MassBiologics
Medicine for Better Lives

Newsletter Name?

MassBiologics and other University News

September 4. 2012 Volume 1, Issue 1

Inside this issue:

September Happenings

- Friday September 7th: "Preeclampsia: Causes and Therapeutics Prospects"
- Saturday, September 8th: UMass Minutemen vs. Indiana University at Gillette Stadium
- Sunday September 23rd: Walk To Cure Cancer

From the Desk of Dr. Mark Klempner

What's In a Name?

In the famous Shakespearean scene, Juliet proclaims to Romeo that it is he who she so passionately loves. No matter what his name she sees in him perfection and pledges every molecule of her being to him. Juliet asks him to renounce his name, Romeo Montague, and to be re-baptized pure "love". She, in turn, will no longer be a Capulet. Their names are of little consequence and should not interfere with their love for one another. But she also says "What's Montague? It is nor hand, nor foot, nor arm, nor face nor any other part belonging to a man." Unlike his surname, the names of these things, and for that matter the names of institutions, tells their stories and mean a lot.

Over our 118 year history we have had many meaningful names that have described what we were about and who we were affiliated with. Our beginning was affiliated with the Massachusetts Board of Health where we were known as The State Labs comprised of a laboratory at the Statehouse and one at the Bussey Institute in Forest Hills where horses were stabled for the production of equine antitoxin for the treatment of diphtheria.

Mark S. Klempner, MD

In 1885, the year after our founding, the renowned and first physician-scientist in America, Theobald Smith, MD, accepted a dual appointment to serve as Professor of Comparative Pathology at the short lived Harvard Veterinary School and to be the Director of the State Labs. Under his leadership The State Labs produced millions of life saving doses of safe, effective equine antitoxin. In 1946 we changed our name to the State Laboratories for Plasma Fractionation and began an over 40 year era of producing human immunoglobulin antisera and antitoxins through plasma fractionation methods developed by the flamboyant

Continued on pg. 7

Pivotal Clinical Trial For Rabies Monoclonal Antibody Begins

A pivotal clinical trial for an anti-rabies human monoclonal antibody (RMAb) being developed through a collaborative partnership between MassBiologics of the University of Massachusetts Medical School and the Serum Institute of India, Ltd., is starting to enroll patients. The study, sponsored by the Serum Institute, will evaluate the efficacy of post-exposure prophylaxis following rabies exposure with RMAb and vaccine compared to standard treatment of human rabies immune globulin (hRIG) and vaccine. Post-exposure prophylaxis for rabies that includes a monoclonal antibody should provide a more affordable, safer alternative to prevent the disease, which

Continued on pg. 2

Administrative Changes at MassBiologics

Beginning this month the University of Massachusetts Medical School Human Resource Diversity & Inclusion (HRDI) team will begin providing their services directly to you on the MassBiologics' campus. This change in approach will give faculty and staff direct access to the central HRDI service providers while at the same time free up the MassBiologics administrative team to take on their expanded roles in the support of business development, contract manufacturing, grants and contracts for externally funded research.

What does this mean to you? Beginning September 4th, led by Jodie Nosiglia, Director of Employee Relations, HRDI will provide an onsite staff person in the Research and Administration Building room #2020 alternating between two and three days per week. The direct line to the phone in room #2020 is (617) 474-4080.

Going forward, Jodie Nosiglia will be responsible to see that your HRDI needs are met. Jodie's contact information is:

Jodie.Nosiglia@umassmed.edu , (508) 856-7789.

The other team members will provide services in their respective areas of expertise as follows:

Talent Management (recruiting)

Michelle Jones-Johnson, Director of Talent Management, Michelle.JonesJohnson@umassmed.edu , (508) 856-1709.

Jim Mack, Senior Talent Specialist, James.Mack@umassmed.edu , (508) 856-3979.

Employee Relations

Ben Moorghen, HR Business Partner II, Ben.Moorghen@umassmed.edu , (508) 856-1284.

Benefits

Katie Temple, Benefits Manager, Katie.Temple@umassmed.edu , (508) 856-1897.

Pivotal Clinical Trial For Rabies cont'd.

is a world-wide public health problem impacting 10 million people a year and resulting in some 55,000 deaths.

