Construction and transcriptional analysis of a tunable polymicrobial community

Cynthia H. Collins[1]*, Michael G. Surette[1,2]

1. Department of Microbiology and Infectious Diseases, Faculty of Medicine, University of Calgary, Calgary, AB, Canada
2. Department of Biochemistry and Molecular Biology, Faculty of Medicine, University of Calgary, Calgary, AB, Canada
*email: ccollins@ucalgary.ca

Abstract

Bacteria have a remarkable ability to adapt to their environment and changing conditions. While this is usually studied in the context of the physiochemical environment, other microorganisms dominate the natural environments of most bacteria. Laboratory-based microbiology has traditionally focused on the isolation of microorganisms and their cultivation in pure cultures. Microbial ecology has exploited sensitive molecular approaches to describe bacteria present in complex communities but has not focused on how these complex communities arise and how they are maintained. The ability to grow microbial communities in the laboratory is challenging because of the tendency of one species to dominate the culture under laboratory conditions. This represents a fundamental challenge in the laboratory with important implications in basic and applied microbiology. Synthetic biology aims to construct organisms with designed functions using naturally occurring component parts. This work has largely focused on engineering genetic regulatory networks with specific behaviors. Recent efforts have been made to extend these engineered networks to multicellular behaviors, in essence engineering simple communities. We are applying systems biology approaches to synthetic polymicrobial communities, through the integration of both community composition data and transcriptional response data, to improve our understanding of how microbial communities behave under various conditions and how cellular physiology affects and is affected by community composition. To engineer synthetic polymicrobial communities, we are developing high-throughput methods for identifying conditions under which the constituents of a community will coexist, without the addition of expensive chemicals such as antibiotics or artificially constructed inter-strain dependency. We have focused on the role of resource competition under nutrient poor conditions. Simple resource competition models do not fit the experimental results. Moreover, we have found that the ratio of two bacterial species, *Escherichia coli* and *Salmonella typhimurium,* in a liquid co-culture can be modulated by the addition of very inexpensive chemicals, essentially defining experimental conditions for tuning population structure. Libraries of transcriptional reporters for each of the species have been employed to assess changes in gene expression under conditions that lead to differing community compositions. Analyzing changes to the transcriptome of each organism provides insight into how changes to the environment that affect community composition affect the physiology of each microorganism. Changes in gene expression observed between conditions leading to different population structures were subtle, indicating that the core physiologies of the microorganisms are similar under the conditions used to tune the population. The ability to change the relative abundance of microorganisms within a mixed population without greatly altering the nature of the constituents of the community increases the potential of multispecies cultures for biotechnological and industrial applications, where employing mixed

cultures could both decrease the strain on a given organism and provide additional levels of control. The elucidation of the molecular and genetic basis of the interactions between strains in these synthetic communities will further enhance our ability to design more complex communities and provide insights into naturally occurring communities.