From Genomics to Proteomics

By Michael R. O’Leary, M.D., CEO

The dream of having the human genome completely sequenced is now a reality, and yet we are just beginning to appreciate the power, and limitations, of the genomic revolution. One unanswered question is: “How do the 30,000 or so human genes translate their genetic messages into cells, tissues, human beings and even cancer?” It happens through proteins, which are organic molecules of varying size and shape, arranged in long chains made up of smaller molecules called amino acids.

Proteins are widely used in cells to serve a number of diverse functions. Some proteins provide the structural support for cells while others act as enzymes to catalyze many cellular reactions. We know the many roles that different proteins play in building cellular structures and in catalyzing metabolic reactions, but where do proteins come from? Since the beginning of evolution, cells have possessed the ability to synthesize proteins. They can manufacture new proteins either for reproduction or to simply replace a degraded one. To synthesize proteins, cells follow a very systematic procedure that first transcribes DNA into messenger RNA and then translates the messenger RNA into long chains of amino acids. The amino acid chains then fold into specific proteins. Encoded proteins carry out most biological functions, and to understand how cells work, one must study what proteins are present, how they interact with each other, and what they do.

Historical Background

The term “proteome” defines the entire protein complement in a given cell, tissue or organism. “Proteomics,” one of the many “omics” buzzwords today, is loosely defined as the systematic analysis of the proteins in an organism, particularly those proteins expressed during a disease state. Although this term originated in the mid-1990s, the roots of this field are closely entwined with the history of clinical chemistry. The first laboratory test for a protein cancer marker, the Bence-Jones protein in urine, was described in 1847. Over the succeeding years, clinical laboratories have developed tests for quantitative and qualitative analysis of hundreds of proteins in biological fluids by the use of activity assays, electrophoresis, chromatography, immunoassays and serologic procedures. Such tests, however, have typically analyzed only one or several proteins at a time, limiting their effectiveness. Recent progress in the use of sophisticated mass spectroscopy offers the potential to analyze hundreds of proteins at a time in miniscule specimens. Such technological advances have greatly expanded potential benefits of proteomic research.

New Biomarkers

Proteomics, therefore, is a powerful biomedical tool for understanding which proteins are present in a particular tissue under given conditions. Instead of tracking a single biomarker, usually a tumor associated antigen whose expression is related to a well-defined cancer (i.e. prostate specific antigen (PSA)), proteomics is attempting to define global patterns of protein expression with diagnostic or prognostic value for a particular form of cancer. Such data sets are obtained using a large number of samples from patients divided into various disease categories versus healthy controls. Proteomic research has been used to study a variety of cancers including liver, prostate, breast, bladder, ovary and esophagus. It appears that there exists certain protein “fingerprints” unique to specific malignant neoplasms that potentially could provide diagnostic and prognostic application. The ability to analyze large numbers of proteins in a single test has greatly accelerated the ability to identify new biomarkers for disease processes.

Proteomics in the Laboratory

Although proteomics is expected to have a large impact on the clinical laboratory, it is not yet clear whether this will appear as a series of new markers adapted to current testing technologies or as new technology further refining the role of known proteins in health and disease. Mass spectroscopy (MS) offers great potential for both quantitative and qualitative analysis of proteins and is expected to play a significant role in the proteomics revolution. Clinical laboratories such as ours with experience in MS methodologies will be poised to be in the vanguard of this very promising technology.
Utilization of HPV Testing Under New 2006 ASCCP Consensus Guidelines

By John Fazio, M.D., Pathologist and Medical Advisor for the Cytology Department

Updated American Society for Colposcopy and Cervical Pathology (ASCCP) consensus guidelines for the management of women with abnormal cervical cytology tests, as well as biopsy proven CIN (Cervical Intraepithelial Neoplasia) and AIS (Adenocarcinoma In Situ), were published in October 2007 in the American Journal of Obstetrics and Gynecology (2007;197(4): 346-355 and 201-222).

Following is a summary of the new guidelines regarding the indications and contraindications for human papillomavirus (HPV) testing.

Under the updated consensus guidelines, recommendations for HPV DNA testing include the following:

• Reflex HPV testing for triage of women 21 and older with a cytology diagnosis of ASC-US (Atypical Squamous Cells of Uncertain Significance).