"We are extremely pleased that this potentially life-saving product has moved forward to the pivotal clinical trial," said Deborah Molrine, MD, deputy director of Clinical and Regulatory Affairs at MassBiologics and an associate professor of pediatrics at UMass Medical School. "Rabies is a major public health problem in Asia and Africa, and we are hopeful that the findings of this study may result in a treatment option readily available in those areas where it is needed most."

The randomized, comparator-controlled study being conducted in India will enroll 200 patients who have had a high-risk (category III as defined by the World Health Organization) exposure to a suspected rabid animal. Study participants will receive proper wound care followed by injections of either the investigational RMAb or standard hRIG treatment in combination with a five-dose rabies vaccine series. The primary endpoint of the study is to demonstrate that the level of neutralizing antibody to rabies virus in the blood of participants who received RMAb and vaccine is at least as much as the level of anti-rabies neutralizing antibody in the blood of those who received hRIG and vaccine.

Death from rabies is preventable with timely post-exposure prophylaxis consisting of wound hygiene, administration of rabies immune globulin, and active immunization with rabies vaccine. Human rabies immune globulin, derived from human blood, is an expensive product and carries a potential risk of contamination with blood-borne pathogens. Equine immune globulin (eRIG), derived from horse serum, is used in many parts of the world, but its use is associated with significant adverse effects such as anaphylaxis or serum sickness. Both products are often in short supply and costly for inhabitants of areas of the world where rabies is endemic. In India alone, it is estimated only 2 percent of patients whose wounds require the rabies immune globulin receive appropriate post-exposure treatment.

After the completion of a phase 1 study in healthy adult volunteers, Serum Institute of India received regulatory approval to proceed with the current pivotal trial. Final results from the current study are expected in the second half of 2013. The trial is registered with Clinical Trials Registry-India (CTRI /2012/05/002709).

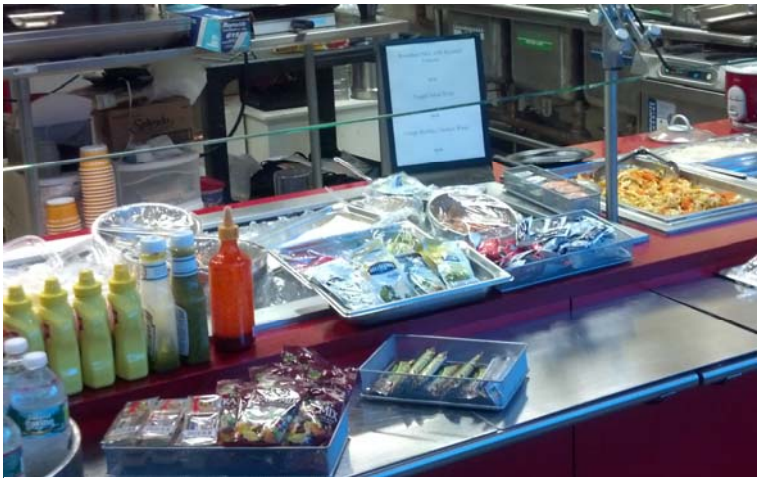
Cafeteria to Adjust Pricing

Due to the rising cost of food, fuel and paper supplies, we will be modestly adjusting the price of certain menu items. The price increases will take effect on Tuesday, Sept 4th, 2012.

MassBiologics will continue to subsidize cafeteria pricing which enables employees to purchase items at reasonable rates. Eurest Dining prides itself on providing quality food, service and variety in its cafeteria and looks forward to continuing to serve you.

If you have any questions, concerns or comments regarding the cafeteria, please contact Jeffrey Way by email or by dialing ext. 4066. The menu will continue to be posted on SharePoint. Comments and suggestions are always welcome.

Thank you in advance for your cooperation.



Quality food at affordable prices continues to be made possible by MassBiologics subsidizing pricing in cafeteria.

Sufficient Documentation is a Key Quality System and it is Everyone's Job

By: Mark Leney, PhD

MassBiologics has demonstrated through interaction with FDA and industry partners that our good documentation practice for licensed and investigational products has been one of our strongest assets. When our critical activities are done, often after significant expenditure of resources, often all we are left with is the documentation.

