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June 2011



The Authority for RESEARCH AND DEVELOPMENT

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# **The Barenholz Prizes** for Applied Research

June 2011

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The Authority for RESEARCH AND DEVELOPMENT

# BARENH(O)LZ



# **Yechezkel Barenholz**

Professor Yechezkel (Chezy) Barenholz, the Daniel G. Miller Professor Emeritus of Cancer Research, heads the Laboratory of Membrane and Liposome Research at the Department of Biochemistry and Molecular Biology at the Hebrew University Faculty of Medicine. All his undergraduate and graduate studies were at the Hebrew University, where he received his Ph.D. in Biochemistry in 1971. While working on his doctoral thesis, he studied at the Animal Research Council Institute at Babraham, Cambridge, England under the supervision of Dr. R.M.C. Dawson and Dr. A.D. Bangham, pioneers in lipid biophysics; Dr. Bangham is considered the "father" of liposomes.

Professor Barenholz has been a faculty member of the Hebrew University since 1971, and a Professor since 1981. He was also on the faculty of the University of Virginia in Charlottesville since 1973, and was a Visiting Professor there (1982-2006). He was a Visiting Professor and taught at the University of Utrecht in the Netherlands as a Donders Chair Professor (1991), at Kyoto University, Japan (1998), at La Sapienza University, Rome (2006), at Shanghai Jiaotong University, Shanghai (2006), at Kings College, University of London (2006) and at the Danish Technical University (DTU) in Copenhagen on 2010.

Professor Barenholz has pursued both basic and applied research. In basic research, he is studying in the biochemistry and biophysics of lipids and membranes, including synthesis, chemical and physical characterization, and the relationship between membrane lipid composition, structure, and function with special focus on sphingolipids

and aging processes. In applied research, his main interests are amphiphile-based drug carriers, especially liposomes - from basic aspects of design of the drug carrier, through animal studies, to clinical trials, and FDA approval - as exemplified by the development of Doxil<sup>TM</sup>, the first liposomal drug and nanomedicine that was approved by the FDA. Doxil, a doxorubicin remote-loaded stericallystabilized liposome, is used for treatment of cancer (sold in Europe as Caelyx<sup>TM</sup>). Doxil was developed as a collaborative effort of Professor Barenholz and Professor Alberto Gabizon and their teams, and of Liposome Technology Inc., Menlo Park, CA (later renamed Sequus Pharmaceuticals Inc., and now part of Johnson & Johnson). Professor Barenholz is now developing other anti-tumor therapies including those based on Doxil combined with other agents that induce programmed tumor cell death (apoptosis), or combined with immunotherapy (liposomal cytokines, especially interleukin-2) as well as two anticancer drug combination in one liposome. The successful preclinical studies in these studies suggest that such combination therapies may be highly beneficial for cancer patients.

Professor Barenholz also studies the applications of liposomes for vaccination against infectious diseases (including influenza, avian influenza, hepatitis B, hepatitis A, and anthrax) and cancer, which led to creation of the vaccine development company NasVax Ltd. His other research activities include the treatment of diseases with an inflammatory component (such as rheumatic arthritis and multiple sclerosis), antioxidant therapy, control of local pain, gene therapy, and the development of a liposomes based medical device for the treatment of osteoarthritis.

Professor Barenholz is the author of over 350 publications, and the editor of three special issues of Chemistry and Physics of Lipids, on "Quality Control of Liposomes" and "Sphingomyelin: Chemistry, Biophysics, Metabolism, Genetics, and Signaling" (together with Prof. S. Gatt), and the 2011 conference special issue, together with Dan Peer. Together with Dan Lasic, Professor Barenholz edited the four-volume Handbook of Nonmedical Applications of Liposomes, CRC Press (1996). For more than ten years, he was one of the Executive Editors of Progress in

