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Keynote Forum





Eugene P. Goldberg

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Microporous biopolymer-microglial cell and implants for spinal cord/CNS repair

There is no clinically effective therapy for repair of spinal cord trauma and other injuries to CNS tissues. More than 250,000 people are affected with 10,000 new injuries annually in the U.S. About 50% are paraplegic or quadriplegic. Annual health care costs exceed \$10 billion. Tissue engineering concepts using various cells, polymer scaffolds, and neural tissue growth factors have been problematic for clinical use. Reported here are results for a study encompassing synthesis, characterization, and in vivo evaluation (including high field NMR) of porous biopolymer-neuroregenerative cell implants. Composite compositions containing microglial cells (MGC) in microporous alginate (ALG), and hyaluronic acid (HA), matrices were prepared and some surface modified with a unique radiation grafted phospholipid nanosurface [Figs. A&B]. Because microglia are natural CNS repair cells, the strategy employed in this research was to develop cell-biopolymer structures designed to facilitate the complex sequencing of biosynthesis and regulation of natural neurotrophic factors at the site of injury; thereby enabling the CNS repair processes and regrowth of neural networks. Using a rat spinal cord injury model, effective wound healing and neural regeneration was demonstrated without cystic cavitation. [see EP Goldberg, WJ Streit, JB Stopek patent publication 60/325,190; PCTUS02]

Biography

Goldberg, FAIMBE, FBSE joined the faculty of the University of Florida in 1975 as the Biomedical Program of Excellence Professor in the Department of Materials Science & Engineering and is now the Genzyme Endowment Professor with adjunct affiliations in the Departments of Chemistry, Pharmacology & Therapeutics, and Biomedical Engineering. He was instrumental in establishing intramural graduate programs in Polymer and Biomedical Sciences. He is now also affiliated with the University's Cancer Center. His biomedical research interests and activities for the past 35 years have been diverse with strong focus on Tissue Engineering and Targeted Lung Cancer Therapy. Tissue Engineering has been primarily devoted to new cell-biopolymer compositions for CNS repair based on matrices (porous implants and injectable gels) derived from alginates and hyaluronic acid incorporating viable brain-derived microglial and stem cells. Dr. Goldberg is the senior author of more than 450 published and presented papers and is on the editorial boards of numerous journals.

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Mahin Khatami

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Chronic diseases and cancer: Stem cells and unresolved inflammation; A wake up call for healthy aging

Despite heavy public investment for over four decades on war against cancer, progress in understanding the complex biology of cancer is fragmentary and dismal. Consequently, few projects have been successful in translating research into effective diagnosis, prevention and therapy while incidence of cancer is projected to rise in the next decade around the globe, particularly for the growing older population. Numerous costly clinical trials and technologies are based on shut-gun findings of molecular entities from hundreds and thousands of molecules (e.g., altered gene, proteins/receptors, enzymes, lipids, cytokines/chemokines, metabolites, or regulatory cell components) and are claimed as 'targeted' therapies without any tangible benefit for the cancer-stricken public. These toxic drugs produce life-threatening side-effects such as cancer cachexia, sarcopenia, thromboembolism, drug-resistance, cancer relapse and multiple organ failure. There is a growing need to properly integrate and connect important available data and identify essential knowledge gaps in order to form a clear vision on cancer biology that would facilitate informed decision making on design of effective drug development. In this presentation, attempts were made to overview the fundamental roles that unresolved inflammation play in altering the dynamics of immune cell responses and increased risks of many chronic diseases and/or cancer. It is suggested that inflammation-induced alterations in integrity and function of cells diversely impact immune-responsive and immune-privileged tissues that would lead to a wide range of age-associated illnesses. The results of our accidental discoveries in 1980's on experimental models of acute and chronic (unresolved) inflammatory diseases are suggestive of the first evidence for a direct link between inflammation and tumorigenesis. Data analyses led to a first report on inflammation-induced developmental phases of immune dysfunction and tumor growth and angiogenesis. Unresolved inflammation was defined as the loss of balance between 2 biologically opposing arms of acute inflammation termed 'Yin' ('tumoricidal') and 'Yang' ('tumorigenic') or apoptosis and wound healing properties of immune system. It is suggested that proper function of stem cells (giant manufacturers of innate and adaptive immune cells) is a key for maintenance of immune/tumor surveillance, body's resistance toward oxidative stress and for delaying the on-set of chronic diseases. Framework for design of clinical trials and therapeutic approaches will be discussed based on the concept that inflammation is a common denominator in the genesis and progression of many chronic illnesses or cancer.

Biography

Mahin Khatami was born in Tehran-Iran. She immigrated to USA in 1969 after training in Chemistry (BS) and Science Education (MS). She received her MA in Biochemistry from SUNY at Buffalo (1977) and PhD in Molecular Biology from the University of Pennsylvania (UPA, 1980). Her postdoctoral trainings were in physiology at the University of Virginia, protein chemistry (proteomics) at the Fox Chase Cancer Institute and UPA. She was a Faculty of Medicine at the Department of Ophthalmology, Scheie Eye Institute, UPA, until 1992. In collaboration with a team of scientists, under the direction of John H. Rockey, MD, PhD, at UPA, she quickly earned her supervisory responsibilities on two major projects; cell and molecular biology of diabetic retinopathy/maculopathy and experimental models of acute and chronic ocular inflammatory diseases. In her junior academic career, Dr. Khatami is considered the most productive scientist in USA as she published 39 scientific articles and over 60 abstracts in conference proceedings in the first decade of her research. In 1998, at the National Cancer Institute (NCI), the National Institutes of Health (NIH), she was a Program Director and health scientist administrator, involved in developing molecular concepts for utilization of patient biospecimen for large clinical trials such as Prostate-Lung-Colorectal Ovarian (PLCO) Cancer Screening Trials.

