# 8.0 The Role of the National Science Foundation (NSF)

The National Science Foundation, particularly through its Directorate for Engineering, appears to have played an important role in the emergence of tissue engineering as a recognized field of activity, and in shaping the character and in determining the direction of the field. In addition to introducing and defining the larger concept of tissue engineering, the Foundation has provided support to key people, ideas, and institutions as discussed below.

## 8.1 Financial Support

From an examination of Fastlane Award data as an illustration of NSF support for tissue engineering, it is evident that the majority of NSF support goes toward individual investigator awards and Centers research (Table 8.1)[132]. NSF is also a strong supporter of workshops, conferences and other meetings, which suggest a prominent role in support of networking activities among individuals active in the field. Analysis of NSF funding by division shows that the vast majority of the agency's support of tissue engineering—more than 80%--emanates from the Bioengineering and Environmental Systems (BES) and Engineering, Education and Centers (EEC) Divisions—both of which reside under NSF's Directorate for Engineering. The role NSF funding has played in research will be explored in the next section.

***Table 8.1: NSF Funding of Tissue Engineering 1988 – 2001, by Award Type***

| | | |
|---|---|---|
| Number of Awards (between 1988 - 2001) | **92** | |
| Total Dollar Value of NSF Awards (Current Dollars) (between 1988 - 2001) | **70,543,307** | |
| Awards for Individual Investigator Research (only) | 12,576,301 | 17.8% |
| Exploratory Awards (SGERs) | 216,866 | 0.3% |
| Awards for Instrumentation | 851,689 | 1.2% |
| Awards for Curriculum Development | 820,602 | 1.2% |
| Awards for Networking and Meetings | 258,000 | 0.4% |
| Awards for Diversity | 1,000,000 | 1.4% |
| Center Awards* | 50,349,031 | 71.4% |
| Career Development Awards (POWRE, PYI, etc.) | 4,070,835 | 5.8% |
| SBIR Awards | 399,983 | 0.6% |
| **Total Dollar Value of NSF Awards (Current Dollars)** | **70,543,307** | **100.0%** |

Source: FastLane Award Data keyword search using term "tissue engineering" supplemented by additional data from the Directorate of engineering

** The Center Award supports includes funds for three Centers – the Georgia Tech/Emory Center for the Engineering of Live Tissues, the University of Washington Engineered Biomaterials (UWEB) ERC, and MIT's Biotechnology Process Research Center (BPEC). Data on these last two Centers was not pulled from FastLane using the keyword "tissue engineering". Their dollar amounts were added manually to the total represented here.* ***As a result, the final dollar value of Table 8.1 does not match that of Table 8.2, which is exclusively pulled from FastLane.***

[132] NSF FastLane search for the period 1988-2001 using the keyword "tissue engineering"

***Table 8.2: NSF Funding of Tissue Engineering 1988 – 2001, by Division***

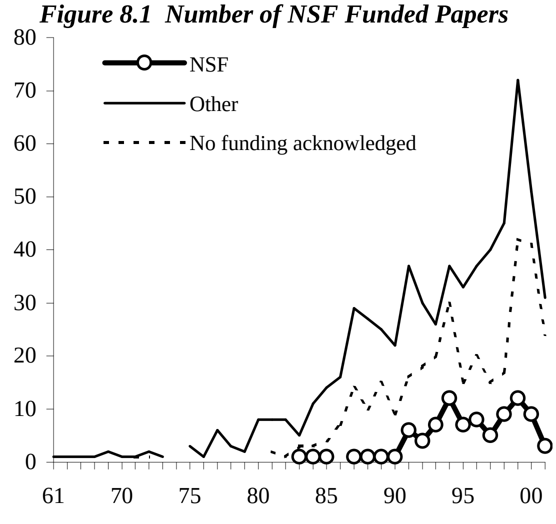
| | Current Dollars | Percent |
|---|---|---|
| BCS Total | 11,000 | 0.0% |
| BES Total | 12,671,526 | 38.5% |
| CTS Total | 311,798 | 0.9% |
| DBI Total | 1,919,379 | 5.8% |
| DMI Total | 399,983 | 1.2% |
| DMR Total | 1,008,863 | 3.1% |
| DUE Total | 74,780 | 0.2% |
| EEC Total | 13,535,560 | 41.1% |
| EPS Total | 2,316,325 | 7.0% |
| HRD Total | 117,579 | 0.4% |
| IBN Total | 214,441 | 0.7% |
| INT Total | 29,000 | 0.1% |
| MCB Total | 300,000 | 0.9% |
| **NSF Total** | **32,910,234** | **100.0%** |

