The *Mycobacterium tuberculosis* drugome and its polypharmacological implications

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1 Introduction

We report a computational approach that integrates structural bioinformatics, molecular modeling and systems biology to construct a drug-target network on a structural proteome-wide scale. The approach has been applied to the genome of *Mycobacterium tuberculosis* (*M.tb*), the causative agent of one of today’s most widely spread infectious diseases. The resulting drug-target interaction network for all structurally characterized FDA approved drugs bound to all putative *M.tb* receptors, we refer to as the ‘TB-drugome’. The TB-drugome reveals that approximately one-third of the drugs examined have the potential to be repositioned to treat tuberculosis and that many currently unexploited *M.tb* receptors may be druggable and could serve as novel anti-tubercular targets. Furthermore, a detailed analysis of the TB-drugome has shed new light on controversial issues surrounding drug-target networks. Indeed, our results support the idea that drug-target networks are inherently modular, and further that any observed randomness is mainly caused by false drug-target connections and biased target coverage. The TB-drugome presented here has the potential to be a valuable resource in the development of safe and efficient anti-tubercular drugs. More generally, the methodology may be applied to other pathogens of interest, with results improving as more of their structural proteomes can be ascertained through the continued efforts of structural genomics.