Last month the Parenteral Drug Association (PDA) published Technical Report No. 56 "Application of Phase-Appropriate Quality Systems and cGMP to the Development of Therapeutic Drug Substances". As a contributing author I watched industry and regulators struggle for consensus. Biopharma and government agree that drug developers must determine their own path, but must do this in a *documented* manner. Sufficient *documentation* of proof-of-concept, sources of biological materials, production and characterization of preclinical lots, pedigree of reference standard, and the application of cGMP documentation to clinical lots, were all emphasized as critical to the development and licensure of biologics while, validation of processes for marketing approval is largely a process of *documenting* that processes work as we think they should.

"...no matter how busy you are, follow this maxim: "Write what you do. Do what you write" and you won't go far wrong"

Some will know that I worked previously as a forensic investigator. Pharmaceutical cGMP and the forensic sciences have much in common; both are highly regulated and require reliable, well qualified processes, while adherence to procedure and meticulous documentation are critical to their integrity. The most important operational rule I learned from my experience in forensics can be usefully be applied to nearly every activity at MassBiologics. Whether writing or executing, making or testing, working in discovery, development, quality or manufacturing – no matter how busy you are, follow this maxim: "Write what you do. Do what you write" and you won't go far wrong.

News from Around Campus

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UMass maintains position as national licensing leader

UMMS research generated 90 percent of total income

The University of Massachusetts has placed in the top 15 nationally for the third year in a row in generating income from the commercialization of its academic research, announced UMass President Robert L. Caret. Approximately 90 percent of the income derived from research innovations was generated by the Worcester campus.

A new report from the Association of University Technology Managers found that UMass generated $35 million in income from faculty-derived discoveries and products during fiscal year 2011. It also signed 25 licenses, created one startup company, and filed 50 patent applications. The University of Massachusetts first cracked the top 15 list in fiscal year 2008.

``We are pleased to continue our streak of being in the top tier of institutions nationally in generating intellectual property income," President Caret said. ``It is a direct result of the outstanding researchers on all five of our campuses whose inventions are helping to fuel the innovation economy in Massachusetts and whose presence in the classrooms and laboratories redound to the benefit of our students. They are also improving the quality of life in the state and around the world. We are grateful for their accomplishments."

With its $35 million in commercialization income, UMass ranked 14th on the list. It was sixth among all U.S. public universities and second among publics and privates in Massachusetts in generating licensing income.

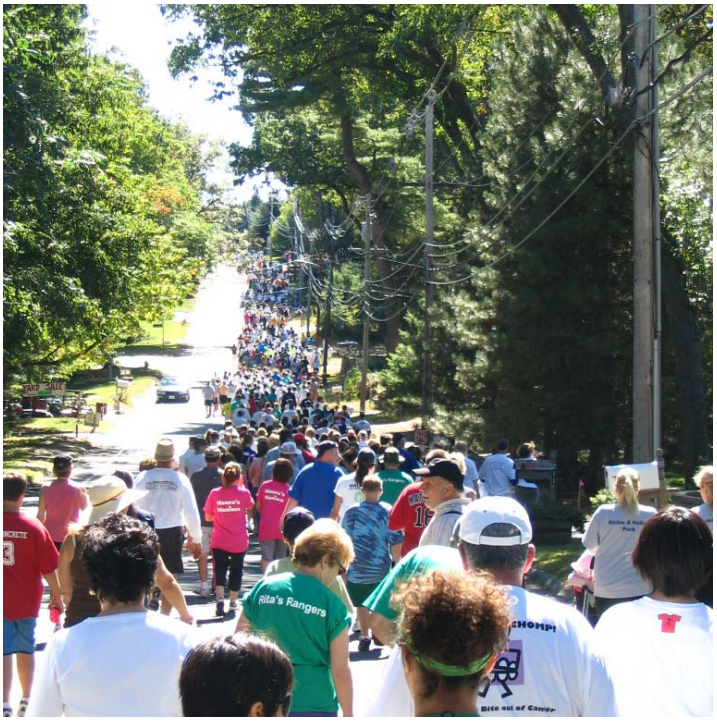
Of the institutions that elected to participate in the survey, two other Massachusetts universities ranked in the top 30: the Massachusetts Institute of Technology ranked sixth with $76.1 million in licensing income, while Harvard University ranked 25th with $13.8 million in licensing revenue.

