FACULTY OF SCIENCE
THE UNIVERSITY OF HONG KONG
香港大學　理學院

DEAN
Professor M Evans

FACULTY SECRETARY
Mrs A O M Tsang

Press Release **For Immediate Release**

HKU Chemists made another hit to the antibacterial drug research

August 29, 2016

Dr Xuechen Li of HKU Department of Chemistry and his research team, together with his collaborators in University of Central Florida (Dr Yu Yuan), USA and the Hong Kong Polytechnic University (Dr Sheng Chen), reported their studies on the synthesis of a newly discovered "game-changing" antibiotic, Teixobactin, in *Nature Communications* recently. This underlies potential application and development of the next-generation teixobactin-based antibacterial drugs.

The globally ever-increasing antimicrobial resistance has become a serious threat to human health. For instance, methicillin- resistant *Staphylococcus aureus* (MRSA) has emerged as one of the most important pathogens, both in hospital (HA-MRSA) and community-acquired infections (CA-MRSA). It is considered as one of the most important super-bugs in Hong Kong and caused huge mobility and mortality. To avoid further aggravation of resistance-related problems, misuse and overuse of antibiotics should be prevented to minimize the emergence of drug-resistant organisms. On the other hand, development of novel antibacterial and anti-resistant agents should be actively pursued. Although there is an urgent public need for the new antibacterial drug, in fact very few pharmaceutical companies have interests in investing on the development of new antibacterial drugs, due to the lower profit compared to medicines used to treat diabetes and cardiovascular diseases. It is evidenced by the fact that no new antibiotics have been introduced to the market over the last decade. To address this issue, researchers in the academia should play a more active role in the search of new antimicrobial compounds.

A team of researchers led by Dr Xuechen Li of HKU Department of Chemistry, took up the responsibility and challenge and have been continuingly working on the development of new antibiotics for the past seven years. In 2013, they developed the first chemical synthesis of an antibiotic daptomycin, which enabled them to search for the next-generation daptomycin-based antibiotics. Recently, his team has made another success by developing a chemical strategy to synthesize another antibiotic, Teixobactin.

Last year, the discovery of the antibiotic Teixobactin by researchers in the USA, was considered as a breakthrough in the antibacterial drug research (*Nature*, 2015, 517, 455). Teixobactin can kill a range of pathogens without detectable resistance, including methicillin-resistant *Staphylococcus aureus* (MRSA), *vancomycin-resistant Enterococcus* (VRE) and *Mycobacterium tuberculosis*. As promising as it is, Teixobactin is not perfect yet as a drug and can be further improved for its clinical properties via its structrual modication. In the history of the antibacterial drug development, modification of the lead compoud has successfully led to many generations of improved penicillin-based antibiotics. Indeed, it is only through chemical synthesis and medicinal chemistry that one can flexibly modify the teixobactin structure to generate various teixobactin derivatives from simple materials. Thus, the development of a straetgy to chemically synthesize teixobactin and

its derivatives has drawn a lot of attention with intense competition worldwide and more than 15 research groups from different countries had strived to develop a chemical strategy to synthesize teixobactin. Collaborating with another chemist from University of Central Florida, USA, HKU team became one of the fastest groups in the world to complete the chemical synthesis of teixobactin, from which they have also generated 10 teixobactin analogues with promising properties (US provisional patent filed). The strategy they developed is very efficient and can generate many teixobactin derivatives in a fast and combinatory manner. Now they are running at a full speed with an aim to synthesize more 100 different teixobactin derivatives within two years to search for analogues with improved pharmacological properties for the clinical development.

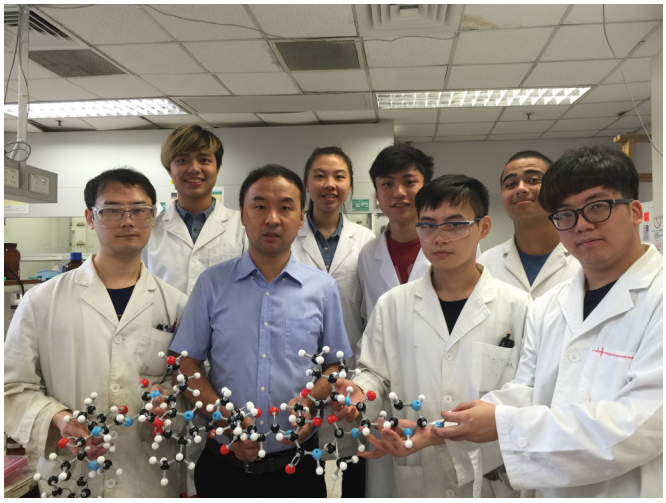
For media enquiries, please contact Ms Cindy Chan, Senior Communication Manager of HKU Faculty of Science (tel: 3917 5286/ 6703 0212; email: cindycst@hku.hk).

Journal article
"Total synthesis of teixobactin", *Nature Communications*
Link: http://www.nature.com/ncomms/2016/160803/ncomms12394/abs/ncomms12394.html

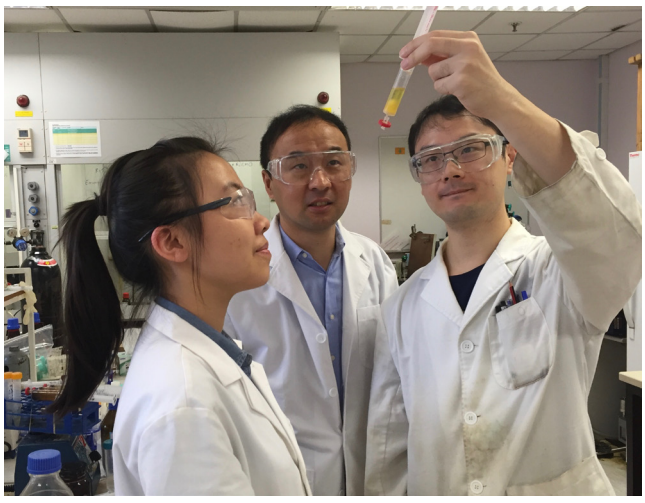
Image download and illustration:
http://www.scifac.hku.hk/news/media?page=1

Photo captions:

1. Dr Xuechen Li (second from the left in the first row) and his teixobactin project-team at HKU Department of Chemistry, including 3 Ph.D students and 4 undergraduate students



2. Dr Xuechen Li working in the laboratory with his research team.



– End –