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The Beat Newsletter

College of Medicine

The Beat

University of South Alabama
College of Medicine

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BEYOND FOLIC ACID: EXAMINING THE ADVANTAGES OF THE NATURAL TETRAHYDROFOLATES FOR THE PREVENTION OF DISEASE

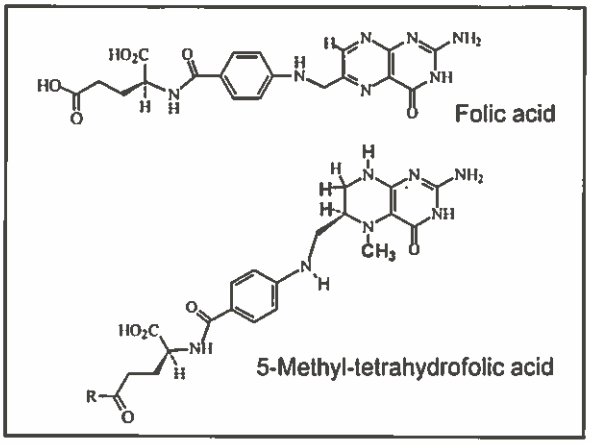
Since 1945 when it was first synthesized folic acid has been used primarily to prevent anemia. In the last decade the role of adequate folate status in the prevention of neural tube defects (NTD), vascular diseases [e.g. coronary artery disease (CAD) and stroke], and cancer [e.g. colorectal and cervical] has become increasingly apparent. Much of the evidence on the importance of folate is epidemiological. For example, the Harvard Nurses' Health Study showed a 75% reduction in risk for colon cancer in women who are long term users of multivitamins containing folic acid, even when controlled for intake of other vitamins and calcium.

The biochemical basis for the protection afforded by folate is uncertain, and probably not the same for every disease. The two areas of folate dependent metabolism that are most often considered are 1) its role in the biosynthesis of thymidylate and the purine nucleic acid bases, and 2) the methylation of homocysteine to produce methionine. Typically, dietary intake of methionine is not sufficient to supply the need for S-adenosylmethionine, the primary methyl donor in mammals which is responsible for many dozens of reactions, including DNA methylation. The spent S-adenosylmethionine ultimately returns to the small pool of homocysteine to be recycled by a one-carbon transfer from 5-methyl-tetrahydrofolate (5-MTHF). Many investigators are pursuing the hypothesis that when folate status is poor, homocysteine increases to levels that may be toxic to the vascular endothelium and other cell types. Whether homocysteine directly causes diseases such as CAD, stroke, and NTD, as often proposed, or is merely a marker for folate deficiency remains to be demonstrated conclusively. None-the-less, it has been estimated that between 13,500 to 50,000 CAD deaths annually in the U.S. alone could be avoided with increased folate intake. More than nine large-scale placebo controlled trials of folic acid in combination with vitamins B6 and B12 are now in progress to test this assertion.

Folic acid, however, is not a significant natural form of folate, and is not found in fresh unfortified foods. All known metabolic processes in higher organisms are performed by the reduced folates. Were it not for the adventitious activity of the enzyme dihydrofolate reductase (DHFR) in promoting a very slow conversion of folic acid to the active forms, the synthetic material would serve no useful purpose. There are several other aspects of folic acid that have not received enough attention considering the growing significance of folate nutrition and health outcomes.

To be utilized properly folic acid must be well absorbed from the digestive tract, distributed in an appropriate fashion to the tissues, and activated by DHFR. In none of these respects is folic acid entirely perfect. Experiments using labeled compounds suggest that in contrast to purified natural folates, there is considerable individual variability of intestinal transport of folic acid. Moreover, although at low dose (less than 200 µg) most folic acid is converted to 5-MTHF (the primary folate in plasma) on crossing into the portal vein, this is not always the case at higher doses such as with the U.S. RDA of 400 µg.

Recent work by Drs. June Ayling and Steven Bailey, Department of Pharmacology, has shown that in some people unreduced folic acid can persist in the blood for over 24 hours. Reports from several groups suggest that, in contrast to 5-MTHF, folic acid in the portal vein is highly sequestered by the liver, and only slowly released to the systemic circulation. Thus, while folic acid is bioavailable for most people, and has been shown to lower the risk of NTD (by about 72%), it is not clear that this is the optimal folate for the



The structure of synthetic folic acid and 5-methyl-tetrahydrofolic acid (R=OH) (5-MTHF), the form of folate found in plasma, milk, and orange juice. In most tissues 5-MTHF is also a major form, but like other intracellular folates is polyglutamylated (R=$glu_{[n]}$ $1 \leq n \leq 11$), an area of research in which the late Dr. Charles Baugh made significant contributions.

