JPIAMR Network Plus 2020 - Alliance for the **E**xploration of **P**ipelines for **I**nhibitors of **C**arbapenemases (EPIC Alliance) Launch Meeting

EPIC Alliance has launched! The consortium that was awarded funding under the JPIAMR Network Plus 2020 and the *Instituto de Salud Carlos III* transnational calls officially convened and held its launch meeting on the 29th of January, 2021. The founder consortium is composed of 11 members and from 7 countries, and are:

- Dr. Elias Dahdouh (Coordinator) from the Instituto de Investigación Sanitaria del Hospital Universitario La Paz (IdiPAZ), Spain
- Dr. Jesús Mingorance from the Instituto de Investigación Sanitaria del Hospital Universitario La Paz (IdiPAZ), Spain
- Dr. Paulino Gómez Puertas from the Centro de Biología Molecular "Severo Ochoa" (CBMSO, CSIC-UAM), Spain
- Dr. Stefano Lorenzetti from the Istituto Superiore di Sanità (ISS), Italy, in collaboration with Dr. Francesca Spyrakis from the University of Turin, Italy
- Dr. Thierry Naas from the Université Paris-Saclay, Hôpital de Bicêtre, France
- Dr. Bogdan Iorga from the Institut de Chimie des Substances Naturelles (ICSN), CNRS, Université Paris-Saclay, France
- Dr. Nathaniel Martin from the Institute of Biology Leiden, Leiden University, The Netherlands
- Dr. Joe Rubin from the University of Saskatchewan at Saskatoon, Canada
- Dr. Luis Martínez-Martínez from the Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC), Spain
- Dr. Thomas Tängdén from the Uppsala University, Sweden
- Dr. Linda Falgenhauer from the Justus Liebig University Giessen, Germany

Carbapenems are among the most potent drugs available to treat bacterial infections that are resistant to other antibiotics. However, several bacteria become resistant to these molecules through the production of enzymes that can break down carbapenems, called carbapenemases. These carbapenemase-producing bacteria threaten our ability to control many infectious diseases across the globe since they render one of the most potent antibiotics ineffective; in addition to frequently being resistant to many other families of antibiotics at the same time. Moreover, there are increasing rates of these carbapenem resistant organisms being reported worldwide. There is thus a great need for strategies to overcome this antimicrobial resistance. One such strategy is the use of carbapenemase inhibitors that might block the action of carbapenemases and could have the potential to reverse the resistance to carbapenems. This approach, though very promising, can be very laborious, time consuming, and costly. Therefore, several groups have relied on computational approaches to detect possible carbapenemase inhibitors. The computational approach is not without its own set of challenges since its success heavily relies on choosing the correct search parameters, algorithms, and databases, in addition to selecting molecules that could successfully pass all the filters before being used in practice.

Within the EPIC Alliance network, we bring together experts from the fields of clinical and basic microbiology, infectious diseases, computational biology & chemistry, bioinformatics, biochemistry, translational biology, biophysics, pharmacology, toxicology, veterinary sciences, and epidemiology

spread across seven countries. All members of the network are leading experts in their fields, and with our combined expertise, we will be able to answer the following question: What is the best approach for data mining on carbapenemase inhibitors and how to translate this data into experiments. Specifically, over the course of two years, the consortium will be addressing the following questions, among others that may arise:

1. What is the best way to predict the carbapenemase inhibiting activity of molecules?
2. How to target carbapenemases with broad spectrums of activity?
3. Which parameters should be chosen for the computational data mining for carbapenemase inhibitors?
4. How can we test candidate molecules *in-vitro*, *in-vivo*, and through clinical trials?
5. What is the cost-effectiveness and feasibility of this approach?
6. Is this approach better than already existing ones?

By answering these questions, we hope to reach a unified strategy for finding and testing these important molecules that can safeguard the use of carbapenems and help in the global effort to fight against bacterial resistance.