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September 10-11, 2018 | Dublin, Ireland

# TARGETING BACTERIAL VIRULENCE TO DEVELOP EVOLUTION PROOF ANTIBIOTICS

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Keeping the antibiotic resistance in mind, it is of greatest need to develop new ways to treat bacterial infections. Evolution-proof antibiotics that disarm the bacterial pathogens without impacting their survival would be an important strategy towards sidestepping the evolution of resistance. Drugs that disarm the pathogen will generate much weaker selection for resistance than traditional antibiotics. Disarming the pathogens is possible by targeting a family of bacterial proteins called AraC family proteins that regulate the bacteria's ability to infect or damage a host, rather than its ability to survive. We tested this exciting hypothesis against Shigella flexneri, a diarrhea causing bacterial pathogen responsible for causing 165 million cases of illness and more than 1.1 million deaths worldwide. We successfully identified several molecules that selectively inhibited an important Shigella protein VirF that is crucial for causing infection. The highly potent molecule SE-1 is found to not impact the growth of the bacteria but prevent bacteria's ability to invade and infect cultured human intestinal cells. SE-1 also inhibits infection pathways in other pathogenic bacteria that cause infections such as diarrhea, pneumonia, and cholera and thus can be developed as a novel agent to treat multiple infections. Targeting such infection pathways may yield non-traditional antibiotics that are more powerful and versatile than our current antimicrobials and would solve the antibiotic resistance issue that has grown to alarming levels.