VAMAS

Synthetic Biomaterials

Technical Work Area 40

Project 3

Comparability measurements of antibiotic interactions with bacterial model membranes

Objectives

The aim of this study is to validate phospholipid model membranes as candidate reference materials for screening antibiotics. The model unilamellar liposomes in solution is titrated against an antibiotic solution. Heat changes associated with binding events are directly measured using Isothermal Titration Calorimetry (ITC) and binding affinity determined.

Background

The composition of bacterial membranes has a profound impact on the susceptibility of bacteria to antibiotics. The growing role of membrane modifications in the spread of antimicrobial resistance conforms to a strong shift by industry towards targeting Gram negative bacteria whose outer membrane remains a formidable barrier for most antibiotics. High-throughput screening methods are being developed to enable pipelines of antimicrobial agents with novel mechanisms of action.

Commercialisation barriers exist for reference methods and materials that will make use of qualitative and quantitative responses of antibiotics to membranes. This need is echoed by existing regulatory policies that limit the wide use of advanced therapies (EC/1394/2007; EC/2001/83).

Standardization needs

There is a pre-standardisation need to focus on:

- ability to produce and characterise materials to common (physical) specifications
- assigned values consistent between laboratories and with the protocols of assembling membranes mimics with different phospholipid compositions
- procedures for quantitative analysis of the values by reproducible measurements of the highest metrological order
- material validation in biologically native and near-native environments as a function of drug concentration and time

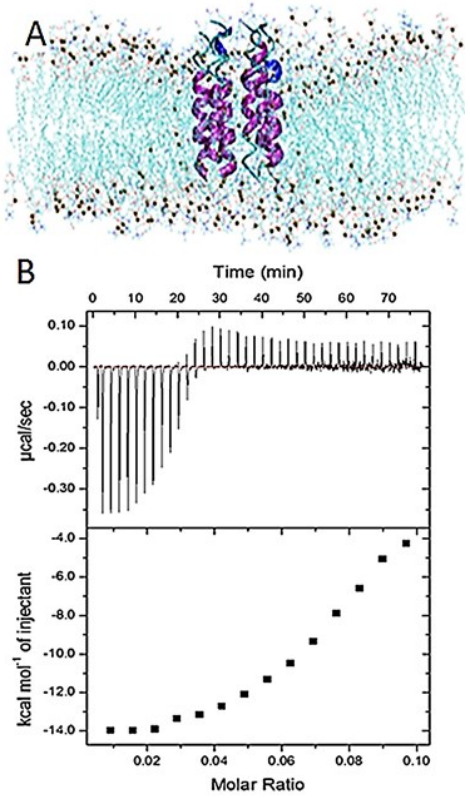
Relevant Standards

ISO Guide 35 Reference materials
ISO 15189: 2012, BS ISO 29301: 2010
ISO 15194: 2009
EU 2017/746: IVD regulation

Relevant Committees

ISO/TC 276 - Biotechnology
ISO/TC 229 - Nanotechnologies
BIPM – CAWG, PAWG

Call for Participation



(A) Molecular dynamics simulation of an antibiotic (magenta) inserted into a bacterial membrane. (B) Isotherm showing the profile of antibiotic-membrane interactions.

Work Programme

- Materials assembled for distribution
- Materials characterised by participating laboratories
- Data analysis with uncertainty evaluation

Second stage analysis

- Procedures developed will be repeated by a smaller group of participants to determine the effect of test parameters on the repeatability and reproducibility of the measurement.

Knowledge Transfer

International round-robin tests, good practice guidelines, peer-review publications and presentations.

Status

Study In progress since July 2018.

Additional Volunteers Welcome

Participants fund their own study in the project

For more information on participation, please contact:

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