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Study identifies new class of antibiotics with potential to fight “superbugs”

Eleftherios Mylonakis, MD, leads team of researchers from Brown, Emory and Northwestern Universities, Massachusetts Eye & Ear Infirmary and Massachusetts General Hospital

Providence – An infectious disease researcher and physician at Lifespan is the senior author of a study just published in *Nature* about the discovery of a new class of antibiotics that could one day help combat the alarming emergence of drug-resistant “superbugs.”

**Eleftherios Mylonakis, MD, PhD**, chief of infectious diseases at Lifespan affiliates Rhode Island Hospital and The Miriam Hospital in Providence, and Charles C.J. Carpenter Professor of Infectious Disease at Alpert Medical School of Brown University, led a multidisciplinary team of researchers searching for drugs to target bacteria that have developed a resistance to conventional antibiotics. Their pioneering methods and discovery of a new synthetic class of antibiotics is the subject of a paper published online in *Nature* this week.

Their research led to the identification of two synthetic retinoids, both of which demonstrated the ability to kill MRSA (*methicillin-resistant Staphylococcus aureus*), a type of staph bacteria that is resistant to several antibiotics. Retinoids, which are chemically related to Vitamin A, are used to treat a variety of health problems, including acne and cancer.

“This is an emergency,” Dr. Mylonakis said, citing a World Health Organization (WHO) projection that “by 2050, superbugs will surpass cancer as the global No. 1 killer. This is a frightening situation. It affects more than individuals in the hospital or the very ill or the very old. It affects everybody.”

Dr. Mylonakis collaborated on the study with researchers from Massachusetts Eye and Ear Infirmary, Massachusetts General Hospital, Brown University, Emory University and Northwestern University. He said that teams like his are stepping in to fill a void left by the major pharmaceutical companies, which for a variety of reasons have not invested in the development of new antibiotics for many years.

“In a simplistic way it’s a math problem,” said Dr. Mylonakis. “It takes the bugs an average of two years to develop resistance to antibiotics. It takes more than 10–15 years of work to get an antibiotic into clinical practice.”

Dr. Mylonakis said drug-resistant staphylococcus is of great concern for several reasons: it’s omnipresent in the environment and on our skin, is highly virulent, and can cause serious blood, bone and organ infections.

The research team developed novel ways to screen a remarkable 82,000 synthetic compounds to identify those that would serve as effective antibiotics but not be toxic to humans. Ultimately, 185 compounds were identified that decreased the ability of MRSA to kill laboratory roundworms.

Of those, two, both synthetic retinoids, were selected as the best candidates for further study. One of the original compounds and a completely novel, more active derivative were effective when tested on a mouse thigh infected with MRSA.

Sophisticated computer modeling and other studies showed that these retinoids impair bacterial membranes. Moreover, these compounds kill so-called MRSA “persister” cells that are drug-resistant dormant cells that are not susceptible to current antibiotic therapies. The ability of the drugs to make bacterial membranes more permeable also appeared to be a factor in why they worked well in tandem with an existing antibiotic, gentamicin.

Chemists at Emory University, as part of the research team, modified the retinoids to retain maximum potency against MRSA, while minimizing toxicity.

“The molecule weakens the cell membranes of bacteria, but human cells also have membranes,” says William Wuest, associate professor of chemistry and a member of the Emory Antibiotic Resistance Center. “We found a way to tweak the molecule so that it now selectively targets bacteria.”

The computer modeling was led by Huaqian Gao, the Walter H. Annenberg Professor of Engineering at Brown University and one of the study’s authors. The powerful computer simulations demonstrated a powerful route toward understanding the molecular interactions between the screened compounds and bacteria membrane and determining the energy barriers for their penetration and embedment inside the membrane.

“This has been a very exciting multidisciplinary project,” said Gao.

**Dr. Frederick Ausubel**, study co-author and professor of genetics at Harvard Medical School and Massachusetts General Hospital said, “The development of new classes of anti-microbial compounds will be critical for combating the ever increasing incidence of antibiotic-resistant infections.”

“The results were extremely positive. We are extremely optimistic,” said Dr. Mylonakis. But he added, “This is still years away from coming to clinical trial.”

The study was supported by National Institutes of Health grant P01 AI083214, National Science Foundation grant CMMI-156290 and National Institute of General Medical Sciences grant 1R35GM119426.

http://nature.com/articles/doi:10.1038/nature26157
Physician compensation report shows gender wage gap nationwide; increases in Rhode Island

SAN FRANCISCO – Doximity released its second annual Physician Compensation Report, one of the most comprehensive surveys of U.S. physician compensation, on March 14. This year’s study found that doctors saw an average 4 percent wage increase nationally from 2016 to 2017. However, compensation varied significantly across metropolitan areas, between genders and across medical specialties. The report is based on more than 65,000 verified U.S. physician respondents, making it one of the largest studies available on physician pay in the United States.