• Subsequent management of women 21 and older with cytologic diagnoses of ASC-US, ASC-H (Atypical Squamous Cells of Uncertain Significance cannot rule out a High Grade Intraepithelial Lesion), LSIL (Low Grade Intraepithelial Lesion) or AGC (Atypical Glandular Cells) when the initial colposcopy shows no CIN 2, 3 or glandular neoplasia (post colposcopy follow-up).

• Subsequent management of women with a histologic diagnosis of CIN 2,3 who have been treated with either a diagnostic excisional procedure or ablation (“test of cure”).

• Initial management of women 21 and older with a cytologic diagnosis of atypical glandular cells (AGC) in conjunction with colposcopy, endocervical sampling, and endometrial sampling (only if patient is over 35 or has clinical indications, such as vaginal bleeding).

• Routine cervical cancer screening (in conjunction with a Pap test) for women 30 years and older (DNA with Pap).

• Reflex HPV testing for triage of postmenopausal women with LSIL is an acceptable choice.

Situations where HPV testing is contraindicated or may not be appropriate include the following:

• HPV testing is not indicated in the management of adolescents (age 20 and younger), regardless of the cytologic diagnosis. Further, if HPV testing is performed, the results should not be used to influence patient management.

• HPV testing should not be used for routine cervical cancer screening in women less than 30 years of age (refers to DNA with Pap).

• HPV testing is not appropriate for initial triage of women with HSIL. These women should all get colposcopy.

• The use of HPV testing alone is not acceptable for the initial triage of women with adenocarcinoma in situ (AIS) as well as all categories of atypical glandular cells (AGC). These patients should all get colposcopy with endocervical sampling, as well as endometrial biopsy (if they are over 35 or have symptoms such as vaginal bleeding), in addition to HPV testing as part of the initial work-up.

Other relevant points:

1. Testing for low-risk (non-oncogenic) HPV types has no role in routine cervical cancer screening or for the evaluation of women with abnormal cervical cytology. Testing should be confined to high-risk HPV types only.

2. HPV testing should not be performed more frequently than once every 12 months. The exception to this is AGC or AIS when no pathology is found on the initial workup, in which case repeat HPV testing at six months may be appropriate. Otherwise, there is no reason to repeat HPV testing at less than 12-month intervals.

3. Clinical judgment should always be used when applying the consensus guidelines to an individual patient because it is impossible to develop guidelines that apply to all situations.

The complete 2006 consensus guidelines as well as management algorithms may be viewed online at the ASCCP Web site, www.ASCCP.org.

For more information or to discuss HPV testing, contact Cytology Department Medical Advisor John Fazio, M.D., at (315) 492-5096 or Cytology Department Technical Manager Janet Miller at (315) 410-7211 or by e-mail to janetmiller@lacny.com.
A Culture of Safety

By Jayne L. Healey, MD, Assistant Director of Laboratories

Up to 85% of clinical decision-making is based upon information obtained from laboratory testing. Laboratory-related errors can result in delayed diagnosis, additional laboratory and/or invasive testing, improper treatment and serious transfusion reactions. Given these facts, The Joint Commission appropriately included safe laboratory practices in their 2008 National Patient Safety Goals (NPSG).

Sources of error in laboratory testing can be broken down into 1) pre-analytical 2) analytical and 3) post-analytical. Although not free from error, modern automation has resulted in remarkable accuracy and reliability in the analytical phases of laboratory testing. As such, pre-analytical and post-analytical problems now represent an increasing percentage of laboratory-associated errors.

Currently, 46% to 56% of errors occur during the pre-analytical phase, with the vast majority being specimen identification errors. A recent College of American Pathologists (CAP) Q-Probe survey reports that 42% of laboratories allow the primary collectors of specimens to re-label misidentified specimens. This troubling statistic underscores the culture of low expectations regarding specimen labeling, despite the potential for serious adverse events. If the 2008 National Patient Safety Goals are to be met, a more proactive and systematic approach is warranted.