Lipid Research; currently he is on the editorial boards of Chemistry and Physics of Lipids, Journal of Liposome Research, Cellular & Molecular Biology Letters, and International Journal of Oncology. Professor Barenholz is a co-inventor of over 30 worldwide approved patent families, two of which serve as a major part of Doxil patent protection. Professor Barenholz was awarded a number of prestigious prizes for his contributions to the medical application of liposomes and to liposome science and technology, including: appointment as the Donders Chair Professor, a special award for his excellent contribution to the field of liposome science at the University of Utrecht (1991); the Kaye Award for Innovation for "A novel approach to obtain efficient and stable remote drug loading of liposomes for clinical use" (1995); the Kaye Award for "The development of liposomal doxorubicin (Doxil) for cancer treatment: from basic research to FDA approval" (1997); the Alec D. Bangham Achievement Award for "Life-long achievements resulting in fundamental and sustained impact on the advancement of liposome science and technology" (1998); and the TEVA Founder Prize for "Major contributions to medical biotechnology" (2000). In 2003, Professor Barenholz established (from Doxil royalties) The Barenholz Prizes for Applied Research to encourage doctoral students to pursue excellence and innovation in applied research for the benefit of the Hebrew University, Israel, and all mankind.

Professor Barenholz is married to Dr. Hanna Barenholz and is the proud father of four daughters and has twelve grandchildren. Professor Barenholz may be reached at yb@cc.huji.ac.il.

# THE BARENHOLZ PRIZES FOR APPLIED RESEARCH



Shaul Lapidot The Robert H. Smith Institute of Plant Sciences and Genetics in Agriculture The Robert H. Smith Faculty of Agriculture, Food and Environment The Hebrew University of Jerusalem Supervisor: Prof. Oded Shoseyov Barenholz Prize Category: Applied Chemistry, Material Sciences and Nanotechnology



Supervisor: Prof. Lazar Friedland Barenholz Prize Category: Applied Physics, Medical Devices and Applied Computer Sciences



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**Cellulose-based Composite Materials** from Renewable Resources

### **Shaul Lapidot**



**BARENHOLZ PRIZE CATEGORY: APPLIED CHEMISTRY, MATERIAL SCIENCES** AND NANOTECHNOLOGY



### PhD student of Prof. Oded Shoseyov The Robert H. Smith Institute of Plant Sciences and Genetics in Agriculture

Shaul Lapidot was born in Israel in 1972 and raised on Kibbutz Tzora where he still resides with his wife, two sons and one daughter (ages 8, 5 and three months). After six years of army service, he thought he would become a wine maker but turned to biotechnology after Prof. Oded Shoseyov opened the magic door of science to him. He recently submitted his Ph.D. thesis on nano structured composite biomaterials under Prof. Shoseyov's supervision. Shaul received the Hebrew Universitv's Kave Innovation Award in 2009. His hobbies are wine, cooking, travelling and mountain biking.

In this invention, methods have been developed for production of Nano Crystalline Cellulose (NCC) from paper mill waste. NCC is further processed into composite foams for applications in the composite materials industry as bio-based replacement for synthetic foams.

The process of paper production involves loss of all fibers with dimensions lower than the forming fabric mesh. Consequently around 50% of the total fibers initially produced are washed as sludge. In Europe alone, eleven million tons of wastes are produced annually by this industry, making it necessary to find alternative uses and different applications for the wastes. We have found that fibers from paper mill sludge are a perfect source for NCC production due to their small dimensions which require relatively low energy and chemical input in order to process them into NCC. We have also developed the application of NCC into nano structured foams.

Foams are used for numerous day-to-day applications, including furniture, car interiors, etc. In the field of composite material they are used as core materials in sandwich panels to achieve high strength, weight reduction, energy dissipation, and insulation. Conventional foams are produced from polymers such as polyurethane, polystyrene PVC, and PET. Since all current foams rely on fossil oil, they present a clear environmental disadvantage.

NCC foams that we have recently developed are highly porous and lightweight. Additional strengthening of the foams was enabled by infiltration of furan resin, a hemicellulose based resin produced from raw crop waste (e.g., sugar cane bagasse, oat hulls, corn cobs and rice hulls). The new NCC reinforced foams display technical performance which matches current high end synthetic foams. The technology was recently licensed from Yissum by Melodea, Ltd., a start-up company which aims to develop it to industrial scale production.

