

Critical Areas of Research: Microbial Sciences

Executive Summary

Research involving microbiology at Harvard Medical School and its allied institutions has been strong in the areas of basic molecular mechanisms and infectious diseases for many decades. The recent discoveries relating to the previously unimaginable extent of microbial diversity in this planet have created enormous interest in the area of microbial ecology and its relation to human health. While Harvard has some existing strength in this area, microbial ecology represents a unique opportunity for the growth of University-wide interdisciplinary research efforts. Studies centered on the ways microbes interact with each other and with their hosts, with particular emphasis on the molecules that mediate these interactions - microbial chemical ecology - should be a research priority for Harvard. The success of the Microbial Sciences Initiative and the planned development of the Allston campus make the current conditions propitious for Harvard Medical School, along with other parts of the University, to assemble a group of laboratories focused on this critical area of research. The group would be composed of existing Harvard faculty as well as new hires in areas that are currently not represented in the University. The best organizational structure for the growth of microbial chemical ecology may be the creation of a new center that is closely linked to the Microbial Sciences Initiative and whose faculty all have their appointments in existing departments across the University.

Area of Biomedical Science Evaluated

Within the broad area of microbiology, this paper is focused exclusively on the outstanding scientific opportunities for Harvard Medical School, and Harvard University as a whole, in the area of **microbial chemical ecology** and its various impacts on human health. Since its inception late in the 19th century, microbiology has enjoyed a splendid history. The discovery that microbes are responsible for infectious diseases as well as most of the transformations underlying the cycles of matter gave birth to a fundamental science. The central role that the study of microbes played in the birth of molecular biology kept microbiology in the limelight during the second half of the 20th century. Throughout all of this history, microbiologists at Harvard Medical School and its affiliated hospitals have played key roles both in making great strides in basic understanding and in applying that knowledge to the improvement of human health. As we enter the 21st century, microbiology once again is at center stage as we recognize the eminent role that microbes play in the shaping of our planet. Microbes make up the majority of the world's biomass; their numbers and diversity greatly surpass those of all other organisms. Yet we remain largely ignorant of most of the ongoing microbial activities in the world. The study and utilization of this virtually unexplored biological reservoir will keep microbiologists busy for decades to come. Harvard Medical School needs to plan accordingly and, as it looks towards the future, make microbial ecology an integral part of its plans for growth.

This paper is focused on microbial chemical ecology. Two papers are attached as appendices to this presentation that serve as evidence that microbiology at Harvard, from a much broader perspective, has recently been reviewed in two different contexts. These reviews should serve as a general background for this much more focused paper. First, the Microbiology and Molecular Genetics Department recently underwent an external review. A key recommendation of that review was that the Department should make every effort to take advantage of the opportunities afforded by the existence of the University-wide Microbial Sciences Initiative (MSI). This white paper presents a focused way for the Department and MSI to integrate their efforts. Second, MSI was recently reviewed by the Harvard University Science and Engineering Committee (HUSEC). The paper that describes MSI and which was presented to HUSEC is also included as an appendix. In that report MSI presents, as it has done from its inception, possibilities for how to include microbial sciences in the development of the Allston campus. This background information should thus help explain the very focused nature of the current proposal in the context of very recent efforts that took a much more comprehensive approach to review microbiology at Harvard.

Related Areas not Considered in this Presentation

By necessity, there are many areas of research in microbiology not considered in this presentation. That is because they have either recently been reviewed elsewhere or because they are part of other nascent planning efforts. For example, numerous investigators across Harvard University are interested in infectious diseases. There is a budding effort to organize an Infectious Disease Initiative through the formation of a broad-based affinity group that includes members of Harvard Medical School and Harvard School of Public Health currently doing research on pathogenesis, virology, and tropical diseases, among others. Also, a Center for Vaccine Research within the Longwood Medical Area might emerge as a logical extension of the successful New England Regional Center of Excellence in Biodefense and Emerging Infectious Diseases.