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entire population. With support from Merck KGaA, Dr. Ayling's group (in collaboration with other investigators) is examining the metabolic consequences of incomplete reduction of folic acid. The extent to which homocysteine can be lowered by folic acid in comparison to 5-MTHF is also being studied. Along with ongoing investigations of the bioavailability of the natural folates in other labs, a means for providing more assured folate nutrition is being established as a way to prevent disease.

DIRECTOR HIRED FOR NEW OFFICE OF TECHNOLOGY DEVELOPMENT

More than $33.5 billion in economic activity and 280,000 jobs were directly attributable to the commercialization of academic research in 1998, according to the Association of University Technology Managers. Universities are a fundamental source of new innovations, and the transfer of these technologies to the marketplace continues to drive the global economic boom.

The University has established a campus-wide office to move USA inventions from lab to market. The Office of Technology Development will serve the entire USA community in identifying, managing, and commercializing the products of research and development. This office gives the University an additional way to expand opportunities for basic and applied studies, to strengthen ties with the local business community, and to increase resources for its educational and research missions.

Nicole Baute has been named Director of Technology Development for the University. She comes to USA from Tulane University, where she was Assistant Director of Technology Development for five years. Tulane consistently ranks among the top twenty universities in the country in the amount of revenue generated by its invention portfolio, and Baute hopes to replicate that success here.

"There is tremendous opportunity at the University of South Alabama to commercialize inventions coming out of the growing research base," Baute said. "By aggressively managing the intellectual property developed here, and by strategically moving inventions into the commercial sector, we can make a positive difference for the University, its faculty, and the Mobile community."

During the past two years, Baute also served as Staff Director for the Louisiana Gene Therapy Task Force, a statewide coalition of universities, politicians, and businesses created by the Louisiana Legislature to build a strategic plan for economic development based on biotechnology research. Baute helped secure $6.8 million in state appropriations for the Task Force proposals and won an award from the Press Club of New Orleans for best public relations campaign based on materials developed for this project.

Baute, 33, is a native of Covington, Louisiana. She earned her bachelor's degree in natural sciences from Loyola University New Orleans in 1989 and was recognized as the outstanding science graduate as well as the top female graduate that year. She also holds a master's degree in public policy from Georgia Tech, with a concentration in technology-based economic development.

In talking about technology development, Baute likes to stretch traditional perceptions. "Typically, people just think of patents when they hear the term "technology transfer," Baute said. "Patents, though, are only one starting point for this whole process. Sometimes you don't even need a patent to produce value from an invention. Looking at all the different facets of technology development will maximize the benefits for each invention."

Baute added: "It is an exciting time to be at USA, and I am looking forward to working together with members of the University community to build a program that supports the growing reputation of the University of South Alabama."

The Office of Technology Development is located in CSAB 253; Ms. Baute can be reached by phone at 460-7932 or via email at nbaute@usamail.usouthal.edu

LAB SAFETY INSIGHTS

In the new Lab Safety Review column, Laboratory Network.com readers will find a monthly series of articles contributed by experts in the field of lab safety. Articles include information on how to select safe products for their applications, describe safer ways to utilize equipment, highlight new innovations in lab safety, and suggest classic techniques for ensuring a safe environment. Each month a different lab safety expert contributes an article about product safety, ventilation, ergonomics, regulatory issues. In addition to these monthly features, the Lab Safety Review will also include a regular update of general lab safety tips.

The lab review column can be found at: http://www.laboratorynetwork.com.

TUFTS UNIVERSITY HELPS CREATE EDUCATION PROGRAM ENCOURAGING ORGAN DONATION

In an effort to increase the rate of organ donations, Tufts University School of Medicine, the United Network for Organ Sharing (UNOS), and Medscape, Inc. launched the nation's first internet-based continuing medical education program on organ donation. The program "Donation and Transplantation: Into the New Millennium", is for health care professionals and the general public, and consists of a series of teleconference lectures by organ donors and transplantation experts. For more information visit http://www.tufts.edu/communications/OrganTransplant.html

If you would like to submit an article for publication, please forward it to:

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GARDNER APPOINTED TO HEALTH COUNCIL BY GOVERNOR

Gov. Don Siegelman has appointed **Dr. William Gardner**, Lenior Locke Professor and chairman of pathology, to the statewide Health Coordinating Council. The council's purpose is to advise the Alabama Health Planning and Development Agency on all health planning and development functions required by law, which governs the state agency.