Source: FastLane Award Data kyword search using term "Tissue Engineering"
Note: BCS: Behavioral and Cognitive Sciences, BES: Bioengineering & Environmental Systems, CTS: Chemical and Transport Systems, DBI: Biological Infrastructure, DMI: Design, Manufacture and Industry, DMR: Division of Materials Research, DUE: Division of Undergraduate Education, EEC: Engineering Education & Centers, EPS: Experimental Program to Stimulate Competitive Research, HRD: Human Resource Development, IBN: Integrative Biology and Neuroscience, INT: International; MCB: Molecular and Cellular Biosciences

## 8.2 Researcher Support

While the interviews did not shed much light on the role of NSF as a funder, bibliometric analysis (see Figure 8.1 and Table 8.3 below, as well as Appendix 5 for the full bibliometrics and patent analysis) revealed that NSF has had a significant role in supporting lead researchers in the field[133]. Figure 8.1 illustrates the relative role of NSF support of TE over the years. NSF support has been acknowledged on 12% of the papers revealed by the bibliometric analysis. The influence of NSF funding on top researchers in the field, however, has been disproportionately large. Table 8.3 shows that three of the most prolific researchers – Vacanti, Langer and Mooney - acknowledge NSF funding on 19%-37% of their papers, including on the

***Figure 8.1 Number of NSF Funded Papers***




[133] In an analysis carried out for this project, subcontractor CHI Research tallied the funding sources acknowledged by papers retrieved through a PubMed search carried out in September 2001, using a search filter that heavily weighted the scaffolds-and-cell-seeding concept of TE. In the group of 1,056 papers generated by this search, 727 explicitly acknowledged a funding source. Of these, 89 papers or 12% acknowledged NSF support. In the absence of an exhaustive manual review of the funding histories of individual researchers active in tissue engineering, there is no way to determine what the corresponding fraction would be for a more inclusive definition of tissue engineering [than used in the bibliometric study].

1993 *Science* paper (this percentage may, in fact, be even higher, as not all papers list acknowledgement of research funding and, further, some researchers fail to mention all of the funding sources that should be cited in acknowledgements). Given the wide range of tissue engineering activities, it is not surprising that NSF support of researchers varies considerably. Notable researchers such as Linda Griffith, Jeffrey Hubbell, P.M. Kaufmann, and Mark Saltzman also acknowledge NSF on a third or more of their papers, while NSF appears to have had no role in supporting other prominent researchers such as Arnold Caplan, Lisa Freed, V.M. Goldberg or Gordana Vunjak-Novakovic.

