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**How to exploit evolutionary trade-offs
to combat antibiotic resistance**

Evolution is at the core of the impending antibiotic crisis. Sustainable therapy must account for the adaptive potential of pathogens. One option is to exploit genetic trade-offs of resistance mutations, which can produce hypersensitivity to other drugs (so-called *collateral sensitivity*). To date, the evolutionary stability and thus therapeutic applicability of reciprocal collateral-sensitivity remains unclear. I will present recent work from my lab, where we explored the potential of collateral sensitivity to constrain the evolution of antibiotic resistance in the model pathogen *Pseudomonas aeruginosa*. Using experimental evolution in combination with genomics and functional genetic analysis, we show that adaptation to a particular antibiotic can result in variation in the evolved collateral effects. Depending on the evolutionary trajectory taken, some populations may evolve collateral sensitivity, while others from the same treatment produce cross-resistance. This level of variation in the evolutionary response may constrain the applicability of collateral sensitivity for treatment. Nevertheless, additional experiments also demonstrated that, if collateral sensitivity did evolve, then it cannot be easily overcome. It thus seems important to identify those cases where such evolutionary trade-offs are common and cannot be easily countered by the pathogens due to a lack of suitable mutations. Such information may help the design of sustainable antibiotic therapy, while additionally enhancing our understanding of the importance of trade-offs during evolutionary adaptation.

Date: Thursday, 12th April 2018, 1:30 pm
Venue: GEOMAR Westshore, Düsternbrooker Weg 20, Lecture Hall
Host: Prof. Dr. Deniz Tasdemir