Outstanding Scientific Opportunities that Motivate Studying this Area

The vastness of the genetic diversity of the microbial world is just beginning to be recognized. Up to now, this vastness has been so daunting that most cutting-edge research has been largely limited to defining “who is there” in different environments. A gram of soil typically contains thousands of different microbial species. What is most astounding is that a different gram of soil will contain a different collection of thousands of species. The same occurs within the human body; it is now clear that each individual harbors a unique collection of thousands of microbial species whose contribution to human health is simply not understood.

The challenge for the future is to begin to understand how these microbes interact with each other and with their hosts. The study of the nature and function of the molecules mediating these interactions - an area of research here defined as **microbial chemical ecology** - is of great basic scientific interest and is likely to yield new compounds with enormous therapeutic potential. Thus, microbial chemical ecology is an emerging area of research through which we will gain an understanding of the principles underlying interspecies interactions in the planet and which in all likelihood will yield great benefits for human health because of its high relevance to translational research.

Harvard's current strengths and challenges in this area of biomedical research

Harvard is well-placed to become a leader in the area of microbial chemical ecology. To make real advances in this area research efforts should be interdisciplinary, involving faculty from across the University. A consortium of six Harvard Medical School laboratories, whose joint efforts are focused on the identification and characterization of small molecule natural products of microbial origin, already exists. This consortium has been successful in securing collaborative grants to develop approaches to understand the ecological function of small molecule natural products as well as to sequence and mine the genomes of twenty strains from the genus *Streptomyces* - probably the planet's most prodigious small molecule producers. This consortium already cuts across traditional departmental boundaries. Four members of the consortium are from the Department of Microbiology and Molecular Genetics (John Mekalanos, Deborah Hung, Suzanne Walker, and Roberto Kolter) and two members are from the Department of Biological Chemistry and Molecular Pharmacology (Jon Clardy and Chris Walsh). In addition, there are other Harvard faculty that provide strength in the area of microbial chemical ecology. Examples are Dennis Kasper and Laurie Comstock of the Channing Laboratories, Roy Kishony of the Systems Biology Department of Harvard Medical School as well as Daniel Kahne and Alan Saghatelian from the Chemistry and Chemical Biology Department in the Faculty of Arts and Sciences. In addition, several faculty members in the Organismic and Evolutionary Biology Department are focused on different aspects of microbial ecology (Anne Pringle, Colleen Cavanaugh, and Peter Girguis). The arrival of Jeanine Wiener-Kronish as Chief of Anesthesia and Critical Care at the Massachusetts General Hospital should also help catalyze Harvard's growth in human microbial ecology. Two members of her team, Sue Lynch (UCSF) and Eoin Brodie (Lawrence Berkeley National Labs) have pioneered cutting-edge methodologies for rapid microbial community assessment.

There are, however, several key areas in microbial ecology in which Harvard is weak. In the last few years there has been an explosion of interest in the analysis of the human microbiota and the role that it plays in human health and disease. Yet Harvard has contributed relatively little to this important research. Major developments in this area have come from the

laboratories of Jeff Gordon (Washington University) and David Relman (Stanford University). Also, considering the remarkable richness of natural products made by the Streptomyces, it is surprising that Harvard has no resident experts that study the genetics and molecular biology of these organisms. This area is being successfully pushed forward by investigators such as Mark Buttner and Mervyn Bibb (John Innes Institute, Norwich). The joint effort of the Fenical-Gerwick-Moore laboratories at UCSD combines chemistry, microbiology and genomics in a way that other universities will try to emulate. The well-organized and recently launched Microbial Science graduate program at MIT is also a significant challenge to Harvard's leadership in the area. Finally, much has been learned recently about the chemical signaling underlying well-studied beneficial symbioses. Here again, while some investigators at Harvard study beneficial symbioses, there is a lack of researchers focused on the chemistry underlying these interactions. The model systems to study actinomycete-insect symbioses developed by Cameron Currie (University of Wisconsin, Madison) represent an important research opportunity in the area of microbial chemical ecology and could potentially lead to a search strategy for therapeutically useful microbial products. In the coming years, Harvard should place a high priority in recruiting new faculty members that will bring expertise in these important areas to the University.