#### Cellulose fibers contain amorphous and crystalline areas



### Production of cellulose nano-particles (whiskers) from the fibers



**Autoresonant Four-Wave Mixing** in Optical Fibers

### **Oded Yaakobi**



PhD student of Prof. Lazar Friedland Racah Institute of Physics Faculty of Science

Oded received his B.Sc. in Physics and Mathematics (in the prestigious Talpiot program) from the Hebrew University (1999). He completed his M.Sc. at Tel Aviv University (2005) under the supervision of Profs. Zilman and Miloh while serving as a Research Officer in the Navy. While studying for his Ph.D., Oded worked as a researcher in Dr. Henis's group at the Soreg Research Center, and collaborated with the research groups of Prof. Wurtele and Prof. Siddigi from University of California at Berkeley. In his doctoral research, Oded studied theoretical aspects of resonant wave interactions. Oded is the first author of eight peerreviewed publications. His scientific achievements were acknowledged by national and international organizations (e.g. APS, ICPSA), reflected by the prizes, scholarships and grants he has received.

### **BARENHOLZ PRIZE CATEGORY: APPLIED PHYSICS,** MEDICAL DEVICES AND APPLIED **COMPUTER SCIENCES**

One of the most important nonlinear processes in optical fibers is four-wave mixing. A four-wave mixing involves the interaction between four waves in which the sum of the frequencies of two waves is equal to the sum of the frequencies of the other two waves. The process of four-wave mixing is used for amplification of weak signals in devices called Optical Parametric Amplifiers (OPA). In OPA one or two strong pumps are injected in parallel to a weak signal wave. During the resonant interaction, energy is transferred from the pumps to the signal and a fourth idler wave is excited. However, in usual uniform OPAs there is a compromise between the spectral width of the amplification and the amplification efficiency at each given frequency.

Autoresonance is a fascinating nonlinear effect enabling the control of systems with varying space-time properties without any feedback. Recently, we considered the process of autoresonant four-wave mixing in optical fibers for the first time. We proposed a novel OPA scheme by using tapered fiber in which the radius of the fiber varies longitudinally. Our results indicate a possibility of an efficient autoresonant OPA in a wide spectral range with significant advantages compared to usual uniform OPAs. For instance, in the proposed tapered fiber scheme, the amplification is larger than in a usual uniform fiber for most frequencies. In addition, the amplification profile in the tapered fiber is flat, whereas in the uniform fiber the efficiency depends strongly on the signal frequency (wavelength).



$$\frac{dA_l}{dz} = i\gamma \left( |A_l|^2 A_l + 2\sum_{j\neq l=1}^4 |A_j|^2 A_l + 2A_m A_n A_k^* e^{i\varepsilon\Psi} \right)$$



Due to its broad band and flat amplification spectrum, the proposed OPA is expected to enable many new applications in the fields of high power lasers and telecommunication. For instance, potential applications are signal amplification, frequency conversion and pulse regeneration and reshaping (noise removing). By choosing the OPA parameters appropriately, it may be possible to achieve an amplification spectrum that has either single narrow line or two narrow lines that are separated by a wide bandwidth. One of the uses of this kind of a spectrum is coherent Raman microscopy.



# BARENHOLZ PRIZES

# THE BARENHOLZ PRIZES FOR APPLIED RESEARCH

### תש״ע Barenholz Prizes 2010

MS. CLARITE AZERRAF PhD student of Prof. Dmitri Gelman, Institute of Chemistry, The Hebrew University of Jerusalem Barenholz Prize Category: Drug Delivery Systems

MR. EHUD SEGAL PhD student of Dr. Ronit Satchi-Fainaro, PhD, Sackler Faculty of Medicine, Tel Aviv University Barenholz Prize Category: Development of Drugs and Carrier-Based Drugs

### תשס״ע Barenholz Prizes 2009

MS. INBAR FREEMAN PhD student of Prof. Smadar Cohen, Ben-Gurion University of the Negev Barenholz Prize Category: Drug Delivery Systems

MS. NAAMA GEVA-ZATORSKY PhD student of Prof. Uri Alon, Weizmann Institute of Science Barenholz Prize Category: Proteomics, Genomics, Lipids and Metabolomics

MR. OMRI ALLOUCHE PhD student in the laboratory of Prof. Ronen Kadmon, Faculty of Science, The Hebrew University of Jerusalem Barenholz Prize Category: Agriculture and Environmental Sciences and Medical Devices