Annual Walk To Cure Cancer on Sunday September 23, 2012

The annual **Walk to Cure Cancer** is approaching. Proceeds raised, from the walk, support research at the University of Massachusetts Medical School as well as fund cancer care at UMASS Memorial Cancer Center.

We have once again created **Team MassBiologics** in support of this event and we encourage representation from each department, with at least one walker and by departments actively asking for pledges from co-workers, family and friends.

Your support is needed to spread the word and to find volunteers from your departments to walk the 5 mile course. The walk takes place on Sunday, September 23, 2012 at 11:00AM at UMASS Medical School in Worcester. This is a family event so those that volunteer to walk are encouraged to bring their family to join us as we support cancer research. Contact Jeffrey Way for more information at x4066.



Thousands of walkers take to the streets to walk 5-miles around Lake Quinsigamond each year to raise money for cancer research.

umass med NOW

News from Around Campus

Discovery points to new pathways, potential treatment for ALS
Team identifies gene that influences survival time

By Jim Fessenden August 28, 2012

UMass Medical School Communications

A team of scientists, including faculty at UMass Medical School, have discovered a gene that influences survival time in amyotrophic lateral sclerosis (ALS, also known as Lou Gehrig's disease). The study, published in Nature Medicine, describes how the loss of activity of a receptor called EphA4 substantially extends the lifespan of people with the disease. When coupled with a UMMS study published last month in Nature identifying a new ALS gene (profilin-1) that also works in conjunction with EphA4, these findings point to a new molecular pathway in neurons that is directly related to ALS susceptibility and severity.

"Taken together, these findings are particularly exciting because they suggest that suppression of EphA4 may be a new way to treat ALS," said Robert H. Brown Jr., DPhil, MD, professor and chair of neurology and a co-author on the study.

ALS is a progressive, neurodegenerative disorder affecting the motor neurons in the central nervous system. As motor neurons die, the brain's ability to send signals to the body's muscles is compromised. This leads to loss of voluntary muscle movement, paralysis and eventually respiratory failure. The cause of most cases of ALS is not known. Approximately 10 percent of cases are inherited. Though investigators at UMMS and elsewhere have identified several genes shown to cause inherited or familial ALS, almost 50 percent of these cases have an unknown genetic cause. There are no significant treatments for the disease.

Wim Robberecht, MD, PhD, lead investigator of the Nature Medicine study and a researcher at the University of Leuven in Belgium and the Vesalius Research Center, screened for genes in zebrafish that blunt the adverse effect of the ALS mutant gene SOD1. Through this process, his team identified EphA4 as an ALS modifier. Dr. Robberecht's team went on to show that when this gene is deactivated in mice with ALS, the mice live longer.

Robberecht then turned to UMMS to confirm that turning off EphA4 in human ALS cells would slow the progression of the disease. Dr. Brown and his team identified two human ALS cases with mutations in the EphA4 gene which, like the zebrafish and the mice, had unusually long survival times. This suggests that blocking EphA4 in patients with ALS may be a potential therapeutic target in the future.

In an exciting, related development, a new ALS gene (profilin-1) identified last month by UMMS scientists works in conjunction with EphA4 in neurons to control outgrowth of motor nerve terminals. In effect, gene variants at both the top and the bottom of the same signaling pathway are shown to effect ALS progression. Together these discoveries highlight a new molecular pathway in neurons that is directly related to ALS susceptibility and severity and suggests that other components of the pathway may be implicated in ALS.

"It is exciting that these two studies identify the same pathway in ALS," said John Landers, PhD, associate professor of neurology and lead author of the PFN1 study. "Hopefully this discovery will accelerate efforts toward finding a treatment for ALS."

Product Discovery: Successful Identification of Lead Tetanus and Diphtheria Antibodies

Dr. Gregory Babcock is pleased to announce that Product Discovery has identified lead antibodies that neutralize both the diphtheria and tetanus toxins. These exciting projects employed a new method for the isolation of fully human antibodies. In the past, genetically modified mice have always been used to isolate human antibodies. For these projects very specific cells, called antibody secreting cells (ASCs), were isolated from the blood of human volunteers recently immunized with the MassBiologics Td Absorbed vaccine. The DNA was isolated from individual ASCs and antibody genes specific to either tetanus or diphtheria were obtained.