The successful Microbial Sciences Initiative (MSI) provides a fertile intellectual atmosphere for research in microbial chemical ecology to flourish rapidly at Harvard. MSI grew out of a grass-roots movement that brought together some Harvard Medical School faculty with colleagues in the Faculty of Arts and Sciences and the School of Engineering and Applied Sciences to pursue interdisciplinary research projects. Today the MSI represents a vibrant community of nearly sixty faculty members and their research teams from across the University. Through weekly informal discussions, a seminar series, a yearly symposium, a post-doctoral fellowship program, and a summer undergraduate research program, MSI is fostering the growth of microbiology in many new directions at Harvard.

One of the key priorities of the MSI is education. Strong evidence of this has been the launching of several new interdisciplinary graduate and undergraduate courses that familiarize the students with the wide ranging implications of microbial sciences. For example, LS110 "A Microbial Planet" brings together a geobiologist (Ann Pearson, Earth and Planetary Sciences), a chemist (Jon Clardy, Biological Chemistry and Molecular Pharmacology) and a microbial geneticist (Roberto Kolter, Microbiology and Molecular Genetics) to provide the students with a broad perspective of microbial activities in the planet. LS190, a graduate level course coordinated by Gary Ruvkun presents a wide spectrum of microbial sciences topics, from origin of life to the ecology of infectious diseases. MSI is currently obtaining approval for the establishment of an undergraduate secondary area of concentration and an entry portal for Ph.D. students interested in carrying out microbial sciences research in laboratories from across the University. These interdisciplinary teaching efforts will be further strengthened by the recruitment of faculty whose expertise lies in the areas of microbial ecology currently lacking at Harvard.

Quite importantly, MSI has provided a community that has successfully recruited stellar faculty to departments that recognized the need to hire microbiologists but had lacked the critical mass to attract the top-notch candidates. Thus, MSI already links microbial scientists from across the University in a very active way. The possibility of growth in the Allston area provides a unique opportunity to develop a strong research and educational program in microbial chemical ecology composed of Harvard Medical School faculty working alongside

faculty from Departments from the Faculty of Arts and Sciences, Harvard School of Public Health, and the School of Engineering and Applied Sciences, all under the aegis of the MSI.

What Limits Harvard's Success in this Area and how to Overcome the Challenges

Today the physical extent of Harvard Medical School and its affiliated institutions has become a limiting factor in growth planning. Thus, future growth depends on establishing additional research facilities physically located beyond the present footprint. Harvard Medical School has tremendous strength in the areas of bacterial pathogenesis, virology and basic molecular mechanisms of bacterial physiology. Growth in all these should assure continued success in those areas. But, there is also a pressing need to increase Harvard Medical School's commitment to research related to microbial chemical ecology.

As Harvard Medical School considers expansion into the area of microbial chemical ecology, the obvious location for this area to develop is the Allston campus. The adjacency of the Allston campus to the Faculty of Arts and Sciences, with its rich tradition in ecology, evolution, physics, chemistry, and engineering would provide the ideal setting for faculty members investigating diverse aspects of microbial ecology to develop and expand expertise in this important area. In particular, the area of microbial chemical ecology is both of great medical importance and underexplored at Harvard as a whole. Moving some existing laboratories of Harvard Medical School faculty, along with some from other departments from across the University, coupled with new hires, would build a strong interdisciplinary group with common scientific interests in an area with enormous translational potential.

Moving some Harvard Medical School faculty to Allston would have the added advantage of freeing-up space within the Longwood Medical Area for additional growth in the areas of virology and molecular mechanisms of bacterial physiology and pathogenesis. Following such a plan would therefore ensure that Harvard Medical School microbiologists stay at the leading edge of their discipline, taking full advantage of the great opportunities afforded by the creation of the Allston campus while at the same time assuring that the Longwood Medical Area remains a vibrant location that will lead the way in biomedical research for decades to come. A trade-off of such a move would be the separation of faculty who have interacted closely for many years. However, by keeping their departmental affiliation and by keeping at least part of their teaching mission based at Longwood, the Harvard Medical School faculty unity would be maintained.

