Biochips for Detecting Polymicrobial Infection

Liping Tang1* and Wenjing Hu2

1Department of Bioengineering, University of Texas at Arlington, Arlington, Texas 76019-0138, USA
2Progenit Inc., Arlington, Texas 76001-5689, USA

Animal models are commonly used to study the pathogenesis of infection and to evaluate the effectiveness of treatments in combating infection. However, microbial infection in laboratory animals may also exert a devastating effect on animal healthcare. Many microorganisms have been found to cause species-specific mycoplasmal and bacterial diseases in animals [1,2]. For example, mycoplasmosis, which is an endemic disease in some rodent colonies, can cause respiratory and genital tract infections [1,3-5]. Pasteurella multocida, a common pathogen in rabbit colonies, can cause upper and lower respiratory tract infections, subcutaneous abscesses, middle and inner ear infections, and reproductive tract infections [1,6]. Interestingly, some animal species may serve as asymptomatic carriers of bacterial infections which can cause severe clinical disease in other species. Bordetella bronchiseptica can reside in a rabbit colony without presenting any symptoms of disease. However, it can trigger severe respiratory distress in guinea pigs [7]. In addition, viral and parasitic infections in laboratory animals may be asymptomatic. However, the infection of these pathogens has a significant influence on the overall immune reactions and can decrease reproductive efficiency [2,8]. Although animal models have been used in numerous studies for investigating mechanisms and therapy for infection, there are limited methods which can be used to monitor the responses of microorganisms in vivo.

Bacterial colonization and inflammatory cell accumulation in several vital organ systems of animals are two major unifying symptoms associated with microbial infection [9-11]. Systemic and localized infection cannot be determined via visual observation. Although inflammatory responses caused by external stimuli can be easily identified, the extent of internal or even subcutaneous inflammation cannot be easily determined. Diagnoses of inflammatory responses and infection are typically carried out via serological tests, microbial assays, and/or histological evaluation. However, the isolation of tissue via tissue biopsy or collections of blood and tissue fluids are invasive and rather random procedures. Furthermore, these standard assays are often time consuming and require specialty equipment and facilities. In addition, such analyses require tedious laboratory procedures and specialized facilities. It usually takes several days to obtain the results. These prolonged processes substantially hinder research progress and increase overall research costs. Therefore, there is a need for the development of a novel technology to screen and determine the extent of polymicrobial infection in laboratory animals. With the rapid development of biochip technology, it is highly desirable that new biochips can be fabricated for detecting polymicrobial infection in laboratory animals.

Although intensive research efforts have been placed on the development of imaging tools for studying the pathogenesis of infection in vivo [12-16], most of these works were carried out using genetically engineered bacteria to emit bioluminescent signals or microorganisms preabeled with various fluorescent dyes. Limited progress has been made on the development of imaging probes capable of specifically targeting and detecting microorganisms in vivo. Several recent studies have made good advancements on this front. For example, recent studies have revealed that 99mTc-labeled peptide derived from human ubiquitin (UB129-41) and lactoferrin (hLF1-11) can be used to detect local Candida albicans and Aspergillus fumigates infection [17]. In addition, maltodextrin-based probes have been developed to detect and to quantify bacteria in vivo [18]. Taking advantage of the unique interaction between antibiotics and microorganisms, divalent vancomycin-porphyrin has been synthesized and demonstrated to have the capability of imaging enterococci [19]. Optical probes carrying two zinc (II) dipicolylamine units have been used for imaging Staphylococcus aureus and E. coli in mice [20]. On the other hand, substantial progresses has been in recent years on the development of imaging probes for detecting inflammatory responses. Specifically, an imaging probe carrying molecules of folic acid has been demonstrated to gather in inflamed tissue via the folic acid receptors on inflammatory macrophages [21]. The accumulation of Polymorphonuclear Leukocytes (PMN) in tissue can be imaged and quantified using imaging probes targeting PMN’s formyl peptide receptors [22]. By incorporating these recent discoveries in the area of inflammatory and infection imaging, it is conceivable that a biochip can be designed for determining and quantifying the extent of inflammatory reactions and bacterial colonization in the blood, tissue and body fluid of laboratory animals. We believe that the information generated from the infection biochip will improve our understanding about the mechanisms of infection and provide critical real-time information needed for developing novel therapeutics to reduce effectively the spreading of polymicrobial infection in laboratory animals and humans.

References


