Addressing AMR in *Helicobacter pylori* by FDA-approved drugs as novel anti-infectives

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BACKGROUND

Nearly 50% of the world's population is infected with *Helicobacter pylori,* a gram-negative, microaerophilic bacterium (Malfertheiner et al., 2023). This infection remains the primary risk factor for gastric cancer, one of the leading causes of cancer-related mortality worldwide (Moss, 2017). Antimicrobial resistance (AMR) in *H. pylori* results in severe global health issues as current resistance rates to commonly used antibiotics for the treatment of *H. pylori* include 25–60% for metronidazole, 15–30% for clarithromycin, and 20% for levofloxacin (Bujanda et al., 2021). The combination of *H. pylori*'s role in carcinogenesis and its high resistance rates underscores the urgent need for novel therapeutic approaches to overcome antibiotic resistance.

OBJECTIVES

We propose to identify novel anti-infectives by screening for compounds targeting *H. pylori*. Our strategy focuses on drug repurposing, which involves screening drugs already approved by the US Food and Drug Administration (FDA) for new therapeutic applications. This efficient and cost-effective approach offers a pathway to identify compounds that inhibit *H. pylori* growth more rapidly than conventional drug discovery methods. Approval timelines are shortened to approximately six years, with costs reduced to a quarter of traditional methods (Nosengo, 2016).

METHODS

We have designed a screening platform to evaluate *H. pylori* growth inhibition in a 96-well plate format. Using the Prestwick Chemical Library, a collection of 1,200 FDA-approved drugs, we classified active candidates as those achieving at least 90% growth inhibition.

RESULTS

Our initial results identified over 200 active candidates, now undergoing further *in vitro* validation. Many of these candidates were confirmed in a secondary screening, where we also determined their minimum inhibitory concentrations (MICs) and minimum bactericidal concentrations (MBCs). Experiments to evaluate the mutation frequency associated with our compounds are currently ongoing.

CONCLUSION

The findings from this drug screening provide new therapeutic alternatives, which could significantly contribute to addressing the challenge of antibiotic resistance in *H. pylori*.