Gardner will serve a three-year appointment. The Health Council's role include reviewing and revising the Alabama health plan when necessary.

NEWS BRIEFS...

A new study published in the medical journal of Contraception finds for the first time that the newer, 'lose-dose' pills with only 20 micrograms of estrogen are just as effective in clearing up skin as are pills with higher doses of estrogen. The study was led by *Ian Thorneycroft, Ph.D., M.D., professor of obstetrics and gynecology*. The study examined 58 healthy patients who took three cycles of 20 microgram treatment. By random selection, half the women took a 20-microgram pill containing the progestin *levonorgestrel*, and the other half took a 20-microgram pill containing the progestin *norethindrone acetate*.

Eighty-five percent of those in the first group, and 67 percent of those in the second group, experienced a significant reduction in acne lesions after treatment. None of the patients experienced weight gain. "The results of this study show that women who take oral contraceptives to improve their skin, as well as prevent pregnancy, now have more options," added Dr. Thorneycroft.

Regina Benjamin, M.D., *associate dean for rural health*, has been selected to serve on the national advisory panel for the Network for Supervising Physicians, a new service from the American Academy of Physician Assistants.

Richard Esham, M.D., *professor of medicine*, participated in the first national training meeting for community-based preceptors, held in Tampa. He gave two workshops and assisted in training sessions. Three hundred educators from across the nation attended the conference.

Bernita Finley, *former USA Bear Student*, received a 1999 UNCF-Merck Undergraduate Science Research Scholarship Award for the 1999-2000 academic year. Ms. Finley will be mentored by a Merck scientist and receive two 10-12 week Merck Summer Internships. The UNCF-Merck Scholarship Awards are intended to help black undergraduate students who are interested in science to further their science education and potentially pursue science careers. Ms. Finley has been accepted to USA College of Medicine and will begin her studies in the fall of 2000. Her stated long term goal is to conduct medical research.

BLAND DELIVERS EMMETT B. FRAZER LECTURE

Kirby Bland, M.D., Chairman of Surgery at the University of Alabama at Birmingham was the honored speaker for the seventeenth annual Emmett B. Frazer Endowed Lecture, March 24th at the USAMC. Dr. Bland's topic was "Management of Early Breast Cancer." He also spoke at the Mobile Infirmary Medical Center on "Prospective Trials in Rectal Cancer."

Dr. Bland, a native of Dothan, Alabama recently assumed the position of Chair of Surgery at UAB, after a distinguished career at the University of Florida and most recently, as Chair of the Department of Surgery at Brown University School of Medicine. His well-known text, *The Breast: Comprehensive Management of Benign and Malignant Diseases*, written with Dr. Edward Copeland, III, is now in its second edition.

The Emmett B. Frazer Lectureship was established in 1982 for the purpose of giving local surgeons the opportunity to discuss current practices with surgical leaders from around the country. Dr. Frazer, who died in 1985, was a Mobile physician for more that 60 years and was internationally recognized for his accomplishment as a surgeon. He was a pioneer in surgical practices and the first surgeon with specialized training in the surgical sciences to practice in Mobile.

NIH LAUNCHES CLINICAL TRIALS REGISTRY

The National Institute of Health has launched the first phase of its congressionally mandated clinical research trial database. The service, ClinicalTrials.gov, is an Internet-based service that currently contains information on more than 4,000 federal and private trials primarily sponsored by the National Institutes of Health. The National Library of Medicine (NLM) spearheaded the creation of this website. In addition to the trails database, extensive links are available to the NLM's consumer health information service, MEDLINE plus. To learn more, visit http://www.clinicaltrials.gov

RODNING INDUCTED INTO LEXINGTON WHO'S WHO

Charles B. Rodning, M.D., Ph.D., Professor and Vice-Chair of Surgery, has been named to the 1999/2000 Edition of the Lexington Who's Who Registry of Executives and Professionals. Lexington Who's Who is an annual publication comprised of detailed biographies dedicated to the recognition of individuals who have demonstrated leadership and achievement in their occupation, industry, or profession.

