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Report of the visiting Committee on Evolutionary Biology

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March 12, 1999

REPORT OF THE VISITING COMMITTEE ON EVOLUTIONARY BIOLOGY
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Preamble

The founding professors in the life sciences departments of Israel's universities did important research on, and teaching of the systematics, ecology and evolutionary biology of the Middle East. They demonstrated that the unique biodiversity, geological history, climatic features and the history of human habitation in the area provided excellent resources for the study of organismic evolution. They also developed comprehensive collections of the flora and fauna of the middle east that constitute a major resource for evolutionists.

Evolutionary biology has, however, undergone a series of fundamental changes in recent years as advances in other parts of biology, medicine, computer science, physics, chemistry and meteorology have become part of the tool kit of modern evolutionary biology. The retirement of the older generation of organismic evolutionists and the absence of a cadre of middle level faculty has left the teaching and research of evolution in Israel in a very precarious position. A leadership vacuum is imminent and the result is a crisis for young professors, graduate students and undergraduates interested in aspects of evolution. In addition, the training of high school teachers with the background to teach evolutionary aspects of biology is in severe danger of elimination.

Proper training in evolutionary biology today includes organismal, molecular, and mathematical components, as well as computer literacy. A commitment on the part of universities and government is necessary to support scholars in all of these areas, to ensure that a critical mass of faculty is maintained at several institutions and to encourage the production of the next generation of broadly trained evolutionists.

As evolutionary approaches become widely used in computer science, medicine and the social sciences, universities as a whole will benefit by the strengthening and maintenance of excellence in evolutionary biology.

The precarious position of research and scholarship in evolution in Israel's universities was stressed throughout our meetings with faculty and students. In what follows, we summarize what we learned from these discussions and our visits to laboratories in the university, and make suggestions regarding short-term and long-term steps that could contribute to improving the condition of this central component of biology in Israel.

We have included as an appendix, a recent initiative of the US National Institutes of Health to encourage (and support) research on "Evolution and Infectious Diseases". At a later date, we will send, as an additional appendix, a report on "Evolution, Science and Society" prepared under the sponsorship of the U.S. National Science Foundation, as well as a report on systematics (Systematics Agenda 2000).

Special Strengths of Israel for Studying Evolutionary Biology

There are reasons why studies in evolution should be a central scientific endeavor in Israel. Some of these involve building on past accomplishments that are impressive, while other reasons include unique geographical and demographic features of the country.

Previous evolutionary studies in Israel have resulted in extremely valuable materials that are now available for study. It would not only be a lost opportunity, but also irresponsible not to exploit these collected materials to the fullest or not to add to them. A carefully designed botanical garden resides in Tel-Aviv University, and an important herbarium exists in Hebrew University. Extraordinary collections of birds, insects and other animals collected throughout Israel are present at Tel-Aviv University. In addition, important collections of invertebrates, fish, reptiles, and paleontological material are held in Jerusalem. These are not only national treasures, but the only substantial collections of this sort between Italy and India. The insect collection is world class and frequently used by scholars visiting Israel, as well as being sent out to investigators in other countries for study. Tel-Aviv University also has an invaluable collection of anthropological remains excavated in Israel and abroad. The collected materials have established the coexistence (or alternation) of modern humans and Neanderthals in Israel for a period of approximately 30,000 years, to give just one example of their importance.

The Institute of Evolution in Haifa maintains invaluable DNA banks in the form of seeds derived from the wild ancestors of wheat, barley and a number of other crop plants. These seeds come from plants that have been carefully documented with respect to numerous genetic traits including resistance to plant diseases. The characterizations of the plants have been computerized, greatly facilitating their use. These seeds are critically important for molecular genetic studies and have direct importance for molecular genetic studies and for agricultural studies in the future.

The geographic conditions in Israel are extraordinary for evolutionary studies on animal and plant diversity. The climatic conditions range from tropical to desert, and from fresh water to extreme salinity in the Dead Sea. In addition, the coral reefs in Eilat allow investigations of marine organisms. The rich and varied fauna of tropical marine invertebrates in coral reefs is particularly well suited to investigations on evolutionary diversity. Moreover, the slow growth rate of the coral reefs is traced in the fine structure of their skeletons, leaving an exact record of water temperature for hundreds of years. In addition, the mountainous terrain in Israel is perforated with caves, providing sources of fossils and information pertinent to cultural evolution and domestication of plants.

Israel is a corridor between Africa and Eurasia, which has added to its biological diversity. No other country in the world has such a variety of physical and geographical conditions, as well as being a bridge between evolutionary hotspots.

The geographical location and cultural heritage of Israel has resulted in both ethnically diverse and isolated populations that can be exploited for studies on human evolution. These studies have clear relevance to the understanding of many ethnically related human diseases. Indeed, an impressive collection of cells from numerous groups in Israel has been assembled at Tel-Aviv University and is sent to investigators that request them throughout the world.

Evolutionary game theory, dynamic systems theory, and other approaches have been developed and used successfully during the last 15 years for interdisciplinary research in

the Institute for Rationality in The Hebrew University, with cooperating faculty and students from Mathematics, Economics, Biology, and Psychology. The research topics include modeling genetical and behavioral changes in biological populations, dynamic changes and equilibria in social and economic systems, and human perception and decision processes. In addition, Professors from the mathematics department at Tel Aviv University have made widely recognized contributions to mathematical evolutionary theory, while the new mathematical genetics group at Haifa University has begun to be internationally known.

Finally, molecular biology, mathematics and computer sciences are highly developed in Israel. These sciences play important roles in evolutionary research. Graduate students in evolutionary biology should be encouraged to take advantage of these resources with the potential results that interdisciplinary dissertations and research programs will emerge.