“Considering the increasing concern about potential doctor shortages, having a clear understanding of physician compensation is more relevant than ever,” said Nate Gross, MD, co-founder of Doximity. “As the largest online medical network in the U.S., Doximity has unmatched insight into issues that affect the medical community, including compensation trends and disparities.”

Key findings include:

Physician Compensation by Metro Area
- The five metro areas with the highest average annual salary in 2017 were: Charlotte, N.C. ($402,273); Milwaukee ($398,431); Jacksonville, Fla. ($379,820); Indianapolis, Ind. ($378,011); and San Jose, Calif. ($376,585).
- The five metro areas with the lowest average annual salary in 2017 were: Durham, N.C. ($282,035); Ann Arbor, Mich. ($302,692); Baltimore ($304,002); New Haven, Conn. ($308,262); and Rochester, N.Y. ($312,503).
- From 2016 to 2017, the metro areas with the largest increase in physician compensation were: Charleston, S.C. (11.6 percent or $33,182 more); Milwaukee (7.3 percent or $52,601 more); Austin, Texas (7.2 percent or $45,605 more); San Francisco (6.9 percent or $58,184 more); and Las Vegas (6.7 percent or $47,256 more).

Physician Compensation by Medical Specialty
- The five medical specialties with the highest average annual salary in 2017 were: neurosurgery ($662,755); thoracic surgery ($602,745); orthopedic surgery ($537,568); vascular surgery ($476,300); and plastic surgery ($473,212).
- The five medical specialties with the lowest average annual salary in 2017 were: pediatric infectious disease ($191,735); pediatric hematology and oncology ($208,524); pediatric endocrinology ($214,911); pediatrics ($221,900); and preventive medicine ($231,838).

Physician Gender Wage Gap
- In 2017, the national gender gap for physicians increased as female doctors earned 27.7 percent less ($105,000) than their male counterparts. The disparity in 2016 was 26.5 percent, when female doctors earned $91,284 less.
- Similar to 2016 findings, there remains no medical specialty in which female doctors earn more than male doctors. Additionally, women earn less than men in all of the top 50 metro areas.
- From 2016 to 2017, the metro areas with the largest increase in gender wage gaps were: Charleston, S.C. (8.6 percent increase); Ann Arbor, Mich. (8.2 percent increase); Riverside, Calif. (8.0 percent increase); Providence, R.I. (6.4 percent increase); and Indianapolis (6.1 percent increase).
- In 2017, the metro areas with the largest gender wage gaps were: Charleston, S.C. (female physicians earn 37 percent or $134,499 less); Kansas City, Mo. (32 percent or $131,996 less); Nashville, Tenn. (32 percent or $118,706 less); Providence, R.I. (31 percent or $108,796 less); and Riverside, Calif. (31 percent or $115,991 less).
- In 2017, the medical specialties with the largest gender wage gaps were: hematology (female physicians earn 20 percent or $78,753 less); occupational medicine (20 percent or $59,174 less); urology (20 percent or $84,799 less); orthopedic surgery (19 percent or $101,291 less); and gastroenterology (19 percent or $86,447 less).

“All health care stakeholders should be aware of the differences in compensation for men and women across the country. Compensation inequity can directly affect where and what physicians choose to practice, which could ultimately affect patient access.”

— Christopher Whaley, PhD, the report’s lead author and adjunct assistant professor at the University of California, Berkeley School of Public Health.

To read the full report, visit: https://www.doximity.com/careers/compensation_report
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CDC Emergency Department data show increases in opioid overdoses

Data from emergency departments (EDs) show that the U.S. opioid overdose epidemic continues to worsen, according to the latest Vital Signs report by the Centers for Disease Control and Prevention (CDC).

The report examines the timeliest data available to CDC on ED visits for opioid overdoses across multiple states. Overall, ED visits (reported by 52 jurisdictions in 45 states) for suspected opioid overdoses increased 30 percent in the U.S., from July 2016 through September 2017. Opioid overdoses increased for men and women, all age groups, and all regions, but varied by state, with rural/urban differences. The findings highlight the need for enhanced prevention and treatment efforts in EDs and for greater access to evidence-based opioid use disorder treatments, including medication-assisted treatment and harm reduction services.

“Long before we receive data from death certificates, emergency department data can point to alarming increases in opioid overdoses,” said CDC Acting Director ANNE SCHUCHAT, MD. “This fast-moving epidemic affects both men and women, and people of every age. It does not respect state or county lines and is still increasing in every region in the United States.”