***Table 8.3: Sources of Support for Prominent Authors and Their Papers in Tissue Engineering***

| | | | | | Funding type | | |
|---|---|---|---|---|---|---|---|
| Author | TE Papers | # agencies | # of NIH institutes | % NSF | NSF | Other | No funding acknowledged |
| Vacanti JP | 92 | 10 | 8 | 19% | 13 | 57 | 22 |
| Langer R | 76 | 11 | 6 | 26% | 17 | 48 | 11 |
| Mooney DJ | 53 | 5 | 5 | 37% | 17 | 29 | 7 |
| Vacanti CA | 31 | 4 | 1 | 5% | 1 | 18 | 12 |
| Atala A | 28 | 2 | 1 | | | 3 | 25 |
| Caplan AI | 27 | 4 | 5 | | | 27 | |
| Aebischer P | 26 | 4 | 2 | 6% | 1 | 15 | 10 |
| Mikos AG | 25 | 6 | 6 | 17% | 4 | 20 | 1 |
| Yannas IV | 21 | 8 | 4 | 7% | 1 | 14 | 6 |
| Freed LE | 20 | 4 | 3 | | | 20 | |
| Goldberg VM | 19 | 4 | 3 | | | 19 | |
| Kim BS | 18 | 4 | 2 | 43% | 6 | 8 | 4 |
| Vunjaknovakovic G | 18 | 4 | 3 | | | 18 | |
| Ingber DE | 17 | 8 | 3 | 25% | 4 | 12 | 1 |
| Mayer JE | 17 | 5 | 1 | | | 12 | 5 |
| Schloo B | 16 | 3 | | 13% | 2 | 13 | 1 |
| Ma PX | 15 | 5 | 2 | | | 8 | 7 |
| Boyan BD | 14 | 7 | 3 | 15% | 2 | 11 | 1 |
| Cima LG | 14 | 5 | 3 | 40% | 4 | 6 | 4 |
| Hollinger JO | 14 | 4 | 6 | | | 6 | 8 |
| Hubbell JA | 14 | 5 | 2 | 75% | 9 | 3 | 2 |
| Spector M | 14 | 5 | | 8% | 1 | 12 | 1 |
| Winn SR | 14 | 2 | 4 | | | 6 | 8 |
| Reddi AH | 13 | 4 | 2 | | | 6 | 7 |
| Upton J | 13 | 4 | 1 | 10% | 1 | 9 | 3 |
| Grande DA | 12 | 4 | 1 | | | 9 | 3 |
| Allcock HR | 11 | 5 | 1 | 11% | 1 | 8 | 2 |
| Athanasiou KA | 11 | 2 | | | | 4 | 7 |
| Bell E | 11 | 3 | 1 | | | 4 | 7 |
| Green H | 11 | 3 | 3 | | | 9 | 2 |
| Hansbrough JF | 11 | 2 | 2 | | | 8 | 3 |
| Wozney JM | 11 | 5 | 2 | | | 7 | 4 |
| Bruder SP | 10 | 2 | 4 | | | 10 | |
| Galletti PM | 10 | 4 | 3 | | | 4 | 6 |
| Schwartz Z | 10 | 7 | 2 | 22% | 2 | 7 | 1 |
| Yoo JJ | 10 | 2 | 1 | | | 1 | 9 |

*See Appendix 5 for a more extensive listing of authors published in tissue engineering.*

NSF funding, however, is not evenly distributed across all aspects of tissue engineering. NSF support is clearly targeted toward the application of engineering principles, especially with the aim of advancing engineering knowledge. Table 8.4 uses the bibliometric study to identify the sub-fields of tissue engineering where NSF-funded researchers have been most active and demonstrates that the agency has held true to its stated mission and goals. Almost 90% of NSF-supported papers are in fields related to engineering or fields that promote the application of engineering principles to solve problems in a variety of realms. Table 8.4 also shows that NSF support has been highest for biomedical engineering (30 of 145 papers or 21%) and general/miscellaneous biomedical research (27 of 212 papers or 13%).

Both the interviews and the bibliometrics assessment explored the role of NSF in supporting the establishment and growth of TE in institutions. Table 8.5 below lists the top institutions with which authors of TE papers were affiliated according to acknowledgements in the papers (a more extensive listing of institutions involved in tissue engineering can be found in Appendix 5).[134] As the Table shows, NSF supported 12% of the papers produced by authors working at these institutions. The Table shows that, among the TE papers (1) by authors from the leading TE research institutions and (2) that contained acknowledgements of underlying research sponsorship(s), 17% of the papers contained acknowledgements of NSF support.

[134] Note that papers whose authors were at more than one institution were multiple-counted. Please see the Appendix for a more complete listing of institutions. Only the top publishing institutions appear in this excerpt.

