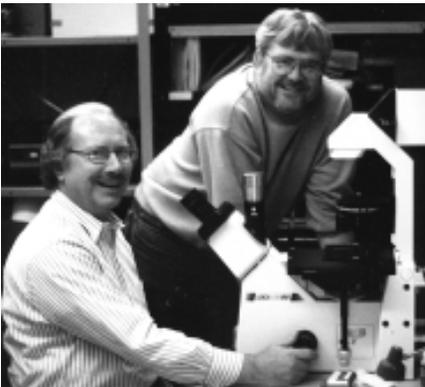




Center for  
Molecular Medicine  
& Genetics

# Advances

## Leon Carlock, Ph.D., and Robert Skoff, Ph.D.: Center Fosters Partnerships Throughout WSU



Robert Skoff, Ph.D., left,  
and Leon Carlock, Ph.D.

Three years ago, Center faculty member Leon Carlock, Ph.D., decided it was time to move away from his research focus of Huntington disease.

Instead, he hooked up with Robert Skoff, Ph.D., professor of anatomy and cell biology, who had long been studying aspects of multiple sclerosis. Together they received a grant from the National Multiple Sclerosis Society.

Today, their partnership has grown and so has their funding. Dr. Skoff is now an associate member of the Center. They have more than \$2 million in funding from several sources, including a \$900,000, four-year NIH grant and two additional Multiple Sclerosis Society grants. And they believe they are on to some important discoveries that will have a great impact on the understanding of multiple sclerosis.

“The Center gave me the opportunity to work with investigators in other units,” says Dr. Carlock. “Bob and I have drawn from unique skills and backgrounds to obtain this funding. Bob needed my molecular biology expertise. I needed his developmental and cell biology expertise. By teaming up we’ve worked across boundaries and have been very successful.”

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### Message from the Director

#### Center Mission Moves Forward with Five-Year Charter Renewal

Revolutionary change demands that you break the rules. Business as usual just isn't enough to be successful.

As researchers around the world rapidly unravel the mystery of the human genome and change the course of medicine as we know it, the Center has focused its mission on pushing these boundaries of knowledge through unprecedented — and sometimes unconventional — partnerships and outreach.

By stretching traditional boundaries and relationships, the Center's faculty is poised to conduct the groundbreaking basic and translational research that will profoundly impact the diagnosis, treatment, and prevention of human disease.

This issue of *Advances* highlights some of the Center's interdisciplinary partnerships and research. Center faculty member Leon Carlock, Ph.D., and Robert Skoff, Ph.D., professor of

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## Center Fosters Partnerships

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"... By teaming up, we've worked across boundaries and have been very successful."

Specifically, Dr. Carlock and Dr. Skoff are investigating one of the causes of the symptoms of multiple sclerosis. Their work looks at the mechanisms underlying the role of proteolipid proteins (PLPs)

in oligodendrocyte death. Oligodendrocytes, vital to all vertebrates, are the supporting cells that ensheath the axons of nerves. Without these cells, axons do not conduct electrical impulses properly, and this causes the symptoms of MS.

For their research, they are studying the ubiquitin-proteasome complex,

which is a major player in protein degradation. Ubiquitin is a small protein that links to proteins targeted for degradation. Using tissue culture systems, they are investigating how normal and mutant PLP proteins are processed by the ubiquitin-proteasome system and how oligodendrocyte death is induced.

In particular, they will examine the molecular consequences of specific PLP mutations in programmed cell death; why overexpression of the normal PLP protein produces cell death; and what role the ubiquitin-proteasome complex plays in regulating protein degradation and cell death.

"By understanding the steps that cause the death of oligodendrocytes, we should be able to develop therapies that prevent their death and this, in turn, could lead to treatment of certain human nervous system diseases," says Dr. Skoff.

To reach Dr. Carlock, please contact him at (313) 577-1013 or via email at lcarlock@cmb.biosci.wayne.edu. To reach Dr. Skoff, please contact him at (313) 577-1165 or via email at rskoff@med.wayne.edu.

### Message From the Director

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anatomy and cell biology, barely knew each other three years ago. Today, they have more than \$2 million in joint funding to investigate multiple sclerosis.

When Scott Dulchavsky, M.D., Ph.D., and head of surgery at Detroit Receiving Hospital, decided he wanted to do more extensive research, the Center was the only Ph.D. program at WSU interested in working with a full-time M.D. Today, Dr. Dulchavsky and advisor Mary Murray, Ph.D., are involved in exciting gene therapy research.

