

Indiana University Cancer Center Newsletter

June 1999

Special points of interest:

- *In the Spotlight*-Randy Brutkiewicz, Ph.D.
- BBF announces Recombinant Protein Purification
- Larry Einhorn, M.D. elected President of ASCO
- ASCO Review and Interpretation 1999
- Seminars/ Meetings/ Conference Schedule

In the spotlight.....

Randy Brutkiewicz, Ph.D.

I am an Assistant Professor in the Department of Microbiology and Immunology as well as an Assistant Member of the Walther Oncology Center. I came to Indiana University by way of the NIH in July of last year. My dissertation research was performed in the laboratory of Dr. Ray Welsh at the University of Massachusetts Medical School in Worcester, studying the role of major histocompatibility complex (MHC) class I molecules in the regulation of virus infections by natural killer (NK) cells. I then went to the NIH for postdoctoral training with Jon Yewdell and Jack Bennink, where I initiated my studies on CD1 molecules. Understanding their function is the major focus of my research efforts here. CD1 molecules are cell surface glycoproteins found mostly on hematopoietic cells (e.g., B cells, macrophages, dendritic cells). Although structurally similar, CD1 and MHC class I molecules only share about 20% homology at the amino acid level. When we began our CD1 studies, much more was known about MHC class I molecules than CD1 molecules. We therefore decided to compare several well-known characteristics of MHC class I molecules in order to determine if CD1 is similar or different. What we found was that CD1 is mostly different. We already knew that MHC class I molecules are very polymorphic, and as such, a wide variety of peptides can bind to them and are then presented to the immune system (i.e., cytotoxic T cells). In contrast, CD1 molecules are relatively nonpolymorphic; that is, individuals within a given species have identical CD1 genes. So, if CD1 molecules are recognized by T cells, it would make sense that an invariant T cell would "see" CD1 as its ligand. In collaboration with Albert Bendelac (at the time still at the NIH), we found that such an invariant subpopulation of T cells (NK T cells), does indeed recognize CD1. Because we had found that CD1 molecules do not require the peptide transport machinery that MHC class I molecules need for cell surface expression and T cell recognition, we were very interested in what was naturally bound to CD1. Was it a peptide? Something else? We already had some information about CD1 molecules that gave us some clues as to the characteristics of a putative natural ligand. Others had shown that certain human CD1 molecules (we work with mouse CD1) can bind and present glycolipids derived from cell walls of *Mycobacterium spp.* In collaboration with Sebastian Joyce (Penn State University), Bob Cotter and Amina Woods (Johns Hopkins University), we found that a major natural ligand of mouse CD1 was a cellular glycolipid—glycosylphosphatidylinositol (GPI). We are continuing these studies in order to have a better understanding of glycolipid antigen presentation by CD1. In our work, we are studying how CD1 molecules traffic within the cell. This will aid in our search for

the cellular compartment(s) within which CD1's ligand becomes bound. Additionally, through the use of CD1 knockout mice, we are investigating the role of CD1 molecules in the host's natural resistance to tumors and infectious diseases. Of interest is that CD1-specific NK T cells are responsible for the antitumor effects observed in mice treated with interleukin 12. Because CD1 is expressed on a wide variety of lymphomas and leukemias, we are also very interested in its cell biology and biochemistry in these tumor cells, as well as the ability of NK T cells to recognize CD1 on these cells. The CD1 and NK T cell field is wide-open, with a number of fundamental questions yet to be answered. For example, what exactly do NK T cells "see" bound to CD1? Is it GPI or something else? What defects in host defense occur in an animal without CD1? Answers to these and other questions will greatly enhance our understanding of CD1 and NK T cells, as well as help in the design of novel intervention strategies in cancer and infectious diseases using the CD1/NK T cell system as a target.