In reducing system error, patient safety must be built into the process of specimen collection. The Joint Commission requires that specimen labeling be performed in the presence of the patient. Pre-labeling of collection tubes or specimen containers should not occur. Appropriate labeling includes two distinct patient identifiers. Examples of acceptable identifiers include name, birth date, or medical record number. Unique identifiers link the specimen to the patient, the requisition and the report and decrease the likelihood of misidentification due to common or similar names. The source of the specimen should be included on the label, when appropriate. Finally, the time and date of collection should be noted on the label, along with the initials of the primary collector. In the case of specimens submitted to the Blood Bank, the specimen label MUST include the time and date of collection along with the initials of the primary collector.

In compliance with the NPSG, Laboratory Alliance requires that unlabeled and mislabeled specimens be recollected (with rare exception for one-of-a-kind specimens). Clinicians should recognize this policy as a valuable safeguard against the release of inaccurate results. A “total testing” approach has been proposed in the literature, which extends quality control for laboratory testing beyond the confines of the analytical phase. Healthcare professionals at each step of patient testing need to adopt a culture of safety. This involves teaching and modeling proper behavior, as well as continuous quality monitoring. Laboratory Alliance embraces this ideal and welcomes the collaboration of its clinician partners in meeting these goals.

Students Visit Laboratory Alliance

By Lonnie Stallcup, Education Services Manager

Two students from the Onondaga-Cortland-Madison Counties Board of Cooperative Educational Services (OCM BOCES) Laboratory Technology Program visited our patient service center at the Corporate Offices on Feb. 25 to observe a demonstration by Phlebotomist Melissa Frizzi. The program is designed for high school juniors and seniors who are interested in a career in clinical laboratory science.

“My visit to Laboratory Alliance was well worth it. Honestly, I enjoyed every second I was there. It was a learning experience. I learned what a professional business is looking for from an employee,” said student Codi Smith.

Laboratory Alliance has gone to great lengths to expose students to clinical laboratory science. By partnering with schools, Laboratory Alliance is advancing knowledge of career options and stimulating interest in health care as a career. The program is designed to introduce high school students to the general laboratory and teach them soft skills. It is not a certification or licensure program.

“Students become familiar with the types of specimens needed for various laboratory procedures, including phlebotomy. OCM BOCES students also gain knowledge in the basic operation, calibration and maintenance of several pieces of laboratory equipment,” explains instructor Janet Clark, a medical technologist.

Last fall, the OCM BOCES students were invited to visit Laboratory Alliance’s Operations Center. “I really was amazed by the Hematology Department,” said student Razhelle Denslow, while student Ryan Misener remarked “I found out that microbiology was really cool.”
Sentinel antibiotic susceptibility prevalence studies for groups A and B streptococci are performed biannually by the Microbiology Department to monitor the emergence of resistance to antimicrobial agents. Group A and group B streptococcal isolates are collected from patient specimens from various physician practices and/or area hospitals throughout Onondaga County so that the results are not biased by geographic location or physician practice specialty.

**Group A streptococcal study results**

The following highlights the results of these studies. From Jan. 1-Feb. 28, 2009, 50 pharyngeal isolates of group A streptococci (GAS) recovered from adult and pediatric samples were randomly selected for testing against penicillin, erythromycin and clindamycin.

All 50 isolates (100%) were susceptible to penicillin whereas only 41 (82%) and 42 (84%) of the isolates were susceptible to erythromycin and clindamycin, respectively.

Compared to the antibiotic sentinel study that was performed in 2007, the 2009 antibiotic susceptibility results showed an alarming increase of group A streptococcal resistance to erythromycin and clindamycin. These comparative results for 2007 and 2009 are shown in Table 1.

**Table 1. Comparative 2007 and 2009 Group A Streptococci Susceptibility Results**

<table>
<thead>
<tr>
<th>Year</th>
<th>Antibiotic Tested (% Susceptible)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Penicillin</td>
</tr>
<tr>
<td>2007</td>
<td>100%</td>
</tr>
<tr>
<td>2009</td>
<td>100%</td>
</tr>
</tbody>
</table>

This limited sentinel study indicates that penicillin continues to be effective therapy for the treatment of GAS pharyngitis in the non-penicillin allergic patient. Unfortunately, however, with the continued widespread use of erythromycin and clindamycin as alternative therapies for the treatment of pharyngitis as well as other suspected respiratory and non-respiratory infections, significant GAS resistance to these drugs has emerged over the last two years that may result in possible treatment failures.

