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P1694 Community for open antimicrobial drug discovery (CO-ADD): crowd-sourcing novel antibiotics

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Background: Antibacterial drugs occupy a unique property space that is vastly different to drugs developed for other therapeutic areas, suggesting that commercially available compounds lack the physicochemical properties ideal for activity against bacteria and a varied source of chemical diversity needs to be investigated. We believe an untapped resource is contained in the laboratories of chemists; synthetic compounds prepared for other projects that have never been tested for antimicrobial potential. The global screening initiative **The Community for Open Antimicrobial Drug Discovery [CO-ADD]** will uncover this significant and rich chemical diversity held outside corporate screening collections by providing low-barrier access to testing.[1-3]

Materials/methods: CO-ADD has developed and validated high-throughput antimicrobial screening methodologies for bacteria and fungi in 384-well micro-broth assay format and has the current capacity to screen >10,000 compounds per week against a panel of nine microorganisms in duplicate. A primary microorganism panel is comprised of the ESKAPE pathogens; *Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* (MRSA), and the fungi; *Candida albicans* and *Cryptococcus neoformans*.

Results: A pilot-study screening ~165,000 compounds against key ESKAPE pathogens, saw commercial compounds with a hit rate of 0.03% against Gram-positive bacteria and 0.008% against Gram-negative bacteria. Conversely, academically sourced compounds gave hit rates of 0.52% and 0.27%, respectively. Since this comparison **CO-ADD** has sourced >210,000 academic compounds from 227 submitters from 43 countries, and has unearthed another >300,000 compounds for prospective screening. Screening of the first 200,000 compounds has identified 1,027 compounds (of which 636 are novel in the space) that pass the hit confirmation criteria, displaying antimicrobial activity against at least one of the target organisms (MIC ≤ 16 µg/mL) with promising selectivity index values, i.e. cytotoxicity (CC_{50}) > antimicrobial activity (MIC). Such compounds may represent promising starting points for antibiotic development.

Conclusions: With support from The Wellcome Trust and the University of Queensland, we have created a not-for-profit open access pipeline to provide unencumbered free antimicrobial screening for any interested researcher. After only 24 months **CO-ADD** has screen >200,000 compounds for their antimicrobial potential, greater than twice the number of any other screening program so far disclosed.[4]

References:

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