Dr. Rodning is also listed in the Directory of Medical Specialists, American Men and Women of Science, Who's Who in Science and Engineering, Who's Who in the South and Southwest, Who's Who in America, and Who's Who in American Education. Together with Dr. Arnold Luterman, Dr. Rodning recently published a pictorial and historical monograph entitled "Tradition of Excellence: A Pictorial History of Surgical Education at the Mobile General Hospital and College of Medicine/ Medical Center".

MATCH DAY HIGHLIGHTS

The National Residency Matching Program (NRMP) is the primary route by which applicants to residency programs obtain training position at U.S. teaching hospitals. Match Day occurred on March 16th, for the 33,528 medical student graduates that registered to participate in Match 2000, 10,839 are non-U.S. citizen international medical school graduates. This is the smallest number of non-U.S. citizen registered since 1995, a decrease of 22.5 percent over last year. According to the NRMP, 25,056 individuals participated in the Match this year, a slight decrease from that of 1999. A total of 20,598 first-year residency positions were offered, an increase of 145 positions from last year. Eighty-nine percent of the first-year positions were filled by U.S. medical school graduates.

The NRMP reported that nearly 25% of matched U.S. seniors will enter primary residency programs. Approximately 14% of U.S. seniors will enter family practice residency programs. Nearly 13% will enter pediatrics residency programs.

Match Day Results:

UNIVERSITY OF SOUTH ALABAMA SENIORS RESIDENCIES RECEIVED BY DISCIPLINE

	Class of 1996		Class of 1997		Class of 1998		Class of 1999		Class of 2000	
PRIMARY CARE:	47	73%	42	65%	41	65%	33	55%	35	59%
Internal Medicine	26	41%	12	18%	16	25%	12	20%	23	39%
Family Medicine	15	23%	22	34%	12	19%	91	5%	7	12%
Pediatrics	4	6%	7	11%	8	13%	8	13%	4	7%
Med/Peds	2	3%	1	2%	5	8%	4	7%	1	2%
Anesthesiology	2		3		1		2		2	
Dermatology	0		0		0		1		1	
Emergency Medicine	2		2		0		1		4	
Neurological Surgery	0		0		1		0		0	
Neurology	0		0		0		0		1	
Ob/Gyn	4		5		5		5		4	
Ophthalmology	1		1		2		3		1	
Orthopedics	0		0		3		0		1	
Otolaryngology (ENT)	0		1		0		1		0	
Pathology	2		4		0		3		0	
Psychiatry	4		0		1		0		1	
Radiology	2		1		2		2		3	
Surgery	0		5		6		5		4	
Transitional	0		0		0		0		2	
Urology	0		1		0		3		0	

NIH AGREEMENT WITH DUPONT ON TRANSGENIC ANIMAL TECHNOLOGY

On January 19, 2000 the National Institutes of Health and DuPont announced that they have signed an agreement on the use of DuPont's proprietary OncoMouse™ transgenic animal technology covered by the Harvard "Leder" patents. The Memorandum of Understanding (MOU) resolves long-standing issues of access by academics to this technology, originally developed through DuPont funding at Harvard University, and licensed exclusively to DuPont. The OncoMouse™ transgenic animal technology relates to animal models that develop tumors as a consequence of containing a recombinant activated oncogene sequence. First described by Dr. Philip Leder, its usefulness in basic medical research is widely recognized as these mice provide key model systems for the study of cancer and in testing the effectiveness of novel cancer therapeutics.

Under the MOU, DuPont will continue to provide, at no cost, the OncoMouse™ transgenic animal technology to academic laboratories for research uses and will allow unencumbered use and transfer of this technology among researchers at not-for-profit institutions. The MOU imposes no limitations on scientific publications or so-called "reach-through" rights. The full text of this agreement is available at http://www.nih.gov/od/ott

USA STROKE CENTER REPORTS TPA STUDY AT INTERNATIONAL CONFERENCE

Researchers with the USA Stroke Center say subtle abnormalities in a CT scan should not prevent a stroke patient who meets all other criteria from receiving the clot dissolving drug TPA. The study, conducted at USA Hospitals by **Drs. Jorge Mendizabal, Francis Greiner** and **Richard Zweifler** of the USA Stroke Center and USA medical student, **Douglas N. Lurie**, was presented by special invitation at the 25th International Stroke Conference of the American Heart Association held in New Orleans, February 10th - 12th. Lurie gathered data for the study and made the platform presentation titled *"Do Early CT Changes Predict An Adverse Outcome in Acute Ischemic Stroke Patients Who Undergo Thrombolysis?"*

TPA study conducted by: (pictured left to right) Dr. Jorge Mendizabel, Dr. Francis Greiner, Douglas Lurie (medical student) and Dr. Richard Zweifler.