**Group B streptococcal study results**

A similar antibiotic susceptibility prevalence study was performed on 50 randomly selected group B streptococci (GBS) recovered from vaginal specimens over a comparable two month time period. As expected, all GBS isolates were susceptible to penicillin. The data in Table 2 stills shows significant resistance to erythromycin and clindamycin.

**Table 2. Comparative GBS Sentinel Study for 2009 and 2007**

<table>
<thead>
<tr>
<th>Year</th>
<th>Antibiotic Tested (% Susceptible)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Penicillin</td>
</tr>
<tr>
<td>2007</td>
<td>100%</td>
</tr>
<tr>
<td>2009</td>
<td>100%</td>
</tr>
</tbody>
</table>

If treatment is indicated for GBS, penicillin remains the agent of choice for intrapartum antibiotic prophylaxis in the non-penicillin allergic patient. Ampicillin is an acceptable alternative but penicillin is preferred because it has a narrower spectrum of activity and is less likely to select for bacterial resistance. Importantly, physicians are reminded that confirmed GBS resistance to penicillin has not been reported to date and, as such, antimicrobial susceptibility testing against this agent is not performed.

For penicillin-allergic women at risk for anaphylaxis, cefazolin, clindamycin and erythromycin are possible therapeutic options as recommended by the Centers for Disease Control. While there is no GBS reported resistance to cefazolin, the results of this sentinel study show that 50% or more of the isolates may be resistant to erythromycin or clindamycin. Since antimicrobial susceptibility testing is not routinely performed on GBS isolates, physicians may specifically request such testing when considering erythromycin or clindamycin as therapeutic options.
**Streptococcus pneumoniae – A Brief Overview of Human Infections, Disease Prevention and Antibiotic Resistance Trends**

By Paul A. Granato, Ph.D., Director of Microbiology

*Streptococcus pneumoniae*, often called the pneumococcus, is a well known human bacterial pathogen capable of causing localized respiratory infections as well as more serious, life-threatening systemic disease. Some of the more common localized pneumococcal respiratory infections include otitis media and sinusitis. Importantly, *S. pneumoniae* is also a major bacterial cause of community-acquired pneumonia accounting for as many as 30% of such infections.

Life-threatening, systemic pneumococcal infections usually involve the spinal cord and blood and are called meningitis and septicemia respectively. These infections can have high morbidity and mortality rates in pediatric and adult patients. Sometimes, these more serious, life-threatening infections may result from a localized primary site of pneumococcal infection, such as otitis media.

Prevention of most pneumococcal infections can be achieved by immunization with a 23-valent capsular polysaccharide vaccine in adults or the 7-valent conjugate vaccine in children. Widespread immunization with a 23-valent capsular polysaccharide vaccine in primary site of pneumococcal infection, such as otitis media.

The Microbiology Department is pleased to announce the availability of a new molecular based (PCR) assay that can reliably characterize of staphylococci in blood cultures. This new molecular-based assay employs the use of a small instrument and test cartridge that automates and integrates sample extraction and purification, nucleic acid amplification and the detection of the amplified target sequence (called amplicons) using a real-time PCR assay. The assay is able to detect multiple nucleic acid target sequences that may be present in the blood culture sample that can result in the characterization of the isolate as MSSA, MRSA or coagulase negative staphylococci.

**Rapid PCR Test for the Characterization of Staphylococci Recovered from Blood Cultures**

By Paul A. Granato, Ph.D., Director of Microbiology

Life-threatening cases of septicemia, caused by the presence of microorganisms in a patient’s blood, is a medical emergency and urgent healthcare concern with over 750,000 documented cases occurring annually in the United States. The mortality rate associated with severe sepsis has been reported as high as 50%. Methicillin-susceptible *Staphylococcus aureus* (MSSA) and methicillin-resistant *Staphylococcus aureus* (MRSA) may account for up to 35% of severe sepsis cases. As such, the early detection and characterization of staphylococci in blood may be critical in the selection of appropriate antimicrobial therapy which, in some cases, can be life saving.