And Mark Hughes, M.D., Ph.D., the Center's director of basic research, has been tapped to head WSU's life sciences initiative.

As a result of making great strides toward its mission, the Center for Molecular Medicine and Genetics has recently received a five-year renewal

of its charter by Wayne State University. This support from the University is further demonstration of the excellent progress and high standards the Center has set since it was created just five years ago.

During this time, the Center has supported and nurtured a wide range of activities in molecular medicine and genetics at Wayne State — through the basic and translational research conducted by our own faculty members and the support by the Center as a whole for cutting-edge molecular medicine and genetics research and facilities throughout the campus. We plan to continue in this direction.

This charter renewal comes at a critical time as the Wayne State University School of Medicine continues its growth and development, the State of Michigan develops a Life Sciences corridor and researchers around the

world are seeking new understanding of the human genome. The Center is well positioned to use this unfolding information and to conduct the novel research that may bring cures and better health to people worldwide.

We will keep you informed about our continued progress and change. I welcome your input and involvement as we move forward. Please feel free to call me at (313) 993-7385.

Sincerely,



**George Grunberger, M.D.**  
Henry L. Brasza Professor  
Director, Center for Molecular  
Medicine and Genetics

## Translational Genomics To Be Major Focus of WSU Life Sciences Efforts

Center for Molecular Medicine and Genetics faculty member Mark Hughes, M.D., Ph.D., will be one of the driving forces in Wayne State University's participation in the State of Michigan's \$1 billion Life Sciences Initiative.

Dr. Hughes, who has already helped WSU to explode into the fast-growing area of translational genomics in the two years since he joined the faculty, has been named scientific director for WSU's life sciences efforts. The University has decided to focus these activities in translational genomics and smart sensors.

In his role, Dr. Hughes will chair WSU's life sciences internal and external steering committee (in development), which will create a 10-year, long-range plan for the University. He will also lead WSU's efforts in translational genomics. Greg Auner, Ph.D., associate professor of electrical and computer engineering, will spearhead WSU's activities in smart sensors.

Dr. Hughes, along with WSU's Interim Vice President for Research and Graduate School Dean George E. Dambach, Ph.D., will also serve on a planning committee for the state's overall Life Sciences Initiative. The committee, which reports directly to Gov. John Engler, will help identify targets for investment and recommend an application process and structure for the new program.

"We have a great opportunity to enhance research very broadly at WSU by building from the base of these two leading edge technologies," says Dr. Dambach. "Human genomics and smart sensors are already outstanding here, and we would like to keep them at the leading edge through the life sciences corridor."

Dr. Dambach says that the dollars available from the state — made available by the Legislature and Gov. Engler from a portion of the state tobacco settlement money — will be allocated to universities in two main

areas: recruitment of the next generation of scientists and collaborative projects that link two or more state universities. A primary goal of the Life Sciences Initiative is creation of a life science industry led by research excellence at the universities that transfers to the private sector.

"The goal of our life sciences program is to develop life sciences at the cutting edge in terms of technological development toward applied science where basic science is on the verge of breakthrough and where it can be developed commercially," says Dr. Dambach. "Because our emphasis is on state-of-the-art technology — in both translational genomics and smart sensors — there will be many opportunities for faculty throughout the campus who are conducting hypothesis-driven research to participate in this far-reaching project."

Watch for the next issue of *Advances* for more information about translational genomics activities already underway at Wayne State University.

## Center's Biotechnology Division Gets New Name



The Center's Division of Research and Biotechnology Development stands poised to serve the needs of WSU's translational genomics efforts and other activities generated by WSU's new life sciences program.

The Division, formerly known as the Biotechnology/ Technology Transfer Laboratory, recently changed its name to more accurately reflect its translational activities.

The Division's unique role at WSU is to use scientific personnel with a dedicated interest in translational research to network and expedite the flow of technology among faculty, the WSU Technology Transfer Office, and local, state, and national biotechnology companies.

"Our mission is to promote academic-industry partnerships and to effectively compete for federal and state funding as these collaborations advance the 'high-tech culture and growth' envisioned as critical for the economic development of Michigan in the next century," says Joan Dunbar, Ph.D.

In fact, the development of a high-tech state was recently mandated by Gov. John Engler in the "State Smart: Michigan Program." This program was the culmination of Gov. Engler's Innovation Forum, a year-long series of meetings addressing the relationship between Michigan universities and industry and the efficient conversion of university knowledge into economic growth.