ED data allow faster tracking of regional and state trends

Data from 16 states in CDC’s Enhanced State Opioid Overdose Surveillance (ESOOS) Program were analyzed, showing quarterly trends by state and rural/urban differences from July 2016 through September 2017. Overall, ED visits for suspected opioid overdoses increased 35 percent in these 16 states hit hard by the epidemic. The data show:

- Eight states from three U.S. regions reporting substantial increases – 25 percent or greater – in the rate of opioid overdose ED visits.
- Significant increases in all states reporting in the Midwest, including Wisconsin (109 percent), Illinois (66 percent), Indiana (35 percent), Ohio (28 percent), and Missouri (21 percent).
- Considerable variation among states in the Northeast and Southeast; some states reported substantial increases and others modest decreases:
  - In the Northeast, large increases were seen in Delaware (105 percent), Pennsylvania (81 percent), and Maine (34 percent), but other states, like Massachusetts, New Hampshire, and Rhode Island showed nonsignificant decreases (<10 percent).
  - In the Southeast, North Carolina reported an increase (31 percent), while Kentucky reported a statistically significant decrease (15 percent).
- Continued rises in cities and towns of all types. Highest rate increases (54 percent) were in large central metropolitan areas (a population of 1 million or more and covering a principal city).

The sharp increases and variation across states and counties indicate the need for better coordination to address overdose outbreaks spreading across county and state borders. Closer coordination between public health and public safety agencies can support identification of changes in supply and use of illicit opioids, further allowing communities to take appropriate action to reduce opioid overdoses.

CDC also examined data from the National Syndromic Surveillance Program (NSSP) BioSense platform, using ESSENCE (Electronic Surveillance System for the Early Notification of Community-based Epidemics) software. Analysis of data from 52 jurisdictions in 45 states, which covers over 60 percent of ED visits in the U.S., found that from July 2016 through September 2017:

- All five U.S. regions experienced rate increases; the largest was in the Midwest (70 percent), followed by the West (40 percent), Northeast (21 percent), Southwest (20 percent), and Southeast (14 percent).
- Every demographic group experienced substantial rate increases, including men (30 percent) and women (24 percent) and people ages 25–34 (31 percent), 35–54 (36 percent), and 55 or older (32 percent).

The report noted the central role of state and local health departments in coordinating responses to opioid overdoses. Health departments can:

- Alert communities to rapid increases in overdoses seen in EDs and coordinate an informed and timely response.
- Increase naloxone distribution (an overdose-reversing drug) to first responders, family and friends, and other community members in affected areas, as policies permit.
- Increase availability of and access to treatment services, including mental health services and medication-assisted treatment for opioid use disorder.
- Support programs that reduce harms which can occur when injecting opioids, including those that offer screening for HIV and hepatitis B and C, in combination with referral to treatment.
- Support the use of the CDC Guideline for Prescribing Opioids for Chronic Pain, which encourages using prescription drug monitoring programs (PDMPs) to inform clinical practice.

“Research shows that people who have had an overdose are more likely to have another. Emergency department education and post-overdose protocols, including providing naloxone and linking people to treatment, are critical needs,” said ALANA VIVOLO-KANTOR, PhD, behavioral scientist in CDC’s National Center for Injury Prevention and Control. “Data on opioid overdoses treated in emergency departments can inform timely, strategic, and coordinated response efforts in the community as well.”

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IN THE NEWS
CHICAGO – More than nine in 10 physicians (92 percent) say that prior authorization programs have a negative impact on patient clinical outcomes, according to a new physician survey released in March by the American Medical Association (AMA). The survey results further bolster a growing recognition across the entire health sector that prior authorization programs must be reformed.

“Under prior authorization programs, health insurance companies make it harder to prescribe an increasing number of medications or medical services until the treating doctor has submitted documentation justifying the recommended treatment,” said AMA Chair-elect JACK RESNECK, Jr, MD. “In practice, insurers eventually authorize most requests, but the process can be a lengthy administrative nightmare of recurring paperwork, multiple phone calls and bureaucratic battles that can delay or disrupt a patient’s access to vital care. In my own practice, insurers are now requiring prior authorization even for generic medications, which has exponentially increased the daily paperwork burden.”

According to the AMA survey, which examined the experiences of 1,000 patient care physicians, nearly two-thirds (64 percent) report waiting at least one business day for prior authorization decisions from insurers—and nearly a third (30 percent) said they wait three business days or longer.

The high wait times for preauthorized medical care have consequences for patients. More than nine in 10 physicians (92 percent) said that the prior authorization process delays patient access to necessary care; and nearly four in five physicians (78 percent) report that prior authorization can sometimes, often or always lead to patients abandoning a recommended course of treatment.

In addition, a significant majority of physicians (84 percent) said the burdens associated with prior authorization were high or extremely high, and a vast majority of physicians (86 percent) believe burdens associated with prior authorization have increased during the past five years.

