

Kirwin Providence section 15

1. Effect of bacteria infection on tissue repair (Project with relevance to Human health and Medicine)
2. Effect of bacteria gene products on neutrophil motility (Project with relevance to Human health and Medicine)
3. Design and use of micro-fabricated devices to study cell motility (Project with relevance to Human health and Medicine)
4. Determining the composition of soil microorganisms (Project with relevance to Environmental science)
5. The role of proteins and protein secretion in Eukaryotic biofilm formation (Project with relevance to Environmental science)

To accomplish my research goals, I utilize molecular biology tools, and an interdisciplinary approach that encompasses the fields of microbiology, immunology, and cell biology. The following background information will introduce you to the model system and tool organisms employed in my laboratory.

Background

Neutrophils, also referred to as Polymorphonuclear leukocytes (PMNs), are a subset of white blood cells that provide a critical innate immune defense against invading pathogens. Many, if not all, prokaryotic microorganisms are potential human pathogens. *Pseudomonas aeruginosa*, for example, is an aerobic, Gram negative opportunistic pathogen that is the major cause of lung damage in cystic fibrosis patients. This bacterium is also a major cause of infections in immunocompromised individuals, such as burn victims or those undergoing chemotherapy. In addition to these characteristics, *P. aeruginosa* is also capable of infecting a wide range of plant hosts, and is important for biofilm formation. As such, research centered around this prokaryotic microorganism directly influences our understanding of microbiology, immunology, environmental sciences, and bioremediation. Additionally, because *P. aeruginosa* is capable of directly interacting with other bacteria in the environment through a cell-to-cell communication system called quorum sensing, research centered around this prokaryotic microorganism also directly influences our understanding of Biochemistry-based cellular events.

My laboratory is engaged in two research projects that stem from the following observations:

1. *P. aeruginosa* and the innate human immune system.
2. The dynamic relationship between *P. aeruginosa* and eukaryotic microorganisms such as algae in the formation of ecologically important biofilms.

Research Project #1:

***P. aeruginosa* and the innate human immune system.**

P. aeruginosa relies on its motility behavior in order to colonize human tissue. This activity can lead to disease if the bacteria are not removed via the process of phagocytosis that is primarily mediated by neutrophils. The moist environment of a fresh wound is ideal to support both flagella-mediated and pili-mediated bacteria locomotion. The wound environment is also rich in extracellular matrix (ECM) proteins such as fibronectin. Fibronectin, has been implicated in mediating *Fusobacterium nucleatum* attachment to human cells. This attachment event is an important initial step in disease progression, and *F. nucleatum* is frequently associated with periodontal diseases, as well as invasive human infections of the head and neck, chest, lung, liver and abdomen. Research from my lab has identified fibronectin as an important ECM protein that also regulates neutrophil chemotaxis. Chemotaxis is defined as a cells ability to migrate toward high concentrations of a stimulant molecule. These stimulant molecules can be derived from the host, or directly released from bacteria.

We have used novel, micro-fabricated devices that allow us to study the role of fibronectin in the host immune cell response to stimulant molecules similar to those released by opportunistic pathogens such as *P. aeruginosa*. Briefly, we borrow technology from the computer and engineering industries that allows us to produce devices that fit on the surface area of a standard microscope slide. These devices generate gradients of stimulant molecules. By coating the bottom of the device with ECM proteins such as fibronectin we were able to study how neutrophils respond to stimulant molecules in the context of adhesion to fibronectin.

Currently, my research group (which includes collaborators at Massachusetts General Hospital, Albany Medical College, and Ithaca College undergraduates) is designing new devices that allow us to study the effect of various ECM proteins on both *P. aeruginosa* and neutrophils, and how this interaction relates to disease progression.

My interdisciplinary approach to this research project engages students at many levels. First, students gain experience in classical microbiology, as well as modern molecular approaches to study microbiology. Second, students are engaged in aspects of immunology and cell biology. This relatively novel approach to research at the undergraduate level emphasizes the importance of studies in related disciplines. Finally, students gain practical experience in “product design” and manufacturing of novel scientific “tools”. The relevance of this skill is highlighted by my experience as a project manager for a start-up Biotechnology Company.

This research project offers several opportunities for undergraduate students. Current research projects include:

- 1. Determine the mechanism by which wound-associated ECM proteins promote *P. aeruginosa* pathogenesis**
- 2. Continue the development of micro-fabricated devices that aid in our study of how *P. aeruginosa* interacts with the innate human immune system.**

Research Project #2:

The dynamic relationship between *P. aeruginosa* and eukaryotic microorganisms such as algae in the formation of ecologically important biofilms.

Ecologically important biofilms are communities of microorganisms that adhere to environmental surfaces such as a rock at the bottom of a stream. Growth of these communities is associated with the secretion of extracellular polysaccharides. These polysaccharides in addition to the microorganisms themselves constitute the base of an aquatic food web. Indeed, the health of an aquatic community is

usually measured by assaying for the quantity and quality of certain prokaryotic and eukaryotic species. Understanding the initial steps associated with biofilm formation allows for the development of better strategies for the management of aquatic ecosystems. It is well documented that cell adhesion to inert substrates is a required step towards biofilm progression. Recent data from our lab suggests that proteins (not polysaccharides) may mediate the adhesion of *Penium* (an algae) to inert substrates. Overtime, these adherent desmids secrete an abundant quantity of polysaccharides that encase the proliferating cells. This developing biofilm quickly becomes colonized with prokaryotes such as *P. aeruginosa*. Little is known about the mechanisms that support the maturation of the biofilm with respect to the specific species of organisms found within.