Inhibition of *Helicobacter pylori* glycoprotein biosynthesis

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The discovery of antibiotics and their ability to combat microbial infections revolutionized modern medicine. However, 90 years after the development of penicillin by Alexander Fleming, an emerging trend of antibiotic resistance has become apparent. To date, over 20,000 resistance genes have been identified, with 'superbug' species like *S. aureus* and tuberculosis pathogens displaying resistances to multiple drugs, reflecting increasing virulence and mortality rates.[1] Tp complicate matters, traditional broad-spectrum antibiotics are increasingly seen as insufficient as they indiscriminately harm beneficial bacteria which inhabit human microbiomes.

One particularly problematic, highly antimicrobial resistant bacterium is *Helicobacter pylori*. Upon entering its host, *H. pylori* colonizes the highly acidic environment of the stomach mucosa. Infected individuals are exposed to a flurry of toxins, damaging tissue and ultimately increasing risk of gastritis, gastric ulcers, and several stomach cancers.[2] *H. pylori* is ubiquitous – it causes approximately 5.2% of all cancers[3] – and it continues to develop new mechanisms of antimicrobial resistance, prompting the WHO to list *H. pylori* as a "high priority" target for the research and development of new antibiotics.[4]

One intriguing avenue of potential therapies is *H. pylori* cell surface glycoproteins. Glycoproteins are structures comprised of a protein and linked chains of sugars – called glycans – which together work to mediate interactions between cells and their environment. *H. pylor*i's surface glycans have been associated with the bacteria's ability to initial establish infection.[5] Bacterial glycoproteins are largely composed of characteristic, species-specific sugars. In fact, bacteria share remarkably few glycan sugars with mammalian cells.[6] Because of their exclusivity, *H. pylori* glycoproteins could be a highly selective target forf1 0 0 1 108.14 473.47 Tm0 g0 G[t)-4(a)9(r)-3(g)11(et)-5(f)-3(o2(a)3o1 0 0 1 108.14 473.47 Tm.d TJET