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David T Harris

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Younger is better: Old stem cells aren't what they used to be

The idea of stem cells as medical therapy has become almost commonplace. Millions of individuals have stored stem cells in biobanks for future use, and tens of thousands of have received stem cell transplants or infusions for regenerative medicine therapies. But often overlooked are everyday factors that may impair the utility of these stem cells, including stem cell age and donor health. There is increasing evidence that both factors can significantly impact the therapeutic potential of stem cells.

The hematopoietic stem cell is the best characterized of all stem cells. Weissman and others have shown significant functional changes with age, a finding confirmed upon analysis of cord blood transplant recipients. Similar findings have also been observed with neural stem cells. In terms of regenerative medicine, many are looking at mesenchymal stem cells (MSC). Numerous studies have indicated that MSCs isolated from older donors, as well as from patients with chronic disease conditions, are neither as prevalent (in terms of the number of cells in the sample) nor as potent as those isolated from younger, healthier donors. MSCs collected from older donors seem less able to differentiate into the different cell types needed for tissue engineering, slower to proliferate and expand to numbers of cells that would allow for multiple treatments, and more prone to dying during culture and use.

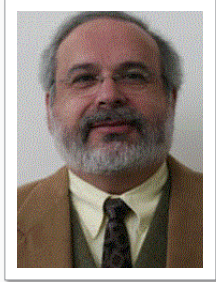
Evidence that MSC quality declines with donor age warrants concern for cell based therapies. The ability of older stem cells to respond to injury may be compromised and could contribute to inferior tissue repair. We have observed such results when analyzing the effects of stem cell age in a chronic wound model. In addition, Shen et al at the University of Texas-Arlington found that aging female mice transplanted with young MSCs had prolonged life span (by 15-20%). In contrast, older MSCs failed to prolong life span at all.

Thus, it seems that stem cells, like the rest of the cells in our bodies, also suffer from the ravages of time. Stem cells (of various types) collected from younger, healthier donors are more effective for transplantation and regenerative medicine than those collected from older individuals, which makes a strong case for the preservation of stem cells at the earliest possible time, and for the consideration of donor age when transplanting stem cells.

Biography

Harris is a graduate of Wake Forest University in Winston-Salem, North Carolina where he obtained Bachelor of Science degrees (cum laude) in Biology, Mathematics and Psychology in 1978. He earned a Masters of Medical Sciences (summa cum laude) from Bowman Gray Medical School in 1980 and his Doctorate in Microbiology and Immunology (magna cum laude) from Bowman Gray Medical School in 1982. From 1982-1985 Dr. Harris was a Post-doctorate Fellow at the Ludwig Institute for Cancer Research in Lausanne, Switzerland. In 1985 he joined the faculty at the University of North Carolina-Chapel Hill as a Research Assistant Professor in the Department of Medicine. In 1989 Dr. Harris joined the faculty at the University of Arizona in Tucson as an Associate Professor in the Department of Microbiology & Immunology. In 1996 Dr. Harris was promoted to Professor of Immunology. Dr. Harris established the first cord blood bank in the USA in 1992. He currently serves as Director of the Cord Blood Stem Cell Bank, is a member of the Arizona Cancer Center, a member of the Children's Research Center, and a member of the Arizona Arthritis Center. Dr. Harris's research interests include stem cells and regenerative medicine, cancer research/stem cell transplantation and gene therapy. He has published more than 300 articles (papers, book chapters and abstracts), given more than 100 talks on stem cells over the past 7 years, and has served as a consultant to the governments of China, Hong Kong, Singapore and South Korea. Dr. Harris has also founded 4 companies while at the University of Arizona; Cord Blood Registry, Inc.; Immune Regen Bio Sciences, Inc.; QuReGen, Inc. and AdiCyte.

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Gene P. Siegal

University of Alabama at Birmingham, USA

Observational biology and its use in developing a common sense approach to the diagnosing of tumor and tumor-like conditions of bone

Many advances in unraveling mechanisms of disease have begun with observational biology. This has been codified in the 'Bedside to Bench to Bedside' paradigm. Pathologists have for centuries taken the lead in this series of endeavors. However, even experienced pathologists are sometimes intimidated by bone biopsies. Histological similarities between reactive lesions and neoplastic processes can cause concern that a bone tumor has been overlooked or fears of under-diagnosis when tumors are present. A common sense approach to the diagnosis of bone diseases using clinical history with correlative appropriate imaging data can help minimize these concerns. In this presentation I intend on surveying interesting diagnostic problems in orthopedic pathology from patients ranging from very young to very old age. Its objectives are to enable participants to construct logical frameworks for categorizing various bone disorders and to be more comfortable in the differential diagnosis of orthopedic diseases. I will begin with a brief introduction to orient participants to the philosophy of diagnosis in skeletal pathology and how best to put the gamut of possible diagnoses into a logical framework based upon age at presentation, clinical history, imaging parameters and histology. This will be followed by use of the case presentation format to challenge audience members to apply the proposed tools to stratify lesions into their most common diagnostic categories..

Biography

Gene P. Siegal is the Robert W. Mowry Endowed Professor of Pathology and Director of the Division of Anatomic Pathology at the University of Alabama at Birmingham. He also serves as Senior Scientist in the UAB Comprehensive Cancer Center & the Center for Metabolic Bone Disease. Professor Siegal is an experimental and diagnostic musculoskeletal pathologist whose research interest for more than three decades has been focused in Cancer Biology. With in excess of 600 peer-reviewed manuscripts and other professional writings, it's no surprise that Dr. Siegal serves on 19 editorial boards, is the current Editor-in-Chief of Laboratory Investigation and has recently been appointed the Executive Editor of the Journal of Cytology & Histology.

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