From Genes to Precision Medicine Cures: Systems Biology of Antibiotic Resistance in Bacteria

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Rapid increase in bacterial resistance to life saving antibiotics is a major threat to human health because antibiotics are becoming ineffective in treating bacterial diseases. Innovative cutting edge approaches are urgently needed to combat bacterial resistance to our precious antibiotics. Central hypothesis is that analyses of determinant genes for Vancomycin resistance in bacteria will reveal evolutionary conservation of essential resistance mechanisms to design effective antimicrobials against antibiotic resistant bacteria. Specific research objectives were to analyze DNA sequences of resistance genes in bacteria against antibiotics and to determine conserved genetic mechanisms in bacteria against major antibiotics, determine modifications to Vancomycin to make it effective against Vancomycin resistant bacteria, and develop a Wikipedia page to empower the public with the knowledge about antibiotic resistance in the world. Digital/synthetic biology approaches including bioinformatics and computational biology and computational chemistry tools as well as comprehensive literature searches were performed. The results showed that the resistance determinants against Vancomycin are diverse and there are different levels of conservation of the gene and protein sequences. In addition, by using computational chemistry approaches, it is possible to modify Vancomycin such that it will effectively inhibit bacteria carrying the resistance determinants against Vancomycin. The Wikipedia page disseminates the new knowledge on antibiotic resistance and solutions using digital/synthetic biology approach. The results are significant because they can be used to develop new antimicrobials or engineer the current antibiotics through computer assisted drug design to save millions of lives.

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