***Table 8.4 Tissue Engineering Research Papers, by Acknowledged Sponsor, Field of Journal, and Character of Research[135]***

**National Science Foundation**

| % Share | TE Papers | Field |
|---|---|---|
| 37% | 30 | Biomedical Engineering |
| 22% | 18 | Misc Biomedical Research |
| 11% | 9 | General Biomedical Research |
| 6% | 5 | Neurology & Neurosurg |
| 6% | 5 | Cell Biology, Cytology & Histology |
| 5% | 4 | Biochemistry & Molec Biology |
| 2% | 2 | Polymers |
| 2% | 2 | Biophysics |
| 2% | 2 | Endocrinology |
| 1% | 1 | Orthopedics |
| 1% | 1 | Surgery |
| 1% | 1 | General Chemistry |
| 1% | 1 | General Biology |
| **100%** | **81** | **Total papers covered by ISI** |
| | 8 | Not covered by ISI |

**Other funders**

| % Share | TE Papers | Field |
|---|---|---|
| 14% | 83 | Orthopedics |
| 13% | 78 | Biomedical Engineering |
| 12% | 70 | General Biomedical Research |
| 11% | 63 | Surgery |
| 9% | 53 | Misc Biomedical Research |
| 7% | 39 | Cell Biology, Cytology & Histology |
| 6% | 37 | Neurology & Neurosurg |
| 4% | 26 | Biochemistry & Molec Biology |
| 4% | 21 | Dentistry |
| 3% | 19 | Immunology |
| 3% | 17 | General & Internal Medicine |
| 2% | 13 | Dermatology & Venereal Disease |
| 2% | 10 | Endocrinology |
| 1% | 8 | Urology |
| 1% | 5 | Cancer |
| 1% | 5 | Polymers |
| 1% | 4 | General Biology |
| 1% | 4 | Biophysics |
| 1% | 3 | Pharmacology |
| 1% | 3 | Cardiovascular System |
| 1% | 3 | Hematology |
| 1% | 3 | Otorhinolaryngology |
| 0% | 2 | Pathology |
| 0% | 2 | Inorganic & Nuclear Chemistry |
| 0% | 2 | Genetics & Heredity |
| 0% | 1 | Misc Clinical Medicine |
| 0% | 1 | Geriatrics |
| 0% | 1 | Physical Chemistry |
| 0% | 1 | Embryology |
| 0% | 1 | Anatomy & Morphology |
| 0% | 1 | General Chemistry |
| **100%** | **579** | **Total papers covered by ISI** |
| | 59 | Not covered by ISI |

**No explicit funding acknowledgements**

| % Share | TE Papers | Field |
|---|---|---|
| 15% | 41 | Urology |
| 14% | 40 | Surgery |
| 14% | 38 | General Biomedical Research |
| 13% | 37 | Biomedical Engineering |
| 9% | 24 | Misc Biomedical Research |
| 8% | 21 | Orthopedics |
| 7% | 19 | Biochemistry & Molec Biology |
| 4% | 11 | Dentistry |
| 3% | 9 | Cell Biology, Cytology & Histology |
| 3% | 7 | Neurology & Neurosurg |
| 2% | 5 | General & Internal Medicine |
| 2% | 5 | Dermatology & Venereal Disease |
| 1% | 4 | Endocrinology |
| 1% | 4 | Immunology |
| 1% | 4 | Cardiovascular Systm |
| 1% | 3 | Misc Clinical Medicine |
| 1% | 3 | Pharmacology |
| 1% | 2 | Otorhinolaryngology |
| 0% | 1 | Pathology |
| 0% | 1 | Gastroenterology |
| 0% | 1 | General Chemistry |
| **100%** | **280** | **Total papers covered by ISI** |
| | 49 | Not covered by ISI |

Notes: Papers not covered by ISI could not be allocated to a field

[135] ISI does not include new journals, some proceedings journals, and some technology journals. New journals are added periodically after they demonstrate quality and importance.

