Protein and Cellular Interactions with Biomaterials: Perspectives for Nanotechnology and Tissue Engineering

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Over the past two decades, the research and development of new biomedical materials has turned from "passive" materials to materials that actively interact and integrate with their biological environment. Unfortunately, this paradigm shift has not been matched by a requisite enhancement of our knowledge of the mechanisms of interaction between the materials and proteins, cells and other materials within the biological environment. Given the unique nature of tissues and organs, we lack biological design criteria for the development of new materials and devices constructed from these materials. Additional constraints in our developing biological design criteria and structure/biological property relationships are our dependence on in vitro studies and non-human models in the development process.

In the early days of biomaterials, 1950 to 1975, the biomaterials development was dominated by the characteristics of the materials intended for prostheses and medical devices. The long-term integrity of the biomaterial as well as its nontoxic nature was considered to be important. Materials identified as suitable for prostheses and medical devices were based on macro in vitro and in vivo studies using simplistic, naïve and, in some cases, inappropriate models for study. Biomaterials were judged on their macro-behavior and little was known of biological interactions at the micro- and nano-levels. From 1975 to 2000, biological interactions with biomaterials began to be more extensively investigated. Advances in our knowledge of biological mechanisms, for example, the coagulation, thrombosis, and complement pathways, led to a better understanding of biological interactions with biomaterial surfaces. In the 1980's, the revolution in techniques for the study of cell and molecular biology led to their application to the investigation of interactions occurring at biomaterial interfaces. The development of antibodies to specific components in biological mechanisms led to the development of assays that were specific and quantitative. These then led to quantitative approaches by which potential biomaterials could be evaluated. Examples here include the development of immunoassays for complement components that enabled a fundamental understanding of complement activation and leukocyte adhesion with kidney dialysis membranes. Another example is the identification of platelet activation by the quantitation of platelet factor 4 and beta-thromboglobulin that identified platelet activation and release, i.e., thrombus formation.

In the 1980's, the revolution in techniques for the study of cell and molecular biology led to their application to the investigation of interactions occurring at biomaterial interfaces. With the advent of tissue engineering and regenerative medicine, heavy emphasis has been placed on biological interactions with biomaterials. In some cases, this had led to an undesirable decrease in the appreciation of material properties and their role in these new scientific areas. An example of these types of problems is presented with biodegradable scaffolds for tissue engineering and their ultimate disposition including changes in form and integrity with resultant changes in the inflammatory and foreign body reactions over the implantation time.

In addressing the theme of this symposium, the real question is what haven't we learned as opposed to what have we learned in some 50 years of biomaterials research and development. Continuing challenges and barriers to the successful use of biomaterials as an enabling technology in the development of new medical devices, prostheses, and tissue engineered constructs will be discussed. These challenges and barriers are areas for significant advancement and areas that must be addressed if we are to successfully move forward in the realization of biomaterials as an enabling technology. The future of new biomaterials is dependent upon an enhanced knowledge base of molecular, cellular, and tissue interactions with materials. Obviously, these interactions span nano-, micro-, and macro-dimensions. Our focus for the future must be on understanding mechanisms of interaction between the new biomaterials and their in vivo environment. This focus on broadening our mechanistic understanding of tissue/material interactions will permit development of design criteria from a biological perspective.