The Microbiology Department is pleased to announce the availability of a new molecular based (PCR) assay that can reliably and rapidly detect *Staphylococcus aureus* from coagulase negative staphylococci in blood cultures. In addition, the assay can detect the presence or absence of the mecA gene in *S. aureus* which is a predictor of the organism’s likely resistance or susceptibility to methicillin/oxacillin. Test results are available within 1 to 2 hours of the detection of gram positive cocci suggestive of staphylococci in a patient’s blood culture. The availability of this rapid and reliable PCR result is 1 to 2 days sooner than using conventional test methods. In the absence of such timely results, clinicians may often have to employ empiric treatment approaches, using more broad-spectrum antimicrobial therapies that can be costly, ineffective and contribute to an increase in drug resistance.

This new molecular-based assay employs the use of a small instrument and test cartridge that automates and integrates sample extraction and purification, nucleic acid amplification and the detection of the amplified target sequence (called amplicons) using a real-time PCR assay. The assay is able to detect multiple nucleic acid target sequences that may be present in the blood culture sample that can result in the characterization of the isolate as MSSA, MRSA or coagulase negative staphylococci.

The Microbiology Department has conducted a thorough, in-house validation of the PCR assay and obtained 100% correlation compared to conventional methods. It is expected that the rapid availability of such reliable results 24 hours a day, seven days a week, will guide the choice of appropriate anti-staphylococcal therapy, when indicated, and have an enormously beneficial impact on patient care and patient outcomes.
Patient Service Center at North Medical Expanded to Accommodate Patients

By Jeff Coyne, Director of Support Services

Due to the ever-increasing number of patients who visit our Patient Service Center at North Medical Center, Laboratory Alliance expanded this location by acquiring an additional 600 square feet. The waiting room was enlarged and two more rooms were built for patient phlebotomy, bringing the total number of phlebotomy rooms to four. This expansion has helped streamline patient visits and has allowed the phlebotomy team to work more resourcefully.

In the News

An article titled “Borrelia Burgdorferi and Babesia microti Coinfection in a 79-Year-Old Camper” was featured in the recent Clinical Microbiology Newsletter (Vol. 31, Issue 5).

The Case Report is co-authored by Russell Rawling, M.S. M(ASCP) SM, RM (NRM) SM, Karen Strouse, MT (ASCP) SM, and Paul A. Granato, Ph.D., Microbiology Department, Laboratory Alliance, and Department of Microbiology and Immunology, SUNY Upstate Medical University, Syracuse, N.Y.

For a copy of the report and discussion relating to the topic, contact Dr. Granato by e-mail at paulgranatophd@lacny.com.

Join us for the Corporate Challenge!

Laboratory Alliance employees, family members and friends are invited to join our team on Tuesday, June 23. The 3.5 mile run, jog or walk on the parkway at Onondaga Lake Park will be followed by food and festivities. This is a fun, non-competitive event, with proceeds donated to local area not-for-profits.

Register online by Friday, May 29, at www.jpmorganchasecc.com. Click on “Syracuse” under the Series Schedule. Then click on “Companies” under About Syracuse. Scroll down to Lab Alliance. Click on “Register for this Team”. Fill in the bold fields and T-shirt size. When it asks for payment info, click on the circle for pay later/my company captain will pay (Laboratory Alliance will be paying the $30 entrance fee for each participant). When done, you will receive a confirmation number and confirmation e-mail from confirmation@jpmorganchasecc.com. Don’t forget to enter the T-shirt size, as we also need it for the company T-shirt.

If you would like to be a tent monitor during the race, or for more information, contact Becky Reynolds, Microbiology at the Operations Center, at (315) 410-7067 (day shift).

A Tribute to Joe

In January, we lost a colleague to cancer. He worked in our Microbiology Department and his specialty was Molecular Diagnostics. He was greatly loved. He had a zest for life and his motto was “Never, ever quit.” His name is Joe Bertolero. Co-worker Debbie Neverette, Cytology Department, writes this tribute to our friend:

On the clear evening of January 19, 2009, Laboratory Alliance lost a dear colleague, friend and mentor. This, Joe, is a farewell to you from all of us here. You have touched each of us with your kindness, witty personality and humble smile. As we go about our daily routines here at work there are many memories and signs reminding us of you. We may shed a tear, look away in the distance for a moment, or just say to another person, “remember when Joe said…”

We will continue to feel your presence throughout the halls of Laboratory Alliance. Thank you for all you have done for each one of us through the years. You will be greatly missed and never forgotten.
Recognizing Great Employees

Congratulations to the following nominees for the CHAMP Award. By consistently demonstrating the attributes of a CHAMP – Caring, Helpful, Accurate, Motivated and Professional – these employees have earned the recognition:


The Employee Recognition Committee thanks everyone who participated. Nomination ballots are now being accepted for the Aug. 1 deadline.