Strengths and Weaknesses of Specific Organizational Models

1. Increased Investment in Existing Units

At this point it would not be absolutely necessary to create any new entity to foster growth in chemical microbial ecology at the University. Harvard Medical School, along with Harvard School of Public Health, the Faculty of Arts and Sciences and the School of Engineering and Applied Sciences, could make a commitment to invest in individual departments to build infrastructure and to recruit new faculty members to help build this area of research. Leadership and governance would, of course, not be altered from the existing structures. However, this model would leave the interacting faculty physically separated, each having their laboratory located within existing department buildings. The current space

limitations of both the Longwood Medical Area and the Cambridge campus would also hinder the ability to recruit new faculty members to strengthen microbial chemical ecology at Harvard.

2. A New Non-Departmental Entity, e.g. a Center or Institute

If a group of laboratories working in microbial chemical ecology is eventually located in the Allston campus, it may be best to organize it as a new center or institute. In such a structure, each faculty member would still remain affiliated with an existing department and have some duties within those home departments. But, naturally, there would be issues that require some local organizational structure. This model would be similar to #1 regarding the commitments for infrastructure and faculty recruitment from across the University, but would have the advantage of providing physical proximity of the researchers involved. By having faculty keep affiliations to existing departments, the strengths provided by those structures would be maintained. If MSI becomes an interdepartmental committee, it would be a natural to work with Schools across the University to advance microbial chemical ecology (see #4).

3. A New Quad-based Department at HMS

Clearly, building a new quad-based department would be counterproductive in the case of microbial chemical ecology. The basic idea is to make this an interdisciplinary area of research that brings together faculty from different departments.

4. A New University Department or Committee

The area of microbial chemical ecology does not justify the creation of a new University department or committee. However, this area of research would fit perfectly as a growth area within the existing MSI. In this regard, it is important to describe the current status of the MSI. MSI is a HUSEC-funded Interfaculty Initiative that will soon seek approval to become an interdepartmental committee (IDC). While the UPCSE report defined IDCs, HUSEC has not yet defined exactly what will be the roles and responsibilities of IDCs. MSI may become HUSEC's first test case. The prevailing sense at MSI is that as an IDC it would seek commitments for new faculty positions to be managed within existing departments, rather than having faculty appointment powers. Thus, in such model, MSI as an IDC could facilitate the creation of a group of laboratories focused on microbial chemical ecology by working together with Harvard Medical School, Harvard School of Public Health, the Faculty of Arts and Sciences and the School of Engineering and Applied Sciences. In short, this model would not be significantly different from #2.

Appendix 1: Authors and Faculty Consulted

This document authored by Roberto Kolter, John Mekalanos, Suzanne Walker and Jon Clardy. However, its preparation rests on extensive consultations with the faculty members of Department of Microbiology and Molecular Genetics, Harvard Medical School:

John Mekalanos, Chair
Jon Beckwith
Tom Bernhardt
John Collier
Ron Desrosiers
David Evans
Mike Farzan
Dan Fraenkel
Lee Gehrke
Darren Higgins
Ann Hochschild
Deborah Hung
Welkin Johnson
Dennis Kasper
Elliot Kieff
David Knipe
Roberto Kolter
Stephen Lory
Max Nibert
David Rudner
Michael Starnbach
Charles Stiles
Suzanne Walker
Sean Whelan
Priscilla Yang

The members of the Steering Committee of the Microbial Sciences Initiative were also consulted:

Colleen Cavanaugh (OEB, FAS)
Roberto Kolter (MMG, HMS)
Daniel Schrag (EPS, FAS)
Ann Pearson (EPS, FAS)
Richard Losick (MCB, FAS)
Gary Ruvkun (GEN, HMS)
Jon Clardy (BCMP, HMS)



HUSEC Presentation

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Microbial Sciences Initiative (MSI) at Harvard

The MSI at Harvard aims to reach a comprehensive understanding of the richest biological reservoir of the planet, the microbial world. Microbes are ubiquitous and have an impact on every aspect of our existence. Yet, their intrinsic invisibility has meant that they have remained largely unknown, their effects and enormous potential often unrecognized. Harvard will play a leading role in the exploration and utilization of microbial resources through the development of interdisciplinary research programs and the training of new generations of microbial scientists.