### תשס״ח Barenholz Prizes 2008

MR. AVI SCHROEDER PhD student of Prof. Yechezkel Barenholz Laboratory of Membrane and Liposome Research, Department of Biochemistry, Faculty of Medicine The Hebrew University of Jerusalem; and Prof. Joseph Kost, Department of Chemical Engineering Faculty of Engineering Sciences, Ben-Gurion University of the Negev Barenholz Prize for Drug Delivery Systems

MS. NAAMA ELEFANT MD-PhD student of Prof. Hanah Margalit Department of Molecular Genetics and Biotechnology, Faculty of Medicine, The Hebrew University of Jerusalem Barenholz Prize for Applied Computer Sciences and Computational Biology

MR. LAVI SHPIGELMAN AND MR. HAGAI LAZAR PhD students of Prof. Eilon Vaadia The Interdisciplinary Center for Neural Computation and Department of Physiology Faculty of Medicine, The Hebrew University of Jerusalem Barenholz Prize for Applied Physics and Medical Devices

### תשס״ז Barenholz Prizes 2007

MR. DANNY GOLDSTEIN PhD of Prof. Simon Benita, School of Pharmacy, Faculty of Medicine Barenholz Prizes in Drug Delivery Systems

MR. IDO BACHELET PhD student of Prof. Francesca Levi-Schaffer, School of Pharmacy, Faculty of Medicine Barenholz Prizes for Novel Drug Design

MR. ASSAF AHARONI PhD student of Prof. Uri Banin Institute of Chemistry and the Center for Nanoscience and Nanotechnology, Faculty of Science Barenholz Prizes in Nanotechnology

## תשס״ו Barenholz Prizes 2006

MS. HILA EPSTEIN-BARASH PhD student of Prof. Gershon Golomb, School of Pharmacy, Faculty of Medicine Barenholz Prizes in Drug Delivery Systems

MR. BENNY GIL PhD student of Prof. Ehud Shapiro Department of Biological Chemistry, The Weizmann Institute of Science Barenholz Prizes in Drug Delivery Systems

MR. TOMMY KAPLAN PhD student of Prof. Nir Friedman and Prof. Hanah Margalit School of Engineering and Computer Science and Faculty of Medicine Barenholz Prizes in Proteomics, Genomics and Metabolism

### תשס״ה Barenholz Prizes 2005

MS. TALI ARNON PhD student of Dr. Ofer Mandelboim, Lautenberg Center for Immunology, Faculty of Medicine Barenholz Prizes in Drug Delivery Systems

MR. ALEX RAV-ACHA PhD student of Prof. Shmuel Peleg, School of Engineering and Computer Science Barenholz Prizes in Computer Sciences

MR. ELI ROTHENBERG PhD student of Prof. Uri Banin Department of Physical Chemistry and Center for Nanoscience and Nanotechnology Barenholz Prizes in Applied Physics

### תשס״ד Barenholz Prizes 2004

MS. AVIVA JOSEF PhD student of Prof. Eli Kedar, Lautenberg Center for Immunology, Faculty of Medicine Barenholz Prizes in Drug Delivery Systems

MR. GABRIEL KERNER PhD student of Prof. Micha Asscher, Institute of Chemistry, Faculty of Science Barenholz Prizes in Computer Science

MR. YANIV BLEDI PhD student of Prof. Michal Linial, Institute of Life Sciences, Faculty of Science Barenholz Prizes in Applied Physics

### תשס״ג Barenholz Prizes 2003

MR. ILAN LEVY PhD student of Prof. Oded Shoseyov Faculty of Agricultural, Food and Environmental Quality Sciences Barenholz Prizes in the Field of the Improvement and Conservation of the Environment

MS. ZEHAVA YEHUDA PhD student of Prof. Yitzhak Hadar and Prof. Yona Chen Faculty of Agricultural, Food and Environmental Quality Sciences Barenholz Prizes in the Field of Agriculture

MR. SHLOMO NEDVETZKI PhD student of Prof. David Naor, Faculty of Medicine Barenholz Prizes in the Field of Proteomics



- 2010 תש״ע
- 2009 תשס״ט
- 2008 תשס״ח
- ז"ס 2007 משס
- 2006 תשס״ו
- 2005 תשס״ה
- 2004 תשס״ד
- 2003 תשס״ה