Animal experiments, developed by the Quality Control (QC) department, were then performed to determine which specific antibodies could protect animals from either tetanus or diphtheria toxin. For both projects, one antibody proved to be the most potent in protecting animals. These antibodies, one for tetanus and one for diphtheria, are now in the cell line selection stage of the development process. Thank you to all of our volunteers at MassBiologics who kindly received the vaccine and donated blood to support our work. This has been a collaborative effort where many people ensured this project's success.

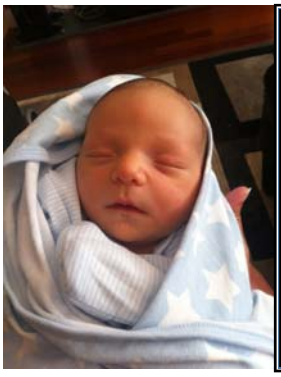
The QC Animal Facilities team dedicated a great deal of time and effort to assisting in the screening of the antibodies while Kirk Rowley and his group developed this new method of isolating human antibodies at MassBiologics and isolating such a potent antibody for tetanus. Finally Dr. Yang Wang and Dr. Leila Sevigny along with their groups identified our lead-candidate diphtheria antibody.

What's Happening at MassBiologics

In future issues, this portion of the newsletter will be reserved for special announcements about MassBiologics employees.

This will be the opportunity to share the comings and goings of faculty and staff, promotions, other employee achievements. We will also acknowledge life events such as births, deaths, marriages or other life milestones for employees and their families.

Please submit contributions to Jeffrey Way (Jeffrey.way@umassmed.edu) by the 15th of each month.



Congratulations to Nicole Mourkakos on the birth of her baby boy. Gregory Mourkakos was born on Friday, July 20, 2012 at a healthy 8 lbs 3 oz.

Process Development: Highly Concentrated MAb Formulation for HCV1

By William D. Thomas Jr., PhD

One of the missions of our Process Development group is to develop MAb formulations that are stable for more than two years in liquid formulation. Over time, we have built a formulation platform that gives a good shelf life for 25 mg/ml MAb preparations using a mild detergent (Tween-80), buffer, and salt as stabilizers. Since the clinical treatment for the HCV1 program requires multiple large doses of HCV1, a highly concentrated formulation was desired for the final product to reduce the treatment volume. However, increasing the MAb concentration could increase viscosity, protein aggregation or particulate formation, ultimately affecting shelf life. We were able to develop a 100 mg/ml formulation after screening for optimal salt, buffer and pH conditions using high throughput methods to detect MAb melting temperatures and aggregation. HCV1 was determined to be a hydrophobic (oily) MAb that had a tendency to aggregate when certain buffers are used and/or salt is present. The final 100 mg/ml formulation developed did not contain any salt and has Tween-80 and a sugar (mannitol) to stabilize the MAb. A preclinical stability study was done under temperature stress conditions to compare the stability of our platform formulation to the higher 100 mg/ml formulation. The stressed samples were then tested by analytical methods that measure aggregation and other stability indicators. These studies predict that the high concentration liquid formulation shelf life will be as long as or longer than our platform formulation. Congratulations to Dr. Paul Casaz and his team for making HCV1 easier to administer to patients.

What's In a Name *contd.*

Harvard protein chemist Edwin Joseph Cohn. The name on our first FDA license (issued #64) to produce "diphtheria antitoxin, vaccine virus and bacterial vaccine made from typhoid bacillus" is the Massachusetts Public Health Biologic Laboratories. Over 50 million doses of purified human albumin and human antisera to such killers as respiratory syncytial virus (RSV), the herpes viruses that cause chickenpox and shingles, hepatitis A virus, smallpox and whooping cough were produced by what became known as the "Cohn Method"

We remained affiliated with the Massachusetts State Department of Public Health and are referred to as the State Laboratory Institute at the 1969 groundbreaking for the new State Laboratory building in Forest Hills. In 1997 we changed our affiliation to the University of Massachusetts Medical School and the name became the University of Massachusetts Biologic Laboratories. Under the leadership of Donna Ambrosino the scientific and therapeutic direction moved to the discovery and production of therapeutic and prophylactic human monoclonal antibodies and MassBiologics was born. Under this name we have produced millions of doses of Td vaccine and human monoclonal antibodies toward the treatment of 7 important diseases including SARS, rabies, C. difficile, hepatitis C viruses, cryptococcus and dysentery.