Three Division members — Dr. Dunbar, Wayne Lancaster, Ph.D., and Joseph D. Artiss, Ph.D., — were active participants in the Forum, which identified biotech-

## Scott Dulchavsky, M.D., Ph.D., Aims High

PROFILE

It's not too often that Ph.D. candidates in the Center for Molecular Medicine and Genetics are paged out of class to operate on a gunshot victim or miss a research seminar to fly to NASA's Johnson Space Center. But Scott Dulchavsky, M.D., has done both.



Dr. Dulchavsky, Ph.D. who received his Ph.D. in molecular biology and genetics from the Center in 1999, wasn't your typical graduate student. He's chief of surgery at Detroit Receiving Hospital and a physician consultant

investigator with NASA's Space and Life Science Directorate.

Dr. Dulchavsky is one of a growing number of physicians associated with the Center whose mission brings physicians and basic scientists closer together so that they can move fundamental discoveries from the bench to the bedside more quickly and seamlessly. The Center was the only Ph.D. program at WSU interested in offering him the opportunity to receive basic science training.

"At that time, I had a major grant with a significant molecular biology component but no background to conduct this part of the research," says Dr. Dulchavsky. "I had asked a Ph.D. lab to help me, but I was uncomfortable farming out such a large portion of the grant. I decided I wanted to be cross-trained as a credible researcher. Robert Rownd (the former Center director), enthusiastically welcomed me. He said translational research is what the Center's mission is all about."

With the support of Ph.D. advisor Mary T. Murray, Ph.D., Dr. Dulchavsky pursued his Ph.D. coursework and thesis, "Biologic Gene Therapy of Mammalian Kidney Ischemia-Reperfusion Injury and Delayed Wound Healing." His research led him to develop the use of a "gene gun" to carry mRNA to wound sites to help in the healing process. He has published one article about his work and has an additional three articles and a patent pending.

"As a trauma surgeon, I am concerned with the healing of wounds, especially as they are affected by diabetes, chemotherapy, and obesity," says Dr. Dulchavsky. "There are ointments available to put on wounds but their effects are often marginal. By delivering the mRNA with a specific vector to a wound site, we can tailor the application for short-term treatment."

Dr. Dulchavsky appreciates the support he received from faculty and staff throughout the Center, especially Dr. Murray. It was an unusual experience for both Dr. Dulchavsky and Dr. Murray, but one from which they both learned a great deal.

"It was unique for a Ph.D. candidate to come to the student-mentor relationship with a whole body of knowledge different than mine, in fact, from the Center's entire faculty," says Dr. Murray. "I learned that many of the things basic scientists take for granted in traditional science can be easily spun off to have clinical significance. And I

helped educate him about how basic scientists see things and their approaches to research."

Dr. Murray and Dr. Dulchavsky are continuing to collaborate on three large grants related to the gene gun (for which Dr. Murray is co-principal investigator), including a \$1 million grant application from the National Institutes of Health. As the Center's graduate officer, Dr. Murray is also involved in a \$1 million NIH grant for "Academic Training in Trauma and Burns," which allows surgical residents to spend two years in basic research.

In addition to conducting exciting, translational research, Dr. Dulchavsky said he believes his Ph.D. is helping him achieve his latest challenge: his goal to be one of the physicians on NASA's Space Station five years from now.

"The NASA space program is very competitive," says Dr. Dulchavsky, who travels to the Johnson Space Center every month in his current role as a physician consultant investigator and also conducts some NASA-related research at Detroit Receiving Hospital. "Forty-eight hundred physicians applied for 19 positions in the astronaut corps. I know that my Ph.D. gave me additional credibility in scientific thinking. It will also help me to conduct research for NASA on bone healing which has implications for long-duration space flights."

## Legislative Update

Several faculty members of the Center for Molecular Medicine and Genetics are part of the State of Michigan's effort to explore legislation that would protect the privacy of genetic information and prevent genetic discrimination. Michigan joins about a dozen other states that are also passing or considering legislation.

Mark I. Evans, M.D., who has a joint appointment in the Center and the Department of Obstetrics and Gynecology, is the committee chair of the Michigan State Medical Society (MSMS) Advisory Committee on Genetic Technology. Other Center committee members include Gerald L. Feldman, M.D., Ph.D.; Anne Greb, M.S.; and Mark Hughes, M.D., Ph.D. The MSMS provides leadership to 13,000 Michigan physicians to help influence state health policy initiatives.

