

## **Summary: Biomaterial-Tissue Interactions- Wataha- Sept, 1999**

### **Description and Definition of Area**

*Definition:* Biomaterial-tissue interactions are best described by the term biocompatibility. Strictly defined, biocompatibility is the ability of a material to elicit an appropriate biological response in a given biological application. This definition implies that any material placed into the body will not be inert and will interact with tissues in a dynamic way, altering both the material and the tissues around it. The biological response to a material is critically dependent on three factors: (1) the composition-structure of the material, (2) characteristics of the host site, and (3) the functional demands on the material. Thus, a material cannot be characterized as biocompatible or not biocompatible until its host site and function are defined.

*Description:* Biomaterial-tissue interactions are relevant to a wide variety of disease states and treatments. Traditionally, this area has focused on materials which can support or replace lost human tissue, for example in dentistry (filling materials/implants/material-tooth bonding), orthopedics (femoral implants), and vascular biology (arterial stents). Biomaterials have also been used in more esthetic applications such as maxillofacial prostheses to restore facial contours after surgical treatment for cancer, or in dentistry to restore tooth esthetics after trauma or dental disease. More recently, biomaterials-tissue interactions have been involved in an area called tissue engineering or bioengineering. Roughly defined, tissue engineering is the manipulation of developmental or wound healing processes to repair or replace lost tissue. In this area, biomaterials have been used as permanent or resorbable scaffolds (for cells or other critical molecules), drug-delivery devices, and barrier materials. For example, cartilage cells may be seeded onto a resorbable scaffold, implanted, and allowed to support cartilage development. Or pancreatic islet cells may be encapsulated in a material which allows transport of only small molecules and nutrients, but not immune cells. In dentistry, collagenous or polytetrafluoroethylene membranes have been used as barrier to prevent growth of epithelial elements and allow regeneration of bone around teeth or implants. In any case, biocompatibility issues are critical to the success of these treatment strategies.

### **Status of this Area at MCG**

To my knowledge much of the biocompatibility research to date has occurred in the School of Dentistry, although there is some research in orthopedics by a former member of the dental school faculty (Steflik), some interest in cranial sutures (Yu, Borke, Pashley) and within the vascular biology group (J Pollock).

Within the dental area, biocompatibility research has an international reputation for excellence, NIH funding (Pashley, Mackert, Schuster for \$0.9M), clinical funding (Dickinson, Browning), and industrial funding (Pashley, Sharawy, Whitford, Ruggenberg, Wataha, and Lefebvre for \$0.4M). To a great extent, there is good translation of basic science research to clinical applications. For example, Dr. Pashley has done exemplary work in resin-dentin interactions at the molecular level which have translated into clinical bonding agents used routinely today in dentistry. Dr. Dickinson commonly relates fundamental mechanical properties of restorative materials to clinical performance. Dr. Ruggenberg has translated basic knowledge of light-curing polymerization to better clinical techniques and devices.

Research in biocompatibility could be expanded successfully outside of dentistry. Many of the techniques and materials used in the dental field are directly applicable to other areas such as orthopedics and vascular biology. The ability of this area to grow will depend on factors which can expand boundaries into other schools and institutes. The dental market is relatively small and will not attract major research dollars by itself.

## **Needs for Expansion of Area**

### ***Programmatic Funding, Translational Funding***

In my opinion, the needs for programmatic and translational funding are the same, so I treat them together. I see the need for the following factors to realize growth in this area at MCG:

- internal education of medical and allied health faculty about the opportunities for biocompatibility research in their fields. Make existing research groups aware of each other.
- internal recruitment of basic science and clinical faculty from all MCG schools and institutes to collaborate in the biomaterials-biocompatibility area.
- meaningful collaboration with engineering programs. The two logical choices are Georgia Institute of Technology and Clemson. These schools are among the top engineering schools and are an untapped source of engineering expertise, new materials development, and instrumentation unavailable at MCG. Collaborative efforts with Georgia State, UGA, and Fort Gordon are also possible. To some extent, collaborations have occurred at the School of Dentistry (GIT: Marek w/ Wataha; GSU: Ghazi w/ Wataha/Pashley; Clemson: Woods w/ Pashley; Fort Gordon: w/ Pashley), but they need to be greatly expanded. I am not aware of collaborations outside of the Dental School in this area, but they may exist.
- external recruitment of bioengineers or individuals with expertise in tissue engineering.