The Unexplored Microbial World. The biological potential of the planet lies in the vast diversity of its life forms and nowhere is diversity richer than in the microbial world. Because of their small size, the effects that microbes have on the planet have remained largely unrecognized, except in the context of disease. But microbes have an impact on every aspect of the natural history of the planet, from rock formation spanning the geological ages to the natural remediation of anthropogenic contamination. Microbes account for the majority of the world's biomass and their numbers and diversity greatly surpass those of all other organisms. There are more microbes in a gram of soil than there are humans alive today, and in that very same gram of soil there are more different microbial genes than there are different genes in all the plants and animals. Yet, this amazing diversity remains virtually unexplored and unexploited.

In the past, microbial scientists relied on their ability to culture microbes as a method to assess diversity. When culture-independent methods were applied to assess diversity a remarkable discovery was made. In most habitats, more than 99% of the diversity had been missed because of our inability to cultivate the microbes residing there. Recent surveys of microbial diversity in every corner of our planet constitute the twenty-first century's equivalent of the "Voyage of the Beagle" - we now recognize that the vast majority of life in this planet is microbial. Yet, we simply do not understand what types of metabolisms most microbes utilize nor what signals from the environment or from other organisms are necessary for their growth, or whether they grow on a time scale that is vastly different from what we have come to expect from cultured microbes in the laboratory. There is a need to understand these and other unknown aspects of microbial science if we are to harness the microbial world for the benefit of humankind. Therein lies the motivation behind the launching of the MSI.

The Need for Interdisciplinary Approaches. In an era of ever increasing specialization and ever increasing enlargement of detailed knowledge, we run the risk of spiraling down increasingly more isolated specialized worlds, unable to communicate except with our closest peers. This is a particular worry in the broad area of microbial studies as the interactions between scientists from many diverse fields are essential to advances in areas outlined above. Mathematics, engineering, geology, ecology, history, informatics, chemistry, evolutionary biology, and molecular biology all need to merge in the study and utilization of microbes. There is a need to train a new generation of scientists, renaissance men and women who can comfortably traverse scientific disciplines. Some universities have approached this challenge by hiring additional microbial scientists into traditional microbiology departments, but have put very

little emphasis on creating bridges between microbial scientists in different fields. Another approach has been to create independent centers for microbial studies. This encourages interaction between microbial scientists but fails to build bridges between those studying microbes directly with scientists in other disciplines whose expertise is required to address the unanswered questions.

Prior to the inception of MSI at Harvard, interactions amongst microbial scientists at the University were limited at best. One department at Harvard Medical School (Microbiology and Molecular Genetics) did have many intradepartmental interactions but these were largely in the context of molecular genetics and medical microbiology. Thus, those interactions lacked the "big picture" of the impact of microbial sciences. Some departments (e.g., Organismic and Evolutionary Biology, Earth and Planetary Sciences, Molecular and Cellular Biology) and the School of Engineering and Applied Sciences have only a few microbial scientists and thus do not have a critical mass for significant intradepartmental interactions. Still other departments whose areas of research are now recognized to be influenced by microbial activity (e.g. Physics, Chemistry and Chemical Biology) do not have microbial scientists as members of their faculty. With so few faculty, a given department might have a difficult time recruiting outstanding applicants in the absence of the initiative. However, MSI has created strong interdepartmental interactions that have made Harvard a much stronger community for the development of the microbial sciences. Indeed, the MSI has played a direct and important role in the recent recruitment of several outstanding microbial scientists.