Kelly Brunelle Named CHAMP

On Jan. 10, Dr. Michael O’Leary, CEO, presented the CHAMP award to Kelly Brunelle. Kelly received this employee recognition at the Laboratory Alliance Holiday Party with her son Joseph in attendance.

Kelly has been in various positions with Laboratory Alliance since Oct. 23, 1991. It is evident from the nominations that Kelly exemplifies the CHAMP in every way.

A nominee must consistently demonstrate the attributes of a “CHAMP”: Caring, Helpful, Accurate, Motivated and Professional. A co-worker of Kelly’s describes her as “always taking the time to assist” and another states, “Kelly is very helpful, professional and patient.”

Kelly not only earned the recognition of her peers as the first 2009 CHAMP, Kelly also received several nominations for the St. Joseph’s S.T.A.R. (Service, Teamwork, Attitude and Reverence) Award. When you see Kelly please congratulate her on these accomplishments.

Employee Anniversaries

April, 5 years:
John Daucher
Bonnie Larusso
San Toscano

May, 5 years:
Smita Christie

June, 5 years:
Curtis Brunelle
Sara Grimshaw
Jessilee Jones
Lauren Roach
Susan Winchell

June, 10 years:
Joni Ducey
Dominick Frijo

New Employees

Please welcome our new employees
At our Operations Center
Dianna Calabria, Phlebotomist
Natalie Cupelo, Laboratory Office Assistant
Lynn Nodine, Phlebotomist
Melissa Skiff, Phlebotomist
Francis Springer, Courier

At our Corporate Office
Roseanne Siefert, Payroll and Benefits Specialist

At our Rapid Response Laboratory at Crouse Hospital
Elena D’Anna, Medical Technologist
Gail Dodsiki, Administrative Secretary

Congratulations

Michael L. Sovocool, MHS, PA(ASCP)
CM, Pathology Associates of Syracuse, P.C., was recently appointed chair of the Board of Trustees of the American Association of Pathologists’ Assistants.

Rachel Elder, M.D., kneeling third from left, front row, is captain of the Lab Crew Soccer Team. Sporting T-shirts with the Laboratory Alliance logo, the team made everyone proud when they won the women’s division and playoffs during the first session at Sportcenter 481. They are currently playing in the second session.

WHO IS YOUR CHAMP?

Caring
Helpful
Accurate
Motivated
Professional
ICE Awareness Can Save Lives

There are over 215 million cell phone users in the United States today. The U.S. Centers for Disease Control and Prevention reported in 2006 that 1,600,000 emergency room patients could not provide contact information because they were incapacitated. So many individuals leave the home each day without any identification or emergency contact information, yet carry a cell phone.

A global campaign calls for individuals to program an In Case of Emergency contact (or ICE for short) into their mobile phones.

**How to ICE your Phone™**

• CHOOSE a responsible person to be your In Case of Emergency (ICE) Contact. Record their contact information.

• INFORM your ICE Contact that you have chosen them as your designated contact and provide them with information that may affect your treatment. Remember MAD or “M” “A” “D”.
  
  • Medicines - List all current medications you are taking, including herbal and organic supplements because they can and do interact with some medications.
  
  • Allergies – List all known allergies, especially to medications, but also to foods.
  
  • Doctors - Include the names and phone numbers of doctors or other medical providers responsible for your regular care.

• ADD this contact as a new entry, with their phone number, in your mobile phone address book under the heading “ICE”. Example: ICE-William or ICE-Dad.

**ICE your phone™ tips**

• To learn how to enter a new contact into your mobile phone’s address book, please contact your mobile phone manufacturer or mobile service provider.

• When entering multiple ICE Contacts, put a number directly behind the word “ICE” in each one to prioritize them for the emergency responders. Example: ICE1 – Mom, ICE2 – Mary.

Learn more at [www.icesticker.com](http://www.icesticker.com)