The discovery of antibiotics more than 90 years was a milestone in the treatment of bacterial infections. However, antibiotics are increasingly losing their potency because antibiotic resistant (AR) bacterial pathogens are becoming more prevalent. Where is our next silver bullet against AR infections? One of the possible strategies to mitigate the resurging threat from these bacteria is to develop chemicals that target bacterial virulence determinants or the disease process instead of functions essential for bacterial growth. In this presentation, I will briefly compare antibiotics with this alternative strategy, introduce functions of bacterial type IV pilus (T4P) in bacterial motility and pathogenesis, and discuss our early attempts to identify chemicals that interfere with T4P biogenesis by targeting an ATPase essential for T4P assembly.