The survey findings show that every week a medical practice completes an average of 29.1 prior authorization requirements per physician, which takes an average of 14.6 hours to process—the equivalent of nearly two business days. To keep up with the administrative burden, about a third of physicians (34 percent) rely on staff members who work exclusively on the data entry and other manual tasks associated with prior authorization.

“The AMA survey illustrates a critical need to help patients have access to safe, timely, and affordable care, while reducing administrative burdens that take resources away from patient care,” said Dr. Resneck. “In response, the AMA has taken a leading role in convening organizations representing, pharmacists, medical groups, hospitals, and health insurers to take positive collaborative steps aimed at improving prior authorization processes for patients’ medical treatments.”

In January 2017, the AMA with 16 other associations urged an industry-wide reassessment of prior authorization programs to align with a newly created set of 21 principles intended to ensure that patients receive timely and medically necessary care and medications and reduce the administrative burdens. More than 100 other health care organizations have supported those principles.

In January 2018, the AMA joined the American Hospital Association, America’s Health Insurance Plans, American Pharmacists Association, Blue Cross Blue Shield Association and Medical Group Management Association in a Consensus Statement outlining a shared commitment to industry-wide improvements to prior authorization processes and patient-centered care.

Earlier this month, the AMA and Anthem announced a collaboration that would include, among other goals, identifying opportunities to streamline or eliminate low-value prior-authorization requirements and implementing policies to minimize delays or disruptions in the continuity of care.

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HIV Update 2018
Saturday, April 14, 2018
7:30 am–1pm

This program is designed to give an update on the diagnosis and management of HIV infection. We will address latest statistics on new infections and trends in the state of Rhode Island and services provided to HIV patients at the Immunology Center. Our speakers are Brown faculty with significant expertise in their topics. Our goals are to increase knowledge to effectively prevent, diagnose and treat HIV infection in primary care practice and to be knowledgeable about common questions arising in the care of the HIV-infected patient.

**Location**
Warren Alpert Medical School
222 Richmond Street, Providence, RI 02912

**For more information**
Contact the Brown CME Office
233 Richmond St., G-R156
Providence RI 02912
401.863.2871
Fax 401.863.2202
CME@Brown.edu
https://Brown.edu/cme

Register online
The University of Massachusetts Medical School (UMMS) seeks a board certified psychiatrist to serve as the Area Medical Director for Central Massachusetts Department of Mental Health (DMH). The Area Medical Director’s primary responsibility is to provide administrative and clinical oversight for the DMH operated and contracted community and facility based service system. As a clinical leader within DMH, we are looking for inspired leadership in the recovery model of care for the people we serve. More specific responsibilities include utilization management, risk management, support for DMH initiatives, and oversight of clinical and psychopharmacology services. A full-time Area Medical Director may spend about 20% working on special projects as directed by the DMH State Medical Director. A UMMS academic faculty appointment will be based on prior experience. There are opportunities for research, including protected time depending on experience and goals. Successful candidates must be a licensed Massachusetts physician with board certification in psychiatry. Preferred qualifications would include facility in teaching professionals, lay public, consumers, as well as trainees such as medical students and residents.

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UMass Medical School is committed to being an equal opportunity and affirmative action employer and recognizes the power of a diverse community. We encourage applications from protected veterans, individuals with disabilities and those with varied experiences, perspectives and backgrounds to consider UMass Medical School as their employer of choice.

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**Multidisciplinary Autoimmune Disease Summit**

**Saturday, April 28, 2018**

7:30 am–4pm

The Multidisciplinary Autoimmune (AI) Disease Summit aims to provide up-to-date information on the diagnosis and management of complex autoimmune diseases with a focus on multidisciplinary care. This conference will present the most commonly encountered AI conditions including dermatomyositis, psoriatic arthritis, inflammatory bowel disease, uveitis, urticaria, scleroderma, interstitial lung disease and hepatitis in the setting of immune suppression. Participants will leave with a better understanding of each disease, its complicated multi-systemic manifestations and treatment options.

Register online

**Location**

Warren Alpert Medical School

222 Richmond Street

Providence, RI 02912

**For more information**

Contact the Brown CME Office

233 Richmond Street, G-R156, Providence RI 02912

401.863.2871 Fax 401.863.2202 CME@Brown.edu

https://Brown.edu/cme

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**Advances in the Treatment of Epilepsy and Movement Disorders**

**Saturday, May 5, 2018**

7:30 am–2:45pm

Medical therapies for intractable epilepsy and for movement disorders such as Parkinson’s Disease are advancing rapidly. This CME conference will provide an overview of recent advances in the medical and surgical care of patients with complex, chronic neurologic conditions, focusing on epilepsy and movement disorders. The goal is to provide caregivers with the understanding necessary to convey existing and near-term potential options to patients, and to foster collaborations among attendees to develop optimal, team-based treatment strategies.

Register online