly to constipation.

## Last Year NIBN Achievements

- ▶ During one single year, NIBN scientists have published over 50 scientific articles in peer-reviewed journals including Science, Proceedings of the National Academic of Sciences and other high-impact publications.
- ▶ NIBN scientists have made headlines by their cutting edge scientific presentations and have been registered over 20 patents.
- ▶ Researchers at NIBN received in the last year about \$3 million in competitive research grants. In addition, a grant of \$3 million from DIP (Deutsche-Israelische Projektkooperation) for 5 years (to Dr. O. Medalia).
- ▶ One spin-off company was established (by A. Sagi, and A. Berman) and the establishment of the second is in progress (osteoporosis diagnosis, V. Shoshan-Barmatz).
- ▶ Two licensing agreements were established by Prof. Smadar Cohen, one with BiolineRx company: investment of \$9 million and the other one with an American company (option letter was signed in October 2005, finalization on December 2005).



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