***Table 8.5: Tissue Engineering Papers by Lead Author's US Institutional Affiliation and Research Sponsor Acknowledged in Papers***

| | | Funding Source Cited | | | |
|---|---|---|---|---|---|
| Institution | TE papers | NSF | Other | No funding acknowledged | % funded that are NSF |
| Harvard University | 317 | 38 | 192 | 87 | 17% |
| MIT | 239 | 50 | 148 | 41 | 25% |
| University of Michigan | 156 | 34 | 75 | 47 | 31% |
| Childrens Hospital Med Ctr/Boston | 142 | 13 | 90 | 39 | 13% |
| University of Texas | 124 | 24 | 71 | 29 | 25% |
| Case Western Reserve University | 83 | 1 | 78 | 4 | 1% |
| University of California at San Diego | 81 | 5 | 62 | 14 | 7% |
| Massachusetts General Hospital | 62 | 1 | 42 | 19 | 2% |
| Rice University | 55 | 6 | 42 | 7 | 13% |
| Johns Hopkins University | 48 | 6 | 29 | 13 | 17% |
| University of Pennsylvania | 36 | 11 | 16 | 9 | 41% |
| Brown University | 35 | 2 | 18 | 15 | 10% |
| University of Massachusetts | 34 | | 18 | 16 | |
| Northwestern University | 30 | | 30 | | |
| University Miami | 30 | | 25 | 5 | |
| Univeristy of Virginia | 29 | 1 | 17 | 11 | 6% |
| Brigham & Women's Hospital | 28 | 1 | 21 | 6 | 5% |
| New York University | 26 | | 17 | 9 | |
| Yale University | 26 | | 23 | 3 | |
| University Minnesota | 25 | 12 | 9 | 4 | 57% |
| University of Pittsburgh | 25 | 1 | 17 | 7 | 6% |
| Washington University | 24 | | 15 | 9 | |
| University Washington | 23 | | 20 | 3 | |
| Genet Inst Inc | 22 | | 13 | 9 | |
| University Rochester | 22 | | 20 | 2 | |

## 8.3 Institutional Development

NSF has played a small but significant role in developing institutions and networks in the field of Tissue Engineering. A sample set of activities is listed below.

***Conferences and Workshops*** As discussed in depth in earlier chapters, NSF has been an early sponsor of workshops and conferences related to TE. To repeat from Chapter 3, the term "tissue engineering" itself was proposed at a 1987 panel meeting convened to consider future directions for the Engineering Directorates's Bioengineering and Research to Aid the Handicapped Program. Strong interest in this concept within the Engineering Directorate (especially through the efforts of Allan Zelman and Frederick Heineken) led to a special panel meeting on tissue engineering, again at NSF, in the fall of 1987, and then to the Granlibakken workshop of 1988, now considered to be the first formal scientific meeting of the emerging field of tissue engineering (see Executive Summary and Chapter 3 for a more in-depth discussion of these early conferences).

In all, about one percent of NSF's total TE support in the period 1987-2001 was devoted to networking and conference support, and many of the individual investigator awards in TE were funds to support presentations of results from research conducted with the NSF support and attendance at non-NSF conferences and meetings.

***MATES*** As a founder and critical participant in the MATES Working Group, the Engineering Directorate, through the leadership of Frederick Heineken, Kiki Hellman, and others, has made a pronounced effort in recent years to engage participation from a range of disciplines (a more detailed discussion of MATES purpose and objectives can be found in Chapter 7 above). The MATES group aims to enhance collaboration and cooperation amongst several federal agencies so that gaps in tissue engineering research can be addressed. An important example is an outgrowth of the MATES initiative, a study published through WTEC, which summarizes the global status of the field[136] and notes where progress is needed.

***NIBIB*** Aside from its participation in MATES, NSF continues to collaborate with other Federal agencies and programs on TE related research and education. In particular, NSF has ongoing collaboration with the newest of the NIH Institutes, the *National Institute for Biomedical Imaging and Bioengineering (NIBIB)*, established in 2000. The first "official" NIBIB interagency activity was a joint NIH/NSF Workshop on Bioengineering and Bioinformatics Education and Training. Since then, the two agencies have established the Bioengineering and Bioinformatics Summer Institutes (BBSI) Program to provide students majoring in the biological sciences, computer sciences, engineering, mathematics, and physical sciences with interdisciplinary bioengineering or bioinformatics research and education experiences[137].

