I. Executive Summary

This bibliometric study of core papers fundamental to tissue engineering produced results in four areas: an overview of the growth of the field, an analysis of NSF's role in the field, a mapping of co-authorship patterns, and an analysis of international patenting

The foundation of the paper side of the study is a database of information on core papers fundamental to tissue engineering. This database was carefully constructed in a process developed to meet the challenge of identifying the boundaries of such an interdisciplinary area. The study focuses on research that synthesized many areas of biomedicine with the aim of seeding autologous cells and growth factors onto three-dimensional biodegradable scaffolds with the aim of forming new functional tissue. Papers and patents in this area were identified using search strategies or "filters" described in the appendices. The set of papers found using the filters was augmented by papers highly cited in the patents and in review papers. Of the papers analyzed in the study, 66% were cited in review articles or patents, and 33% were found using the search strategies described by the filter.

The analytical results revealed that the number of core papers fundamental to tissue engineering has been growing strongly since about the mid 1980's. The paper most cited in reviews of the field is: Langer & Vacanti, "Tissue Engineering," Science 1993 May 14;260(5110):920-6. This paper was cited 39 times in the reviews and 11 times in patents. This paper acknowledges funding from NSF as well as funding from other sources.

Analysis of the use of the term "tissue engineering" in titles and abstracts of papers indexed in PubMed suggests that there were three phases in the spread of the concept of tissue engineering. In the first phase, researchers imagined the possibility of designing replacement tissue. This is exemplified by papers in 1984/85 by Wolter and Meyer examining a prosthesis removed from an eye after 20 years. Wolter and Meyer discussed: "the significance of the successful adaptation of the plastic materials of the prosthesis to the tissues of the cornea and the fluids of the inner eye for the future of tissue engineering in the region of the eye." In the second phase, 1989 through 1997, the term "tissue engineering" began to be used regularly in abstracts and titles. During this period, the term was applied to work concerning all the main organs closely connected to tissue engineering: bone, cartilage, blood vessels, liver, skin, neurons and also to biomedical materials. The third phase of dramatic growth began in 1998 and continues. In this phase we also see a few papers concerning other organs, and in fact the return of papers concerning eyes. Overall, the growth in the use of the term "tissue engineering" in titles and abstracts seems not unlike the growth in number of core papers fundamental to tissue engineering.

We find that NSF supported about 12% of the papers in the field overall. However, NSF focused its support on basic research and biomaterials. Therefore, when clinical research is excluded from consideration, NSF's share rises to 20%. 86% of NSF-supported work is published in the most basic journals or in the two leading biomaterials journals: *Biomaterials* and the *Journal of Biomedical Materials Research*. In contrast, 52% of research supported by other funders is basic or in those two journals. NSF's research is also focused on the core participants in the field. 17% of the papers from leading institutions acknowledge NSF support compared to 2% of papers

from institutions that appeared only once on a core paper fundamental to tissue engineering. More peripheral, and one-off participants are much less likely to acknowledge NSF research support. Thus it is no surprise to find that NSF played a larger than expected role in supporting the work of leading researchers such as R Langer, JP Vacanti, and DJ Mooney.

The patterns of co-authorship in the field are portrayed in an innovative series of figures, tables and maps developed for this study. These reveal the highly collaborative nature of the work undertaken by R Langer and JP Vacanti, with whom most lead authors in the area have worked at least once. Papers by Langer and Vacanti list over 250 coauthors. Several leading authors appear to have started as students of Langer or Vacanti, and several more appear only as their co-authors. Six multi-dimensional maps of the paper-by-paper development of lead authors' work in the area were developed for authors supported by NSF. These reveal the interweaving of public and private knowledge and the public and private sectors in the development of tissue engineering research, and precisely position NSF support in relation to this.

In parallel with the analysis of tissue engineering literature, CHI was engaged to do a patent analysis to study the international patenting trends in tissue engineering. We found:

1. Patenting in the area is increasing steadily and has not yet peaked.

2. Most of the patents are coming from US inventors and assignees.

3. Most of the key inventions are coming from US assignees, especially MIT, Advanced Tissue Sciences, and Regen Biologics Inc.