TPA is a groundbreaking drug that has been shown to be highly effective in treating ischemic strokes when administered within 3 hours of a stroke's onset. The drug works by attacking clots that obstruct blood flow to the brain. The study retrospectively looked at 36 stroke patients who received TPA at USA Hospitals over a two year period. Some of these patients had the abnormalities in their CT scans, yet had positive outcomes. The USA Stroke Center has been using TPA since it was approved for use in stroke patients by the FDA. For more information on stroke or the TPA study, contact the USA Stroke Center at (334)470-5801.

NOBEL LAUREATE PRESENTS DISTINGUISHED SEMINAR

The University of South Alabama College of Medicine will host a Distinguished Scientist Seminar presented by Nobel Laureate Arthur Kornberg, M.D., on April 12 at 4 p.m. in the Medical Sciences Building Auditorium at USA Main Campus. His lecture is entitled, *Biotechnology: Impact on Science, Medicine and Industry.*

Dr. Kornberg was invited to speak at the medical college by the USA Basic Medical Sciences Student Organization (BMSSO). "We are extremely fortunate to have Dr. Kornberg come to Mobile and share his vast experiences with us," said Cathy Webb, president of BMSSO. "His work and his dedication to the search for answers to scientific questions is a strong motivator for students beginning their research careers."

In 1959, Dr. Kornberg shared the Nobel Prize in Physiology or Medicine with Dr. Severo Ochoa for their discovery of mechanisms in the biological synthesis of RNA and DNA. This breakthrough research answered basic biological questions, and today serves as the basis for new scientific discoveries in medicine.

Dr. Kornberg has devoted his life to research in biochemistry, particularly enzymes. First at NIH and then at the University of Washington and Stanford University, he spent decades isolating and purifying the enzymes that form the basis of cells. In fact his autobiography is titled *For the Love of Enzymes.*

A steadfast advocate of biochemistry as the path to understanding fundamental biological processes, Dr. Kornberg could, despite his medical degree, be taken as the quintessential basic scientist. His contribution to the field of Biochemistry is enormous. In addition to his work associated with the Nobel Prize award, he and his laboratory were first to achieve the artificial synthesis of viral DNA - "creation of life in a test tube," as the journalists - to his displeasure headlined it.

Dr. Kornberg's achievements and contributions go beyond his own research, his role as an educator and a mentor have led to others to search for answers. Many of these scientists have also been recognized with a Nobel Prize award. His three sons are successful researchers in molecular biology. At the University of Washington and at Stanford, he headed groups of scientists who became leaders in the emerging fields of genetic recombination and biotechnology. Many of the enzymes he isolated are the same ones used in today's sophisticated sequencing and cloning techniques.

By: Paul Taylor

ONLINE QUESTION BANK FOR U.S. MEDICAL LICENSING EXAM (USMLE)

On March 15th - Kaplan, the nation's premier educational and career services company, introduced the only customized online exam preparation service for Step One of the United States Medical Licensing Exam (USMLE) at www.kaptest.com. Called Qbank, the new service enable medical students the unique ability to custom design their own practice test online for the USMLE Step One Exam, the first of three exams necessary to become a licensed U.S. physician. More than 46,000 U.S. medical students and foreign doctors take the USLME annually.

The Qbank will become the foundation for a full range of online educational tools that will be introduced later this year. Distance learning tools are quickly becoming an integral part of student preparation. Kaplan's technology now allows medical students to create a completely tailored study session each and every time they use the Qbank. This new technology will meet the needs of all kinds of students, ranging from those pressed for time who want nothing more than a quick assessment tool, to those taking center-based courses who seek additional computer-delivered questions.

LUNDBERG TO SPEAK AT INFOFAIR 2000

InfoFair 2000 will take place April 12-13th in the College of Medicine Conference Room on USA Main Campus. The keynote speaker will be Dr. George Lundberg, current Editor in Chief of Medscape and former Editor of JAMA. Dr. Lundberg, a figure of national prominence and highly respected in medical and publishing circles, will be a welcome addition to the InfoFair experience. Dr. Lundberg's seminar is slated for April 12th at 9:00am in the MSB auditorium. His topic is entitled *"New Developments on the Medical Internet."*

InfoFair 2000 will showcase the services of the Biomedical Library and Media Productions Services and will highlight exhibits of interest to health care professionals, educators and students.

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