Another important outgrowth of the NIBIB is a recent solicitation (dated December 30, 2002), likely influenced by the work of MATES and the WTEC report, seeking proposals to address key research challenges in TE[138]. The initiative is expected to draw biologists, clinicians, and engineers to work together to address issues such as cell sourcing, cell identification and characterization, engineering design, and other enabling technologies necessary to move the field forward. A total of $8 million dollars has been earmarked for the initiative.

***Center Support*** NSF's Directorate for Engineering has provided significant support toward institutional development for TE through its funding of Centers. These include the Georgia Tech/Emory ERC, which was awarded in 1998, and the University of Washington Engineered Biomaterials (UWEB) Center. Aside from NSF, the bulk of institutional support in TE has been provided by the Whitaker Foundation, through its role in building the field of biomedical engineering, and especially in providing institutional development funds for the creation and expansion of bioengineering departments– not only at the academic centers highlighted in Chapter 5, but at many other institutions across the nation. These departments are increasingly taking over from departments of chemical and mechanical engineering as the focus of academic research activity in tissue engineering, and the drive to create and expand TE focus areas in many of these emerging departments has created opportunities for young investigators completing their training at the institutions that have led the way in TE research.

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[136] http://www.wtec.org/loyola/te/final/te_final.pdf

[137] http://bbsi.eeicom.com/

[138] http://grants1.nih.gov/grants/guide/rfa-files/FRA-EB-010.html

Not evident in these funding analyses, but worthy of note, is that NSF has been an important source of support over the years for the work of Douglas Lauffenburger, a highly productive researcher on the fringes of tissue engineering who has trained many younger investigators involved in the field. Since 1999, Lauffenburger has served as director of the MIT Biotechnology Process Engineering Center (BPEC), an NSF-funded ERC, in its second incarnation in 1995. BPEC has developed new research thrusts that have moved the focus of its activity toward the boundary between tissue engineering and several adjacent fields, with projects led by several MIT investigators prominent in tissue engineering.

***Young Researcher Support*** As a complement to the bibliometric study, review of NSF's own records in FastLane indicates that during the 1987-2002 period NSF has provided important early career development support for a large number of promising young researchers in tissue engineering, both through specially-designated young investigator and career development awards and through regular project awards, including (listed with current affiliation)[139]:

- Kristi Anseth (University of Colorado)
- Ravi Bellamkonda (Case Western Reserve University)
- John Frangos (La Jolla Bioengineering Institute)
- Linda Griffith (MIT)
- Jeffrey Hubbell (ETH Zurich)
- Jens Karlsson (Georgia Tech)
- Tony Keaveny (University of California Berkeley)
- Michelle LaPlaca (Georgia Tech)
- Cato Laurencin (Drexel University)
- Surya Mallapragada (Iowa State University)
- Howard Matthew (Wayne State University)
- Andrew McCulloch (University of California, San Diego)
- Prabhas Moghe (Rutgers University)
- David Mooney (University of Michigan)
- David Odde (University of Minnesota)
- Michael V. Pishko (Penn State University)
- Robert Sah (University of California, San Diego)
- W. Mark Saltzman (Yale University)
- Christine Schmidt (University of Texas, Austin)
- Lonnie D. Shea (Northwestern University)
- Darrell Velegol (Pennsylvania State University)
- Jennifer West (Rice University)
- Joyce Wong (Boston University)
- Martin Yarmush (Rutgers University)

## 8.4 Overall Assessment

While available evidence suggests that no single organization engendered monumental changes in the field of tissue engineering, NSF's Directorate for Engineering did create an environment that encouraged the crystallization of an emerging concept, both with its innovative Engineering Research Centers (ERC) Program and its ongoing internal efforts to define productive future directions for its bioengineering program. NSF hosted the first meetings at which the concept of tissue engineering as

[139] The data here are not meant to be exhaustive and was gathered by entering the names listed in Appendix 2: Roster of Tissue Engineers into the FastLane Awards database and manually filtering the records retrieved for those applicable to tissue engineering.

a focus of research was defined and strategies for its future growth and potential discussed. The field definition drafted at the October NSF 1987 meeting and reported in the preface of the Granlibakken workshop proceedings was to become a standard citation in later articles, including the well-known 1993 paper by Langer and Vacanti (which listed NSF as a funding source).

