

Stop AMR Global Media Monitor

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Bacterial enzyme could become a new target for antibiotics

An enzyme, the hydroxy-L-proline dehydratase, found in a high number of species of bacteria from the human gut, including Clostridioides difficile. This enzyme is capable to dismantle the tough triple-helix structure. Catherine Drennan, an MIT professor of chemistry said that it could be a potential target as this enzyme does not exist in humans. This enzyme could become a powerful antibiotic slowing down the bacteria's growth.

Source: EurekAlert!, 17 March 2020

Hopeful results from trials of dengue vaccine candidate

Phase 2 and 3 randomized, controlled clinical trials of Takeda's tetravalent dengue vaccine candidate show that it is safe, produces immunity in children, and protects against the disease-regardless of previous exposure to different strains of the virus, according to studies published in yesterday's The Lancet.

In the phase 3 double-blind trial, 20,099 children 4 to 16 years old at 26 centers in endemic areas of Asia and Latin America were randomly assigned to receive two doses of the live TAK-003 vaccine or two doses of placebo 3 months apart from September 2016 to August 2017.

In the first 11 months, researchers found overall vaccine effectiveness of 80.2%, with 61 cases of dengue in the TAK-003 group and 149 cases in the placebo group.

In the first 17 months, overall effectiveness was 73.3%. The vaccine was effective in 76.1% of children seropositive at baseline, 66.2% in those seronegative at baseline, 90.4% against dengue-related hospitalizations, and 85.9% against severe dengue.

Takeda's product is the second dengue vaccine to enter clinical trials, after Sanofi Pasteur's Dengvaxia.

Sanofi's vaccine was 56% to 61% effective in preventing dengue in children, but it was tied to severe illness in dengue-naive children who received the vaccine and then contracted the virus.

Source: CIDRAP, 18 March 2020

Study questions role of antibiotics in kids' pneumonia

A new study looked at 294 children between 3 months and 18 years old diagnosed with a suspected community acquired pneumonia. They compared two groups of children, by receiving or not antibiotics. Despite the fact that most cases are caused by viruses, antibiotics are commonly prescribed. It appears that no statistical differences emerge on the number of treatment failure between the children who received antibiotics and those who did not.

Source: CIDRAP, 16 March 2020

Dr. Jekyll and Mr. Hyde -- Enzyme targeted by TB antibiotic later stops the drug destroying it

D-cycloserine is an antibiotic used since more than 50 years against drug resistant tuberculosis by targeting a specific enzyme, the alanine racemase, helping to build TB bacteria's cell walls. A new study demonstrated that even after exposure to the antibiotic, a fraction of the enzyme was still functioning. Due to a process called hydrolysis, the enzyme was capable to inactivate the drug.



However, D-cycloserine is still an effective antibiotic as it targets secondarily another enzyme.

This discovery could lead to new drugs by trying to prevent its hydrolysis.

Source: EurekAlert!, 16 March 2020

<u>New kind of CRISPR technology to target RNA, including RNA viruses like coronavirus</u>

As CRISPR-based genetic screens already helped scientists to achieve undeniable researches and progress, they can only edit or target DNA. For certain area of the human genome or even organisms such as some sort of viruses, this may not be an effective approach.

However, scientists recently discovered a new CRISPR enzyme called Cas13. This enzyme, despite the traditional Cas9, targets RNA instead of DNA.

"This is the kind of technology innovation that we foster and develop at the New York Genome Center. This latest CRISPR technology from the Sanjana Lab has exciting implications to advance the fields of genomics and precision medicine," said Tom Maniatis, PhD, Evnin Family Scientific Director and Chief Executive Officer, New York Genome Center.

"We are particularly excited to use the optimized Cas13 screening system to target noncoding RNAs," said fellow co-first-author Méndez-Mancilla. "This greatly expands the CRISPR toolbox for forward genetic and transcriptomic screens." In the study, the researchers noticed a marked difference in protein knockdown when targeting different protein-coding and non-coding elements of messenger RNAs and found evidence that Cas13 competes with other RNA-binding proteins involved in transcript processing and splicing.

The team recently leveraged their guide RNA predictive model for a particularly critical analysis: The COVID-19 public health emergency is due to a coronavirus, which contains an RNA - not DNA - genome. <u>New research shows promise to treat female group A</u> <u>streptococcus genital tract infections</u>

In this novel study in The American Journal of Pathology, published by Elsevier, scientists report on the discovery of group A streptococcus surface proteins involved in female reproductive tract infections such as puerperal sepsis that may pave the way to developing vaccines and more effective treatments.

GAS is a major pathogen causing more than 700 million human infections a year worldwide and 15 million cases each year in the United States.

Although the main site of infection is in the throat, GAS can also colonize the female genital tract and cause severe neonatal infections and diseases in the mother during and after labor such as puerperal sepsis.

Both GAS neonatal infections and puerperal sepsis have high morbidity and mortality rates.

"We are still way behind the curve of understanding the molecular basis of puerperal sepsis," explained lead investigator James M. Musser, MD, PhD, chair of the Department of Pathology and Genomic Medicine at Houston Methodist Hospital and the Fondren Presidential Distinguished Chair at the Houston Methodist Research Institute, Houston, TX, USA. "Our understanding of GAS genes contributing to interaction with the female genital tract is a knowledge desert, in part because of limited relevant animal models. It is therefore an important area for translational research to develop vaccines or treatments."

Investigators developed two new animal models for the study of GAS infection biology and used transposon mutant library screens to identify pathogen genes contributing to colonization of the vaginal tract mucosa and infection in the uterine wall.

Notably, they found that genes encoding surface protein SpyAD, and immunogenic secreted protein Isp2, are crucial for GAS fitness in the female genital tract.

Source: EurekAlert!, 19 March 2020

Source: EurekAlert!, 16 March 2020

Low prevalence of Salmonella in Sweden's dairy herds

In Sweden, a study was led to calculate the prevalence of Salmonella in the dairy cattle herds. Results have been published and the prevalence of Salmonella is low but there is a variation of prevalence across the country. The highest prevalence was found in Öland and Gotland. In Öland, the prevalence was of 24%, as high as in a local survey from 2009. Gotland's prevalence raised from 5.5 % in 2013 to 22% in 2019. They do not explain this significant raise and will investigate further.

Source; Food Safety News, 20 March 2020

New drug combination passes safety test in pancreatic cancer

A novel peptide antagonist in combination with a PD-1 inhibitor has been tested to be safe and tolerated by patients with advanced refractory pancreatic and rectal cancer. The study wanted to determine the maximum tolerated dose, safety and tolerability of this new peptide, the LYS2510924. the highest dose of LY2510924, 40 mg, daily is safe and well-tolerated and should be used in the next phase of studies. The researchers also reported that a best response of stable disease was seen in 44% of patients in the trial.

Source: EurekAlert!, 19 March 2020