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Potentialiation of Gram-positive specific antibiotics against Gram-negative bacteria through outer membrane disruption

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Propositions

Accompanying the thesis

Potentialiation of Gram-positive specific antibiotics against Gram-negative bacteria through outer membrane disruption

1. During SAR studies, FICI should not be the sole selection criterion as compounds with both low MSC and MIC values can also be potent leads. (*Thesis Chapter 3*)
2. Screening all members within an antibiotic class for synergy with serum is strongly advised. (*Thesis Chapter 4*)
3. The influence of growth media used in the MIC assays should not be underestimated. (*Thesis Chapter 5*)
4. Reported endotoxin-binding compounds can inspire the development of outer membrane disrupting synergists. (*Thesis Chapter 3*)
5. The permeabilizing properties of the outer membrane (OM) synergists necessarily involve partial disruption or disorganization of the OM, and a major concern of these permeabilizing agents is their effects on eukaryotic membranes, which should be included in their evaluation. (*Annals of Medicine*. 2001, 33:3, 167-171)
6. The negative effect on AMR described for drug repurposing of antibiotics by Talat *et al.* should also be considered for drugs that have been repurposed as antibiotics. (*Front. Pharmacol.* 2002, 13:833005)
7. In the future the effect of antibiotic (over)use on the microbiome and subsequently an individual's health should be taken into consideration when prescribing antibiotics. (*Science*. 2016, 352:6285, 544-545)
8. The current, trusted standard worldwide of MIC assays with Mueller-Hinton Broth should be improved upon by using physiological relevant conditions. (*Nat. Protoc.* 2021, 16, 761-3774 and *EBioMedicine*. 2017, 20, 173-181)
9. Challenging the status quo should especially be aspired to within the scientific world as the twice rejected paper that first described the asymmetrical distribution of the outer membrane was deemed "thermodynamically impossible" is at present the status quo. (*MMBR*. 2003, 67:4, 593-656)
10. "Sweatpants are a sign of defeat. You lost control of your life so you bought some sweatpants" this might be a confronting but accurate representation of the lockdowns during the corona pandemic. (*quote by Karl Lagerfeld*)