Biochemistry Biotechnology Facility Announces Recombinant Protein Purification

The Biochemistry Biotechnology Facility has begun to establish a new service for recombinant protein purification. During the past month we have been diligently training a technician for this service and have successfully completed several purifications. We are very interested in assessing the level of interest on this campus for such a service. Appropriate uses of this service would be 1) to support, or to start, new X-ray crystallography projects; 2) to support ongoing structural projects involving mass spectrometry or BIAcore technology; 3) to provide stocks of commonly used recombinant proteins in various laboratories; 4) to provide larger scale purifications for those who are not equipped or do not desire to do so. This service will be provided for repetitive purifications using established vectors only. It will not be a service for testing expression from new constructs. In the near future we will be posting guidelines for this service on our Web site (<http://www.bbf.iu.edu/>). Each project will be performed on a contractual basis and will be billed to cover the cost of reagents and technician's time contingent upon satisfactory results. Before starting any purification projects we will ask to meet with investigators to discuss their needs and their expression and purification systems. We believe that this will be a successful and valuable service. If you may be interested in using this service please respond to this notice or set up an appointment with us (274-6647) to discuss possible projects.

~John Hawes, Director BBF

Einhorn elected President of ASCO

Dr. Lawrence Einhorn, Distinguished Professor of Medicine, has been elected President of the American Society of Clinical Oncology (ASCO) beginning in May 2000. He will serve as president-elect beginning this May.

ASCO is a professional association representing clinical oncologists who specialize in the treatment of patients with cancer and in clinical research.

Dr. Einhorn has been a member of ASCO since 1974. He served on the board of directors from 1981 to 1984 and was an associate editor for the *Journal of Clinical Oncology*, the official ASCO journal, from 1988 to 1996.

Congratulations Dr. Einhorn!

ASCO Review and Interpretation 1999

The Review and Interpretation of the 1999 American Society of Clinical Oncology (ASCO) Meeting will take place June 21, 1999, from 8:00 a.m. to 5:00 p.m. at the University Conference Center and Hotel.

Experienced faculty members from the section of Hematology/Oncology went to the 1999 ASCO meeting where they attended and analyzed some of the more important papers presented. Thus, the purpose of the course is to analyze, interpret, and discuss these major presentations. In addition, two guest faculty will be presenting their data and viewpoints:

Steven D. Passik, Ph.D., will discuss the issues of pain control and psycho-oncology, and Howard I. Scher, M.D., from Memorial Sloan-Kettering, will discuss genitourinary malignancies.

For more information and/or registrations forms contact the Indiana University School of Medicine, Division of Medical Education at 274-8353.

Seminars/Conferences/Meetings

Wednesday, June

7:00 a.m. Skull Base Group Conference. *UH 2005*.

8:00 a.m. **“What it Takes to Have a Shapely Dose Distribution.”** Lech Papiez, Ph.D., Assistant Professor, Radiotherapy Physics, Dept. of Radiation Oncology, IUSM. *UH 0633*.

12:30 p.m. Radiation/Gynecologic Oncology Conference Case Presentation/Didactic.

4:00 p.m. **NO COMBINED SEMINAR SERIES LECTURE**

4:30 p.m. Rad/Onc Resident Conference. **“Heterotopic Bone.”** Dr. Joseph Montebello, Rad Onc. *Library Radiation Oncology*.

Thursday, June 3

2:30 p.m. **“Tyrosine Phosphorylation in Androgen Refractory Human Prostate Cancer”.** Ming-Fong Lin, Ph.D., Associate Professor, University of Nebraska Medical Center. *Cancer Research Institute Auditorium 101*.

4:00 p.m. **“Telomeres and Hematopoiesis.”** Lucio Luzzatto, M.D., Dept. of Human Genetics, Memorial Sloan Kettering Cancer Center. *Medical Science 326*.

Monday, June 7

4:30 p.m. Hematology Fellows Lecture. **“Antiemetics”.** Fellow. *RT 425*.