So what is in our name? I would say a remarkable story that involves seminal scientific discoveries mixed with the astounding advances in actually producing safe, effective medicines to address diseases critical to the public's health. With our new official name as "MassBiologics of the University of Massachusetts Medical School (UMMS)" we will strive to live up to our history of innovation and excellence.

Softball Season Ends in a Nail Biter

By: Paul Bergonzi

MassBiologics just finished their fifth season of softball. Although the results were not as good as last year's division championship we all had a great time playing and ended up finishing in seventh overall. We had a lot of players improve considerably this year and our team batting average was .478 with Kelso Brown leading the team batting with .771.

This year's playoffs had us matched up against the second seed in the division, Organogenesis 1(Organo 1). Organo 1 came into the playoffs hot, winning their last five games and finishing the season 9-3. MassBiologics showed up with their best line-up of all and were primed to deliver an upset to the number two seed. We got off to a quick start and scored two runs in the first before allowing Organo 1 to come back with a quick four runs to finish the first leading by two. MassBiologics showed great defense by only allowing three additional runs in the following five innings while scoring three of our own. We led off the last inning trailing by two. Once again the bottom of the order came up huge, both Katherine Baptista and Erin Burns got on base allowing the top of the order to drive in two runs tying the game 7-7. Unfortunately, MassBiologics could not hold off the number two seed as Organo 1 drove in the winning run to advance to the divisional semi-final round. It was a great game played by both sides and a great season for MassBiologics.

"Katherine Baptista and Erin Burns got on base allowing the top of the order to drive in two runs, tying the game 7-7"

Jessie Ciras at bat for MassBiologics

MassBiologics News

University of Massachusetts Medical School
460 Walk Hill Street
Boston, MA 02126

Phone: 617-474-3000
Fax: 617-474-3250
Web: www.massbiologics.org
Email: information@massbiologics.org

MEDICINE FOR BETTER LIVES

In Our Next Issue…..

Our next issue will be released in early October.

Department News: Catch up on the latest developments across the organization with updates from your Deputy Directors.

A recap of the UMASS Minutemen v. Indiana game

Walk to Cure Cancer highlights

'Leaders in Innovation Seminar Series' feature

Information Services to give update on setup for SmartPhone email

Plus much more...

Contest: Name the Newsletter

This newsletter is the first of many monthly newsletters to come. Just as we need an identity or name for our organization we also need a name for the newsletter. This is where you come in. We are asking employees to submit ideas for what they think the name of our newsletter should be. All entries will be considered and the winner will be announced in next months newsletter with their name for the newsletter officially in place. Please submit all entries to jeffrey.way@massbiologics.org by September 21st.

Administrative Changes cont'd.

As a comprehensive HRDI team each representative will assist you in facilitating all of your human resources needs. Should your question be general in nature and you are not sure of the specialty contact, you can always phone the HRDI main number (508) 856-8323 or email the HRDI department at human.resources@umassmed.edu

Please note that Marlene Tucker will continue to serve as your primary Diversity and Equal Opportunity Office and can be contacted at 508-856-6396 or Marlene.Tucker@umassmed.edu

The first month of the schedule is provided in the following table including photos of the new points of contact you will begin to see on campus. In subsequent months the onsite schedule will be included in the calendar on the last page of the newsletter. To ensure this transition goes smoothly your input will be sought. Please expect intermittent checks with those of you who have received HR services for feedback on HR Services delivery.

September HRDI Schedule Room 2020

Monday	Tuesday	Wednesday	Thursday	Friday
3 **Labor Day Holiday**	4 HRDI Onsite: Michelle Jones-Johnson, Talent and Jim Mack, Talent	5	6 HRDI Onsite: Ben Moorghen, Employee Relations	7
10 HRDI Onsite: Jim Mack, Talent	11	12 HRDI Onsite: TBD	13	14 HRDI Onsite: Jodie Nosiglia, Employee Relations
17	18 HRDI Onsite: Michelle Jones-Johnson, Talent	19	20 HRDI Onsite: Jodie Nosiglia, Employee Relations	21
24 HRDI Onsite: TBD	25	26 HRDI Onsite: TBD	27	28 HRDI Onsite: Ben Moorghen, Employee Relations