Most importantly, the life sciences community at Harvard tends to be limited to traditional concepts of "life sciences" and remains only marginally connected to the physical sciences, mathematics, and the environmental and planetary sciences. MSI is forming bridges between these heretofore segregated scientific communities. A focus on microbial sciences, with the emphasis on much more than just medical research, is a major change for Harvard and is an excellent opportunity for Harvard to "lead the way", since the breadth of microbial sciences has been overlooked at equivalently great institutions.

MSI started as a grassroots movement due to the interest amongst several faculty members to initiate interdisciplinary research that addressed key questions in microbial sciences. The strength of the MSI arises from the grounding of the faculty in their home department, and the collective knowledge, techniques, and insights each brings to the MSI. The MSI was officially launched in April 2004 after having received approval and seed funding from the Life Sciences Executive Committee and the Dean of the Faculty of Arts and Sciences, William Kirby. Quickly, MSI gained momentum thanks to the involvement of many faculty along with their students and post-doctoral fellows in regular discussions and collaborative research. In June 2006 the MSI was approved by the Provost's office as a University-wide Initiative and received an operating budget for four academic years. Part of the approval process involved preparation of a strategic plan that proposed hiring about ten MSI faculty over the next several years. These faculty would still hold primary appointments in a home department but would be hired and evaluated with the involvement of the MSI.

The last two years have seen a large increase in the interest that was already growing for MSI in many sectors of the University. On a weekly basis at least a dozen faculty members from the Faculty of Arts and Sciences, the School of Engineering and Applied Sciences, and Harvard

Medical School, along with many of their students and post-docs, gather for informal discussions and for "chalktalks" presented by Harvard faculty, students, and post-docs. Already these have led to collaborative research amongst laboratories whose interests range from geology to chemistry to medicine. There are many post-doctoral fellows and students now bridging laboratories between the various parts of the University. Currently, six of these post-doctoral fellows are funded by the MSI. In addition, MSI sponsored twelve undergraduates this past summer (2007) who carried out research in MSI-associated laboratories. MSI also organizes monthly seminars and a yearly Symposium, with ~300 attendees each of the past 4 years from Harvard and from institutions all over Boston and New England.

Last, but not least, largely because of the existence of MSI, remarkably talented microbial scientists have been recruited to faculty positions in non-traditional departments. Examples of these are Anne Pringle, Chris Marx and Peter Girguis in Organismic and Evolutionary Biology, and Colleen Hansel in the School of Engineering and Applied Sciences. The MSI was a key factor in their decisions to accept Harvard's offers and these young faculty members are finding in MSI the perfect community in which to advance their scientific interests. We envision that during the next few years additional junior faculty with close ties to MSI will be hired through both MSI and departmental positions in Organismic and Evolutionary Biology, Molecular and Cellular Biology, Chemistry and Chemical Biology, Earth and Planetary Sciences, Physics, the School of Engineering and Applied Sciences, and Harvard Medical School.

Teaching Mission. MSI considers education to be of central importance for its mission, and we are developing a broad educational plan. Our first step has been the creation of several new interdisciplinary microbial science courses for both undergraduate and graduate students that are being offered this academic year (2007-2008). These courses are: Life Sciences 110 (Spring 08) - "A Microbial World" - to be taught by Ann Pearson (Earth and Planetary Sciences, FAS), Roberto Kolter (Microbiology and Molecular Genetics, HMS) and Jon Clardy (Biological Chemistry and Molecular Pharmacology, HMS). It will cover the broad spectrum of microbial sciences from biodiversity to the crucial impact of microorganisms on geological history, the environment, climate, and world health. Life Sciences 190 (Fall 07 & Spring 08) - "Diverse Microbial Strategies for Metabolism, Pathogenesis, and Chemical Signaling", is currently in progress. Organized by Gary Ruvkun, it involves many MSI-associated faculty. This is an interdisciplinary graduate level course in which students explore topics in molecular microbiology, microbial diversity, and microbially-mediated geochemistry in great depth. Finally, Life Sciences 100r - "Experimental Research in the Life Sciences" now includes two microbial projects every term. Eventually, MSI will launch its own projects laboratory course that will expose students to various and diverse aspects of microbiology. A teaching laboratory appropriate for this course should be made available for the MSI.

