1.0 Introduction

NSF provides the funding that sustains many research fields as advances in these fields expand the boundaries of knowledge. Equally important, the agency provides seed capital to catalyze emerging opportunities in research and education. It supports a portfolio of investments that reflects the interdependence among fields, promoting disciplinary strength while embracing interdisciplinary activities. Its investments promote the emergence of new disciplines, fields and technologies.[1]

Engineering and technology are not static bodies of knowledge and practice, but dynamic processes characterized by constant change. In supporting fundamental research in engineering, the National Science Foundation is necessarily planting the seeds of continued change, for the knowledge gained is itself the fuel for this ongoing transformation.

But new knowledge does not affect solely the particulars of specific technologies and branches of engineering. More fundamentally, it may transform our understanding of knowledge itself, of its organization and of the means of creating and utilizing it most effectively, pointing to new ways of thinking about engineering challenges and, ultimately to the emergence of new areas of research and practice that in time come to be recognized as distinct fields of activity. Thus, in fulfilling its mission to preserve and enhance the vitality of engineering in service of the nation, NSF must constantly be alert not only to opportunities for continuing advances within established lines of inquiry, but also to the possibility that entirely new directions for research may offer compelling benefits for engineering and for society – indeed, that they may be essential to continued progress.

In practice, to what extent has NSF served as a catalyst for the timely emergence of productive new domains of engineering research? What are the specific mechanisms by which it has done so?

They are difficult questions to answer, for the innovation system of which engineering research is a part – and in which NSF plays an important role – is actually a complex ecosystem characterized by noisy signals traversing tangled pathways of influence and feedback among the system components. Gathering the data that may enable one to make sense of the system is challenging, both because the system is only imperfectly "instrumented" with routine measures of its behavior, and because *ad hoc* observations are costly both to the system and to its observers. Finally, the complexity of the pathways of influence that govern the system can make attribution of causality problematic, and the idiosyncratic variety of the particulars in different domains of engineering and innovation make generalization perilous.

This report examines the emergence of the research field of tissue engineering (TE), focusing on developments in the United States. Its purpose is to document the evolution of tissue engineering into a distinct area recognized as such by scholars, to document NSF's involvement through its Directorate for Engineering, and to evaluate the significance of NSF's role in the broader context of the field's evolution.

As a topic of study, tissue engineering is interesting for several reasons. First is the field's inherent human interest. The ultimate goal of the field is to develop powerful new therapies – "biological substitutes" – for structural and functional disorders of human health that have proven difficult or impossible to address successfully with the existing tools of medicine. This goal is made all the more provocative by its science-fiction vision of man-made, living "replacement parts" for the human body,

1 "NSF's Role", p. iv, *NSF GPRA Strategic Plan FY 2001-2006*, September 30, 2000, http://www.nsf.gov/pubs/2001/nsf0104/nsf0104.pdf (URL verified December 30, 2002).

and more compelling by its framing in terms of the lives lost through the ultimately irremediable shortage of transplantable organs.

Of special interest to research managers is the unusual breadth and depth of TE's interdisciplinarity: the knowledge needed to meet the technical challenges posed by TE spans many subdisciplines not only of engineering, but also of science and of clinical medicine. To reach their ultimate goal – successful therapies – tissue engineers must integrate many very different kinds of knowledge and ways of thinking.

Finally, from the perspective of an evaluator, the study of an emerging, strongly interdisciplinary field – a complex, ill-defined, moving target – represents a challenge of the first order, demanding ingenuity and flexibility as much as narrowly-defined methodological rigor, in pursuit of the real prize: qualitative insight that is well-founded in empirical observation and credible in its logic.

Where does one begin such a study? In the contemporaneous historical analysis of an emerging, strongly cross-disciplinary field, it can be difficult to specify the object or scope of the inquiry precisely at the outset. Almost by definition, the conceptual frameworks that define the substantive extent of the field remain fluid, while the field's institutional infrastructure is typically both limited and not fully apparent to a superficial review. The investigation will often take on a "bootstrap" character, in which part of the task of the inquiry is to delimit its own scope through analysis of the evidence that is gathered.

Within a biomedical context, the term "tissue engineering" points naturally to a central concept that is simple, powerful and intuitive: the creation of living tissues for therapeutic purposes. It is not obvious, however, how far this concept should extend. What counts as a "tissue"? (For example, are encapsulated pancreatic cells that function autonomously a tissue? Is blood a tissue? Are unorganized stem cells a tissue?) Must the "engineering" be done *in vitro*, or is induction of tissue growth *in situ* in a living organism also "tissue engineering"? Must the engineered product be implanted, or is improvement of the function of extracorporeal devices through the introduction of living cells to be considered "tissue engineering"? Must the product be directly therapeutic, or is the use of complex, cell-based products in diagnostic applications also a type of "tissue engineering"? To what extent or under what circumstances should fundamental research on underlying concepts or enabling technologies be considered tissue engineering?

Thus, the present study began not with a precise definition of tissue engineering, but rather with a set of plausible entry points for inquiry: the names of a few key researchers widely considered synonymous with the field, a handful of review papers, a list of NSF awards in support of TE research and ancillary activities – and the term "tissue engineering" itself, which could be presented as a filter to search engines used to scan bibliographic and research funding databases as well as the Internet. Following a chain of referrals, citations and links from these initial sources, the investigation accumulated many alternative definitions for the term, as well as a growing list of suggestions by expert interviewees of domains of research activity that they believed could or should be considered part of the field.

A central and ongoing task of the study was to analyze the character and overall coherence of the scope of activity delineated in this way. Specific findings in this respect are presented in appropriate context in the later sections of this report. However, it is worth noting here that no simple boundary-setting rule could be identified that maps cleanly to the scope of activity of researchers who think of themselves, or who are thought of by others, as being tissue engineers. In the end, our own concept of tissue engineering remained a pragmatic and operational one. In particular, because part of the charge for this project was to understand the role of NSF in shaping the field, and because funding agencies act through support of people and their activities, final judgment of what to include in the story was shaped as much by the sociological structure of the field – the people and institutions involved – as by its intellectual or substantive structure.

To understand the emergence of a research field, one must understand also something of what came before. Thus, we begin in Chapter 2 by examining the roots of tissue engineering in existing areas of research. In Chapter 3, we discuss the emergence and evolution of a shared concept for this new enterprise, delineating what participants believed to be its essence, through an examination of the origin and varying meanings and usages of the term "tissue engineering". Chapters 4 and 5 address the reality of tissue engineering: Chapter 4 discusses its scope and substantive character and Chapter 5 describes the community of tissue engineers, outlining some of its general characteristics and introducing specific individuals and institutions that have played central roles in the emergence and growth of the field and the most important genealogic relationships among them. Chapter 6 provides an overview to activities and major contributions in the emerging years of the corporate sector. Chapter 7 completes the spectrum of participants in the field by reviewing other prominent institutions participating in the goal of tissue engineering. Finally, we end in Chapter 8 with a discussion of the role of the National Science Foundation and its Directorate for Engineering in the emergence of tissue engineering. Supporting material is presented in the appendices. Appendix 1 describes our approach to data collection for the study; Appendix 2 presents a roster of individuals currently active or who have previously played an important role in tissue engineering, with information about their training and (where applicable) current employment; Appendix 3 lists the personnel interviewed for this study; and Appendix 4 contains our interview protocols. Finally, Appendix 5 includes a separate analysis conducted by CHI research on bibliometrics and patents, key findings from which are also included in the main report. A separate wall chart graphically illustrates the genealogy of the field.