### ***Where to put MCGRI Funding?***

The most meaningful short-term (1-3 years) use of MCGRI funding would be to provide startup funds for collaborative efforts between (1) faculty members of different MCG schools/institutes, (2) faculty members at MCG/GIT-UGA-GSU (some mechanisms already exist in this regard), and (3) guest seminars in relevant areas such as tissue engineering.

Longer term (> 3 years) use of funds would best be spend on recruiting and supporting faculty in any collaborative efforts which emerged. To some extent we will have to focus within this area to be competitive. MCGRI funds would be best placed in focal areas which emerge as a result of shorter-term efforts.

## **Needs for International Recognition**

Biocompatibility issues are much 'hotter' in Japan and Europe than in the US. For example, a great deal of my funding comes from Swiss and German companies. There are quality research groups abroad in the biocompatibility area (France, Germany, and Japan). The dental area already has an international reputation for research in this area. In my opinion, this reputation could serve as a foundation for expansion of our research into other areas. It is possible that some recruitment of faculty from Europe or Japan would improve our international stature.

## **Relevance to GA Constituency**

The greatest strengths of the biomaterials-tissue interactions area are (1) its ability to be understood and appreciated by the lay public (including legislators), (2) its ability to be applied to a variety of disease processes, and (3) its ability to provide a collaborative base among Georgia universities. In this sense, no matter which areas MCG finally selects as research foci, the biocompatibility area can be an added 'dimension' which provides good PR and a basis for clinical translation of more basic discoveries.

## **Impact of Early Retirement Program**

Fortunately, the early retirement program at MCG will not significantly impact this research area. Dr. Gene Dickinson, one of the clinical researchers in the dental group will retire, but it is expected that Dr. Bill Browning will succeed him in this regard. This succession has been planned for several years.

## **Outline of Specific Needs for Next 3 Years:**

To achieve the goals proposed above, the following specific support is proposed:

### **A. To encourage collaboration between groups with overlapping interests in the Biomaterial-Tissue Interactions area.**

1. Fund travel and honoraria for external speakers in the areas of biocompatibility of materials, tissue engineering and biomimetics, materials for drug delivery, and new materials with promising biological properties. The speakers may also be potential candidates for recruited positions or visiting scholars (see below), and these presentations would serve as a pre-recruitment contact with these people. Speakers would present as part of a new or existing seminar series which has school-wide contact.

Estimated cost: \$36,000 (4 speakers/year, \$3000/speaker, 3 years duration)

2. Fund 4 special research awards for collaborative interdisciplinary research involving biomaterial-tissue interactions. Awards would have to show collaboration among individuals at MCG from different disciplines. Priority would be given for novel collaborations with greatest potential for significant (> \$300,000) extramural funding in the biomaterials-tissue interactions area. Awards would be for 2-3 years duration, maximum amount of \$75,000.

Estimated cost: \$300,000

### **B. Recruitment of individuals to MCG with special training in the biomaterials-tissue interaction area. Goals would be to recruit:**

1. Two individuals with engineering training and expertise which would enhance collaborative efforts at MCG and enhance collaborations with engineering schools. Areas of bioengineering and tissue engineering would be most desirable. Ideally, one individual would have expertise in polymer fabrication, degradation, and characterization, and one individual with expertise in alloys or ceramics (depending on the collaborations which develop or appear feasible at MCG). If possible, a joint appointment with Georgia Tech or Georgia should be explored for these individuals.
2. Two clinical individuals with interests and experience in clinical research in the biomaterial-tissue interaction area. These two individuals could overlap with other positions requested from other areas. For example, a position in the cardiovascular area could find an individual with clinical interests in vascular stents. These individuals would have combined degrees (DMD/PhD or MD/PhD) and have experience in clinical research. Ideally, one individual would have experience in vascular materials and one would have experience in the orthopedic materials.

### **C. Support training program in biomaterial-tissue interaction areas in the following areas:**

1. Stipends for post-doctoral individuals, preferably from engineering or bioengineering areas or the biocompatibility areas of strength in Europe and Japan. These individuals would bring their expertise to MCG and could also benefit from the

medical-dental expertise here. Visits would be for 1 year. Selection of these individuals would be based on their potential to provide interactions which would strengthen areas of focus in this area at MCG. 4-5 positions are proposed.

2. Recruit graduate students and fund tuition and stipends for students in the biomaterial-tissue interaction areas. Recruit these individuals from traditional biological areas as well as from bioengineering and engineering programs. It would be prudent to try to consider graduate students with joint programs at Georgia Tech and MCG. Support for 5 for more graduate students for 4 years is proposed.