The MSMS committee is addressing the implications and merits of a series of bills (SB 589-595) that focus on various genetic privacy issues. In June, the committee met with representatives from the offices of Gov. John Engler and State Sen. John J.H. Schwartz, M.D.

Three of the bills (SB 589-91) prohibit insurance companies from requiring individuals to undergo genetic testing or from asking about genetic test results. Another bill (SB 592) ensures that parents are informed about the nature of newborn screening for genetic

conditions and about the option of retaining a sample for later identification purposes. SB 593 requires physicians to obtain written informed consent before ordering genetic testing. SB 594 and 595 require the subsequent destruction of DNA samples used for forensic purposes or for the establishment of paternity. The Senate is expected to consider the bills this fall.

For additional information about this series of bills, browse the Web at <http://www.michiganlegislature.org/>.

## Michigan Teratogen Information Service Now Available for Expectant Parents



Above, Robin Gold, M.S., speaks at the grand opening of the miTIS.

A new service that advises expectant parents about how substance exposures may affect their unborn children kicked off earlier this year at the Children's Hospital of Michigan.

The Michigan Teratogen Information Service (miTIS) provides facts about teratogens — drugs, medications, chemicals, and environmental toxins — that can cause birth defects.

Expectant parents, community members, and health care providers are encouraged to call miTIS with questions about exposure to substances during pregnancy. Using an extensive research database, miTIS answers most questions immediately and responds to all inquiries within 24 hours. Referrals to genetic

counselors, high-risk pregnancy specialists, and community services are available. All information is confidential and services are provided free of charge.

miTIS is under the direction of Medical Director Yvette R. Johnson, M.D., M.P.H., an assistant professor of pediatrics at WSU in the Department of Pediatrics/ Neonatology at the Children's Hospital of Michigan. miTIS program coordinator is Robin Gold, M.S., an associate member of the Center.

miTIS is affiliated with WSU, Children's Hospital of Michigan, and Hutzel Hospital's Division of Reproductive Genetics. For more information, please call (313) 966-9368 or 1-(877) 52-MITIS (64847). You may reach Robin Gold via email at [rgold1@dmc.org](mailto:rgold1@dmc.org).

## Center Holds Second Annual Scientific Retreat in November

The Center will hold its Second Annual Scientific Retreat on November 19-20, 1999, at the Maumee Bay Resort and Conference Center on Lake Erie in Ohio. The planned activities include a scientific poster session, lectures, and invited speaker. Mark Hughes, M.D., Ph.D., retreat organizer, welcomes any comments, suggestions, and volunteers. You may reach Dr. Hughes at (313) 993-1353 or via email at [mrhughes@erols.com](mailto:mrhughes@erols.com).

## FACULTY NEWS

**Joseph D. Artiss, Ph.D.**, associate professor of pathology and associate member of the Center, recently received a National Institutes of Health (NIH) STTR Phase I Grant for "A New Homogeneous Aptamer-Based Binding Assay." Co-investigators on the grant are **Russell L. Finley, Jr., Ph.D.**, and **William F. Walters, Jr.**, vice president of technical operations at Pointe Scientific, Inc., in Lincoln Park, Mich. The project will develop a new platform for an aptamer-based binding assay that will be used in the development of a quick, simple, non-isotopic homogeneous assay for analytes of clinical interest. The one-year grant for \$106,000 is from the NIH's National Institute of General Medical Sciences.

**Erawati Bawle, M.D.**, and **Joan V. Conard, M.S.**, were members of the faculty and organizing committee of "Craniosynostosis: Advances in Diagnosis, Management, and Genetics," a review and update program for primary care providers hosted by the Wayne State University School of Medicine at the Children's Hospital of Michigan in August.

**Morris Goodman, Ph.D.**, served as chair of a planning meeting of the American Academy of Arts and Sciences at the House of the Academy in Cambridge, Mass., in August. The goal of the meeting was to explore how the Academy can help create a multidisciplinary international program of research and education on humankind's evolutionary origins.

**Anne Greb, M.S.**, was elected as a new member of the Wayne State University School of Medicine's Curriculum Committee by the Faculty Senate.

**George Grunberger, M.D.**, Center director, served as an expert medical panelist on diabetes for the Federal Highway Administration (FHA) of the U.S. Department of Transportation. This panel of four physicians will help the FHA consider the overall assessment and management of risk associated with commercial driving by individuals being treated with insulin.

