Meeting Report

Highlights of the Ninth Annual Beaumont Symposium on Molecular Pathology

DNA Technology in the Clinical Laboratory

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The ninth edition of the Beaumont DNA symposium was held April 13–15, 2000 at William Beaumont Hospital in Royal Oak, Michigan. As in previous years, the symposium was structured to include sessions on new technology in molecular pathology, molecular cardiology, molecular oncology-hematology, and molecular microbiology, as well as roundtables. Pre-meeting workshops were offered this year by biotechnology companies.

New Technology in Molecular Pathology Session

This session opened the meeting with the presentation on "Comparative genomic hybridization: a powerful molecular cytogenetic technique" by Dr. Dagmar K. Kalousek from the University of British Columbia. The overview of this new molecular cytogenetic approach encompassed the theoretical basis of comparative genomic hybridization (CGH), the advantages in comparison to cytogenetic analysis by fluorescent *in situ* hybridization (FISH), and the extensive applications to detect genetic changes in malignancies and to evaluate tissues from abnormal pregnancies.

The second presentation was devoted to "Perspectives in Pharmacogenetics" and was given by one of the founders of this field, Dr. Werner Kalow, Professor Emeritus in the Department of Pharmacology at the University of Toronto. The presentation began with a historical perspective of pharmacogenetics, then focused on human genetic variation as basis of interethnic differences in pharmacogenetics, the monogenic variation of drug responses, multigenic variations, and interethnic frequency differences of enzyme variants.

New technology was also the focus of Dr. Marilyn J. Stapleton's presentation, "Applications of Immobilized Sample Amplification." This novel method was designed to adhere and immobilize intact cells on solid support to

amplify nucleic acid targets directly in specimens. Applications in molecular oncology and in measuring gene expression were exemplified with research performed at Gene Tec.

The keynote address for the entire DNA symposium closed the New Technology session. The speaker was Dr. Robert L. Strausberg, Director of the Cancer Genomics Office at the National Cancer Institute (NCI). His topic was "The Cancer Genome Anatomy Project," a bold new initiative with the goal of achieving the comprehensive molecular characterization of normal, precancerous, and cancerous cells. Dr. Strausberg reviewed the project's current status, its applications in prevention, early detection, diagnosis, and therapeutic strategies, and also future prospects of the NCI Cancer Genome Anatomy Project's Tumor Gene Index, existing public database for gene expression in human cancers, and the Mammalian Gene Collection new project.

Molecular Cardiology Session

The first speaker was Dr. Jeffrey A. Towbin from Baylor College of Medicine, who presented "Genotype and Severity of Long QT Syndrome," offering a comprehensive overview of the molecular genetics of inherited diseases in which arrhythmias are prominent features, the resulting ion channel abnormalities, the genetic testing for Long QT, and the use of therapeutic targets based on ion channel mutations.

The second presentation was given by Drs. Demetris M. Demetriou and Domnita Crisan from the Departments of Cardiology and Clinical Pathology, respectively, at William Beaumont Hospital. The topic "Angiotensin-Converting Enzyme Genotype, Coronary Artery Disease, and Restenosis after Coronary Stenting" was reviewed, as well as the promising but sometimes contradictory re-

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ported findings in disease associations of angiotensin-converting enzyme polymorphism. The Beaumont experience in assessing the value of angiotensin-converting enzyme genotype for restenosis risk after stenting was also presented.

"Molecular Genetics of Hypertension" was the next topic, presented by Dr. Steven C. Hunt from the University of Utah. He offered an excellent update on what is considered one of the most complex tasks facing human geneticists today. His review covered a variety of issues, from subsets of hypertension and gene-environment and gene-gene interactions to reviews of genes associated with or linked to hypertension, genome searches for linkage, clinical application, and risk assessment of genetic information.

The Molecular Cardiology session was concluded by Dr. Pascal J. Goldschmidt from Ohio State University with a presentation of "Genetics and Pharmacogenomics of Unstable Coronary Syndromes." His overview showed clearly that the cardiovascular field has entered a new era and that coronary artery disease (CAD) and coronary restenosis after percutaneous coronary intervention represent examples of complex traits already benefiting from genomic information. The role of glycoprotein GP IIIa PIA2 polymorphism and its association with adverse events post-stenting were reviewed, as well as the far-reaching implications of a pharmacogenetic approach to therapy.

Molecular Oncology-Hematology Session

The first speaker of this session was Dr. Thomas S. Frank from Myriad Genetic Laboratories and the University of Utah. His excellent and extremely informative overview of "Hereditary Cancer Syndromes" set the stage for the entire Oncology session by covering the biological basis of inherited cancer risk, the common hereditary cancer syndromes, genetic testing, and management options for individuals with hereditary susceptibility to cancer.