While the Directorate for Engineering has no doubt provided funding support to key researchers in the field, it is more difficult to attribute specific research contributions and breakthroughs to the Directorate. In fact, in general, the broad and interdisciplinary nature of the field make it difficult to classify any number of research contributions as seminal. As documented in Chapter 2, efforts to "engineer" tissues to restore structure or function predate the events of 1987-88 by many years. However, if there is a research development that marked the emergence of a recognizably distinct field on this foundation of many related, pre-existing lines of research, it appears that the consensus in the research community and through our own best judgment points to the January 1988 publication by Langer, Vacanti and colleagues describing the strategy of using resorbable artificial polymer matrices seeded with cells as a vehicle for cell transplantation. This early phase of the Langer/Vacanti collaboration, catalyzed by the shared experience of working under Folkman, brought together at least four of the conceptual elements that are central to tissue engineering today: the use of polymeric materials in biological applications, the use of live cells to restore lost physiologic function, the vision of controlling tissue morphogenesis through the use of signaling molecules, and the powerful motivation of the shortage of transplantable organs.

Further, the seminal development in *awareness* of tissue engineering in the scientific community as a distinct domain of research is also attributable to Langer and Vacanti. The October 1987 Panel Meeting at NSF and the subsequent Granlibakken workshop in 1988 and Keystone workshops in 1990 and 1992, while significant, appear to have "spoken" to a much narrower audience; among our group of interviewees, few who were not directly involved in one or the other of these events report any awareness of their direct impact, although, again, the field definition drafted at the October meeting is acknowledged.

So, where does NSF fit within the larger picture of support for tissue engineering over the fifteen years since 1987? Comments by our interviewees suggest that while NSF funding is highly valued by those who have received it, the agency is not widely perceived as a major force in the field. The Foundation is seen today to play a less critical *overall* role, but rather, an important and distinctive *niche* role related to its early career support for several now prominent young researchers and its role in bringing in new disciplines to the field. As a founder and critical participant in the MATES Working Group, NSF's Directorate for Engineering has made a pronounced effort in recent years to engage participation from a range of agencies and disciplines. Examples of such efforts include support of the WTEC study, and the close collaboration with NIH, which has produced a new solicitation to support research in fundamental knowledge gaps in TE.

NSF's Directorate for Engineering also appears to have played a large role in incorporating the biomechanics community into the emerging field. The events of 1987-88 engaged pioneers of an engineering approach to orthopedics and hemodynamics, such as Richard Skalak, Van Mow, and Robert Nerem, in the development of a shared concept for the field just as the emergence of the scaffolds-and-cell-seeding approach, occurring in parallel with and independently of the Foundation's activities, was providing a renewed and powerful impetus for efforts to construct cell-based therapeutic solutions.

One might also note the delayed efforts of the Foundation to engage biologists in the endeavor. All of the participants in the Foundation's 1987 discussions were well-aware of the importance of fundamental research in biology as part of the mix required to make tissue engineering a success. As an agency concerned with the full range of fundamental research and not directly with clinical applications, NSF might have been the natural locus for an effort to mobilize basic biological scientists as well. However, as an NSF initiative, tissue engineering arose from the engineering directorate, and judged by data available from the NSF FastLane grants database, remained largely contained within the engineering directorate.

As noted earlier, tissue engineering continues to be characterized by a tension between *ad hoc* and more fundamental or systematic approaches, with many observers concerned that the balance remains too far toward the *ad hoc*. On this deeper level, the involvement of engineers should be an important contribution to making TE truly an *engineering* discipline, characterized by rational design based on integration of fundamental principles. In practice, however, this theoretical rationalization has not made much progress. The challenges addressed by tissue engineering are *hard* problems. This perception underlines a dilemma faced by the Foundation as a whole. In the future, NSF will be challenged to define and fulfill a role that allows it to continue to have a noticeable impact on the field.