**Fazlul Sarkar, Ph.D.**, associate professor of pathology and associate member of the Center, was the co-principal investigator on a recently released study which found that tomatoes may offer protection against cancer. The study was presented at the American Association for Cancer Research in April by **Omer Kucuk, M.D.**, Wayne State University professor of internal medicine and oncologist at the Barbara Ann Karmanos Cancer Institute.

The following individuals at Wayne State University associated with the Center for Molecular Medicine and Genetics are newly certified by the American Board of Medical Genetics. They are: **Mohamed El-Naggar, M.D.**, a current Center graduate student, certified in molecular genetics and cytogenetics; **Barouh Feldman, M.D., Ph.D.**, a fellow in



*Welcome to **Gerald L. Feldman, M.D., Ph.D.**, who is joining the Center faculty as Wayne State University's new director of Clinical Genetics Services. He will also be medical director for the Center's Genetic Counseling Program and program director of WSU's Medical Genetics Residency Program. He will continue in his role as director of the Detroit Medical Center's Molecular Genetics Diagnostic Laboratory. Dr. Feldman, a pediatrician who specializes in medical genetics, most recently served in the Department of Medical Genetics at Henry Ford Hospital. He is board certified by the American Board of Medical Genetics in clinical genetics, molecular genetics, and biochemical genetics.*

medical genetics in the Division of Reproductive Genetics at Hutzel Hospital, certified in clinical genetics; **Kristin Monaghan, Ph.D.**, alumni of the Center, a member of the Department of Medical Genetics at Henry Ford Hospital and associate member of the Center, certified in molecular genetics and medical genetics; **Trieu Vo, Ph.D.**, alumni of the Center, a member of the WSU Department of Pathology and associate member of the Center, certified in molecular genetics; and **Yuval Yaron, M.D.**, in the Division of Reproductive Genetics at Hutzel Hospital, certified in clinical genetics.

The following WSU genetic counselors are newly certified by the American Board of Genetic Counseling. They are: **Rajani Aatre, M.S.**, Department of OB/GYN; **Amy Decker, M.S.**, Department of Medical Genetics at Henry Ford Hospital; **Leigh Anne Flore, M.S.**, Department of OB/GYN; **Karen Krajewski, M.S.**, Department of Neurology; **Heather Lee**, Department of OB/GYN; and **Nancie Petrucelli, M.S.**, Department of Medical Genetics at Henry Ford Hospital.

## FACULTY NEWS

Four CMMG faculty members were recently honored by the Wayne State University School of Medicine. **Li Li, Ph.D.**, received its Research Excellence Award in recognition of excellence in biomedical research. **Leon R. Carlock, Ph.D.**; **Russell L. Finley, Jr., Ph.D.**; and **Mary T. Murray, Ph.D.**, received College Teaching Awards for dedication to excellence in teaching and contributions to the professional development of students.



Genetic Counseling Masters Program graduates first class.

## STUDENT NEWS

Congratulations to **Carol Baker, M.S.**, **Barbara Corey, M.S.**, and **Alicia Salkowski, M.S.**, who recently became the first graduates of the Wayne State University School of Medicine's Genetic Counseling Graduate Program. They each earned a master of science in genetic counseling. Genetic counseling helps individuals understand their risks for inherited conditions and birth defects so they can make informed decisions about genetic testing. Wayne State's genetic counseling program is one of only 23 graduate programs worldwide, which together graduate about 100 students each year.

The Center welcomed seven new students into the Ph.D. training program in Molecular Biology and Genetics this fall. They are **Raymond Esper**, **Rami Khoury**, **Wenijian Li**, **Wei Lu**, **Subhadra Ramanathan**, **Aleric Howell Soans**, and **Lin Tang**.

Two Center students recently completed their Ph.D. degree requirements in Molecular Biology and Genetics. They are **Scott Dulchavsky, M.D., Ph.D.**, and **Rolland Reinbold, Ph.D.** **Sompong Vongpunsawad** earned his M.S. degree. Hearty congratulations to them all!

## Division Gets New Name

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nology and life sciences as one of three "industries" to become potential areas of excellence in Michigan. Dr. Dunbar was a presenter at the final meeting in which recommendations of the Forum's subcommittees were reported to Gov. Engler.