We anticipate that the MSI will form the basis for a new graduate program in the near future. The Initiative has two features that make it particularly suited to launch such a program. First, it is highly interdisciplinary thus offering graduate students training at the intersection of multiple scientific disciplines. Second, it will link graduate education to research programs in multiple departments in the Graduate School of Arts and Sciences and to programs at Harvard Medical School and the School of Public Health. Such a program will be an exceedingly attractive draw for outstanding graduate students in a wide range of disciplines with interests in the microbial

sciences; it should become one of, if not the, leading Microbial Sciences program in the world. Our target date for the admissions of the first entering class is Fall 2009.

The Near Future - A Physical Presence on the Cambridge Campus. For the next three years, a key development to build a stronger MSI will be to create a physical presence on the Cambridge campus. To this end, MSI will require 8,000 square feet of space dedicated to MSI activities. One half of that space (4,000 square feet) will provide enough space for offices to accommodate faculty members from other parts of the University as well as visiting scholars, seminar rooms, small conference rooms, and administrative offices. MSI and the Origins of Life Initiative have agreed to share the administrative space. Both initiatives will also be recruiting a shared Executive Director and Financial Administrator. An additional 4,000 square feet of fully equipped laboratory space will be used by students and post-doctoral fellows from laboratories from around the University who are engaged in collaborative research so that they can work side-by-side in a synergistic fashion, having access to the latest technologies for imaging and analyzing the microbial world. Indirect cost recovery to support this laboratory would come from fundraising efforts as well as grants obtained by the faculty members whose students and post-docs utilize the space. Dr. Ann Pearson, current member of the MSI steering committee, will oversee the overall supervision of this laboratory space.

Long term plans. Harvard's anticipated expansion in Allston creates unique opportunities for growth of the sciences in new directions. In about two years MSI will be perfectly poised to take full advantage of this but now may be the best time to initiate planning. MSI is already flourishing with numerous faculty members and associated students and post-docs involved in diverse interdisciplinary collaborative projects. Soon it may make perfect sense for several of the MSI-associated faculty to have their main laboratories located in a single building in the new Allston campus. These faculty members will include already appointed faculty and new junior faculty members recruited by MSI in conjunction with different departments. Appointments would come in increments of two per year during three years. Such an eclectic group of investigators, drawn from a large number of departments and intersecting in their microbial science interests and expertise, would form a very exciting core to pioneer new ways to interact and to carry out research. The MSI faculty at Allston, in conjunction with the rest of the MSI at Harvard, will be positioned to address the very large goals and important questions that have become manifest as a result of the explosive growth in our knowledge of the microbial world. Examples of such goals include, but clearly are not limited to:

Microbial Chemical Ecology. Define and characterize the functions of microbial secondary metabolites in diverse ecosystems, including the human body.

Define the composition and activities of the "not-yet-cultured" microbiota of diverse ecosystems, including the human body. This would require the combination of our existing strengths in microbial biology with environmental and medical scientists.

A comprehensive description of the microbial metabolic potential. Every microbial energy source, mechanism of electron transport, and metabolic pathway on earth can be

defined through genome sequencing , metabolic decoding of genomic information, and analyses of gene expression.

Funding. NIH and/or NSF training grants will be secured in the near future, but MSI should not depend solely on such awards for its support. There are several philanthropic foundations that should also be approached for support, among them the Gates Foundation for Microbial Disease, The Ellison Medical Foundation, The Moore Foundation, and The Agouron Institute. All of these already fund research in the areas of medical microbiology, marine microbiology and geomicrobiology. Further, it is our hope that the MSI figure prominently in the University fund raising efforts. To this end all of the members of the MSI Steering Committee want to work closely with the various University Development Offices.

The MSI Steering Committee: Colleen Cavanaugh (OEB, Co-Director), Roberto Kolter (MMG, Co-Director), Dan Schrag (EPS), Ann Pearson (EPS), Richard Losick (MCB), Gary Ruvkun (Genetics) & Jon Clardy (BCMP). DECEMBER 2007.