The second presentation focused on the "Molecular Pathology of Colorectal Cancer" and was given by Dr. William E. Grizzle from the University of Alabama at Birmingham. He reviewed translational research relying on molecular markers to characterize neoplastic lesions of the colorectum for early detection, diagnostic, and prognostic value, with identification of aggressive subsets of tumors and the near future perspectives of using molecular characterization for selection of novel therapies.

The hematology part of this session was introduced by Dr. Viviana Van Deerlin from the University of Pennsylvania, who spoke about "Bone Marrow Engraftment Analysis after Allogeneic Bone Marrow Transplantation." Her comprehensive presentation covered the multiple issues related to assessment of bone marrow engraftment including analysis methods, such as restriction fragment length polymorphism (RFLP), polymerase chain reaction (PCR), tandem DNA repeats, identification and selection of informative loci, and quantitative amplification of short tandem repeats (STRs) and discussed the clinical significance of marrow engraftment analysis as an important

adjunct to the care of allo-bone marrow transplantation patients.

The Hematology session was closed by Dr. L. Jeffrey Medeiros from the University of Texas, M. D. Anderson Cancer Center with an update on "Chromosomal Translocations and their Detection in Non-Hodgkin's Lymphomas." Types and general mechanisms of translocations in non-Hodgkin's lymphomas were discussed, followed by a comprehensive review of the detection methods with their respective advantages and limitations and a presentation of the major translocations with an extremely useful commentary on practical aspects for each translocation.

Molecular Microbiology Session

Dr. David Hillyard of ARUP Laboratories opened this last session with his talk on "Viral Load Update: HIV and HCV." Dr. Hillyard discussed the indications for use of viral load assays. Commercially available kits were described in respect to format, methodology, reportable units, linear range, and sensitivity.

Dr. Gail Woods from the University of Texas Medical Branch at Galveston spoke on "Molecular Techniques in Mycobacterial Detection." Dr. Woods discussed commercially available techniques for the rapid molecular detection of *Mycobacterium tuberculosis*. She presented data supporting the subsequent cost savings realized due to earlier diagnosis of tuberculosis, earlier initiation of therapy, and shortened hospital stays.

"Peptide Nucleic Acids (PNAs) for Bacterial Detection" was presented by Dr. Jens Hyldig-Nielsen of Boston Probes, Inc. Dr. Hyldig-Nielsen introduced this new class of DNA mimics to the audience by describing the structure of this uncharged molecule and its special properties, such as PNA/NA hybrids with high T_m values, which result in fast hybridization kinetics and increased specificity. Applications such as detection of *M. tuberculosis* in sputum and harmful organisms in food products were discussed.

The session was closed with a presentation on "Human Herpesvirus (HHV 1-8) Quantitation: Technical and Clinical Considerations" by Dr. Brian Dawson from the University of Texas Southwestern Medical Center in Dallas. Dr. Dawson discussed technical details (ie, use of internal quantitation standards) of quantitative and semiquantitative detection methods for these viruses. Methods included PCR, reverse transcriptase-PCR, real time PCR, and asymmetric PCR. He reviewed several cases demonstrating the clinical use for viral quantitation, which included HHV-6 in sudden infant death and Epstein-Barr virus in a liver transplant patient.

Roundtable Presentations

Roundtable presentations were also very informative on a variety of subjects, including "Image and Ploidy Analysis" by Dr. Rebecca Hankin, William Beaumont Hospital; "Viral Markers for Specific Lymphomas in HIV Positive Patients" by Dr. Brian Dawson, University of Texas; "Med-

ical Technologists in Molecular Pathology," a panel discussion with input from medical technologists from different institutions; "Programmed Cell Death: Clinical Relevance and Detection" by Dr. Frederick L. Kiechle, William Beaumont Hospital; and "Improving and Understanding Molecular and Clinical Pathology Reimbursement" by Dr. John D. Schaldenbrand, St. Joseph Mercy Hospital. Based on participants' comments, the roundtables were a useful forum for exchanging information and networking.

Pre-Meeting Corporate Workshops

Several companies conducted very informative workshops before the opening of the meeting. The workshops were well received by the attendees and included "Laser Capture Microdissection: Single Cells from Fixed Tissue,"

Arcturus Engineering, Inc.; "An Introduction of the Becton Dickinson's Probe Tec ET system" Becton Dickinson; "HemaVision: Multiplex RT-PCR Reactions to Identify Translocations or Chromosomal Rearrangements and Breakpoint or Splice Variants," Bio-Rad Laboratories; "Countdown to Automation: Nucleic Acid Purification Strategies For Keeping Pace with the Demands of the Future," Gentra; "Hepatitis C Virus Genotyping Using Innogenetics' INNO-LiPA HCV II Assay," Innogenetics; "Critical Factors for Successful PCR and RT-PCR," QIAGEN, Inc.; "Automation of Mutation Detection: A Novel Enzymatic Approach Using the READIT Technology," Promega; "The Use of the LightCycler in Molecular Pathology," Roche Molecular Biochemicals; and "Hemostasis Testing Using the Invader Assay," Third Wave Technologies.