To advance academic-small business collaborations, the Division actively promotes and facilitates STTR grant applications to the National Institutes of Health and National Science Foundation. (Please see page 6 for a recent success story.) The Division is working with other faculty members and local as well as national biotechnology companies on additional STTR applications.

Further information about the Division's activities will soon be available on the Great Technologies Web site at [www.GreatTechnologies.org](http://www.GreatTechnologies.org). This Web site was initiated by the Governor's Innovation Forum as a further mechanism to promote and market the technologies and successes of Michigan's universities and industry.

You may also contact Dr. Dunbar at (313) 577-5542 or via email at [jdunbar@cmb.biosci.wayne.edu](mailto:jdunbar@cmb.biosci.wayne.edu) or Dr. Lancaster at (313) 577-0028 or via email at [wayne@cmb.biosci.wayne.edu](mailto:wayne@cmb.biosci.wayne.edu).

Ph.D. candidate **Stanley A. Forfa** presented the poster, "Translational Masking via a Translation Regulatory Particle (TRP) Isolated from the *Xenopus laevis* Oocyte," at the Fourth Annual RNA Society Meeting in Edinburgh, Scotland, in June.

## Attend the Second Annual International Motor City Diabetes Symposium

"From Beta Cell Dysfunction to Curing Type 1 Diabetes Mellitus" is the theme of the Second Annual International Motor City Diabetes Symposium on October 29-30, 1999, at the Wayne State University Medical Campus in Detroit.

Symposium organizers are **George Grunberger, M.D.**, Center director, and **Anders Sima, M.D., Ph.D.**, professor of pathology.

Featured speakers include investigators of international reputation such as **Stefan S. Fajans, M.D.**, University of Michigan; **Franz Matschinsky, M.D.**, University of Pennsylvania; **Christopher B. Newgard, Ph.D.**, University of Texas Southwestern; **David E. Sutherland, M.D., Ph.D.**, University of Minnesota; and **Gordon C. Weir, M.D.**, Harvard Medical School.

Registration is \$100 (reduced for WSU faculty and free for WSU graduate students) and includes refreshments, course materials, and processing of CME credits. For more information or to register, please call (313) 993-8029, email [g.grunberger@wayne.edu](mailto:g.grunberger@wayne.edu), or browse the Web at <http://www.med.wayne.edu/diabetes/symposium99>.

## Seminar Series: "Molecular Medicine, Genetics, and Gene Therapy"

Learn about some of the latest research and trends in molecular medicine and genetics at the Center's Molecular Medicine, Genetics and Gene Therapy Seminar Series. Presentations by leading experts are held every other Thursday at noon in Room 2268, Scott Hall. The following is a list of highlights from the fall semester. For the most up-to-date information on the series, please visit the Center's Web site at <http://cmmg.biosci.wayne.edu>.

### November Events

- 4 Jay Tischfield, Rutgers University: "Loss of Heterozygosity" or: "How I Learned to Stop Worrying and Love Mitotic Recombination."
- 11 Bruce Edgar, Fred Hutchinson Cancer Research Center.
- 18 Peter White, Children's Hospital of Philadelphia: "Navigating the Human Genome with CompView."

### December Events

- 2 Lucia Schuger, Wayne State University School of Medicine: "Cell Shape and Smooth Muscle Myogenesis."
- 16 Jerry Workman, Pennsylvania State University: "Multiprotein Complexes that Regulate Transcription by Modifying Chromatin Structure."

For more information, please contact Li Li, Ph.D., at (313) 577-8749 or via email at [llli@med.wayne.edu](mailto:llli@med.wayne.edu).

*Advances* is published by the Center for Molecular Medicine & Genetics.

This newsletter is edited by

**Anne E. Greb, M.S.**

313-577-6298

[agreb@cmb.biosci.wayne.edu](mailto:agreb@cmb.biosci.wayne.edu)

**David D. Womble, Ph.D.**

313-577-2374

[dwwomble@cmb.biosci.wayne.edu](mailto:dwwomble@cmb.biosci.wayne.edu)

The online version of the newsletter and other information about CMMG are available at the CMMG Web site: <http://cmmg.biosci.wayne.edu>.

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Center for  
Molecular Medicine  
& Genetics

Wayne State University School of Medicine  
3216 Scott Hall  
540 East Canfield  
Detroit, MI 48201  
313-577-5323  
[cmmg@cmb.biosci.wayne.edu](mailto:cmmg@cmb.biosci.wayne.edu)  
<http://cmmg.biosci.wayne.edu>