4:30 p.m. Rad/Onc Resident Conference. **“Desmoid Tumors.”** Dr. Joseph Montebello, IUSM. *Radiation Oncology Library*.

Wednesday, June 9

12:30 p.m. Radiation/Gynecologic Oncology Conference Case Presentation/Didactic. **“Radiation Therapy Complications in GYN Cancers.”** Dr. Shailaja Reddy, Radiation Oncology *RT 425*.

4:00 p.m. **“ABC Transporters: What are they and what do they do?”** Victor Ling, Ph.D., British Columbia Cancer Research Center, Vancouver, British Columbia. *Cancer Research Institute Auditorium 101*.

4:30 p.m. Rad/Onc Resident Conference. **“Keloids.”** Dr. Joseph Montebello, IUSM. *Radiation Oncology Library*.

Thursday, June 10

4:00 p.m. **“Biological Therapy of Cancer: Direct and Indirect Approaches.”** Douglas Williams, Ph.D., Vice President for Research, Immunex Corp., Seattle, WA. *Medical Science 326*.

Monday, June 14

4:30 p.m. Hematology Fellows Lecture. **“Special Lecture”** Dr. Alan Sandler, IUSM. *RT 425*.

4:30 p.m. Rad/Onc Resident Conference. **“Pterygium.”** Dr. Joseph Montebello, Dept. of Radiation Oncology. *Radiation Oncology Library*.

Tuesday, June 15

12:00 p.m. Experimental Therapeutics Research Program Meeting. **“TBA.”** *Cancer Research Auditorium 101A*.

Wednesday, June 16

12:30 p.m. Radiation/Gynecologic Oncology Conference Case Presentation/Discussion. *RT 425*.

4:00 p.m. **NO COMBINED SEMINAR SERIES**

4:30 p.m. Rad/Onc Resident Conference. **“Midline Granuloma.”** Dr. Joseph Montebello, Dept. of Radiation Oncology. *Radiation Oncology Library*.

Monday, June 21

8:00 a.m. **“Review and Interpretation of the 1999 ASCO Meeting.”** University Conference Center and Hotel.

4:30 p.m. Hematology Fellows Lecture. **“Special Lecture.”** Dr. Alan Sandler, IUSM. *RT 425*.

4:30 p.m. Rad/Onc Resident Conference. **“Peyronie’s Disease.”** Dr. Joseph Montebello, Dept. of Radiation Oncology. *Radiation Oncology Library*.

Wednesday, June 23

12:30 p.m. Radiation/gynecologic Conference Case Presentation/Didactic. Jean Hurteau, M.D. *RT 425*.

4:00 p.m. **“Oxidative Stress, Protection, and Imaging of Free Radicals”.** Dr. James Mitchell, Radiation Biology, National Institutes of Health. *Cancer Research Institute Auditorium 101*.

Monday, June 28

4:30 p.m. Hematology Fellows Lecture. **NO LECTURE.**

4:30 p.m. Rad/Onc Resident Conference. **“Unknown Primary.”** Dr. Joseph Montebello, Dept. of Radiation Oncology. *Radiation Oncology Library*.

Wednesday, June 30

12:30 p.m. Radiation/gynecologic Conference Case Presentation/Didactic. **“Role of Radiation Therapy in the Treatment of Non-epithelial Ovarian Cancers.** Dr. Ethel Dijamco, M.D., Dept. of Radiation Oncology. *RT 425*.

4:00 p.m. **“Chromatin, Corepressors, and Cancer”.** Dr. Alan Wolffe, Chief, Laboratory of

Molecular Embryology and Chief, Section of Molecular Biology, National Institute of Child Health and Human Development, National Institutes of Health. *Cancer Research Institute Auditorium 101.*

4:30 p.m. Rad/Onc Resident Conference. **“Skin Cancer.”** Dr. Joseph Montebello, Dept. of Radiation Oncology. *Radiation Oncology Library.*

Questions? Suggestions? Announcements?
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