In summary, the topography, geographical location, ethnic diversity, and invaluable collections of biological specimens make Israel uniquely poised to be a leader in evolutionary studies. In Israel there is an essentially unlimited supply of important evolutionary problems that can be pursued at the cultural, organismic and molecular levels. It is clearly of great value and importance to exploit this rich evolutionary resource.

Structure and Future of Evolutionary Biology

Every characteristic, whether anatomical, physiological, behavioral, or biochemical, of every species is the result of an evolutionary history. None of the characteristics of organisms can be fully understood without considering the history and evolutionary processes that brought them into existence.

Evolutionary biology is the discipline that attempts: (a) to describe the history of living things and their characteristics, and (b) to understand the processes that have shaped this history. On the one hand, evolutionary biology provides unity to biology by providing a theory of processes and principles that apply to all organisms. On the other hand, it aims to explain the extraordinary diversity of organisms and their differences in the life history, behavior, physiology, morphology and genetics. Evolutionary biology is therefore inseparable from systematics and ecology, the other disciplines that are directly concerned with biodiversity.

It is useful to recognize the sub-disciplines of the broad field of evolutionary biology, some of which are intimately related to biological areas that are not explicitly evolutionary. Some of the sub-disciplines are:

Evolutionary Genetics, including population genetics.
The basic events of evolution are changes in the genetic properties of populations and species; evolutionary genetics provides the central theoretical and empirical core of the analysis of evolutionary mechanisms. Many of the mathematical theories and analytical methods developed in population genetics are applied both in basic research and in fisheries biology, forest management, biological Control of pests, and human genetics (including forensics and studies of genetic diseases).

Quantitative genetics, which is closely related to population genetics, is employed in both evolutionary studies and plant and animal breeding.

Molecular evolution includes analyses of the evolution of gene sequences and genome structure. It is closely related to evolutionary genetics and to systematics. Comparisons of gene sequences provide data on relationships among species, and often provide inferences about processes such as mutation and the role of natural selection, genetic drift, and other processes in the evolution of genes and genomes.

Evolutionary developmental biology ("evo-devo") is a dynamic new field that analyses how the development of organisms has changed during evolution. It holds mutualistic relationships with developmental biology. Phylogenetic comparisons of development among organisms have added to understanding of developmental processes. The diverse organisms that develop in radically different, often harsh conditions in Israel provide an opportunity to find important developmental specializations that can be associated with evolutionary adaptations.

Evolutionary systematics includes analysis of variation within species and especially the phylogenetic relationship of species to one another. These relationships provide a basis for inferring the history of evolution of characteristics, as well as for classifying species in a way that reflects evolutionary origins. Some systematic studies, such as identifying and discriminating, naming, and cataloging species, are not explicitly evolutionary, but are done best if guided by evolutionary principles. Systematics provides the indispensable basis for ecology, palaeontology, and in fact all of biology. Molecular data (e.g., DNA sequences) play an important role in contemporary systematics. Similar analytical methods for inferring phylogenetic relationships are applied in such diverse areas as molecular biology and linguistics. Many analyses of adaptive evolution of physiological, behavioral, and other characteristics are now pursued within a phylogenetic framework.

Palaeontology supplies a window into the past that is not otherwise available, and provides an all-important time frame for evolutionary studies.

Behavioral evolution (or behavioral ecology) is one of several fields that analyses the diverse adaptations of different species (Evolutionary physiology is another). Theory, experimentation, and field observation are used to understand making strategies, social behaviors and other aspects of animal behavior. Extensions of this field to human behavior have been enlightening but often controversial.

Evolutionary ecology includes study of the evolution of ecological features of organisms (such as life history and diets), as well as evolutionary changes in interactions between species, such as parasites and their hosts. The evolution of infectious diseases and their control has become an active field of study. The evolutionary perspective is becoming increasingly important for understanding the factors that determine the diversity and structure of ecological communities and ecosystems.

Quantitative evolutionary reasoning is also invading and even creating new fields in biology and other sciences. Examples are as follows:

Psychiatry is increasingly adopting "evolutionary" interpretations of its phenomena at both individual and group levels. Without grounding in the fundamentals of social biology, the psychiatrist of the future will be handicapped in choosing natural treatments.

New interpretations describable as "conflictual genomics", are increasingly affecting physiology and developmental biology. Numerous states of abnormality and disease are proving explicable through the evolutionary understanding of the conflicting adaptations of different components of the genome. These show up through extreme physiological states and reactions, sometimes mediated through a process known as chromosomal imprinting. Preeclampsia is an example of a pathological condition in pregnancy that appears to be mediated by opposed physiological effects in mother and fetus which has been attributed to a conflict between the maternal and fetal genomes. In general, it is fair to say that truly modern medicine cannot be taught without understanding of evolution and many mistakes in medicine and public health may have been avoided had medical scientists and physicans been better informed about evolutionary principles.

An old assumption of medical treatment that genetic differences of individual humans (quite apart from the specific states of mutational genetic disease) are unimportant with respect to the treatment of diseases is being increasingly eroded by experience. Real understanding in medical science of such diversity in human populations requires understanding of the evolutionary forces that naturally produce it.

Evolutionary ideas that are based ultimately on the neodarwinian model are creating the new applied science of evolutionary computation. Specifically, this field seeks computational solutions to difficult problems of optimization. Currently well known techniques are "genetic algorithms" and "neural nets"; both involve life-inspired processes, such as mutation, recombination and selection. Without doubt, further highly economically useful sub-fields of computer-aided technology will soon be added. Effectiveness in the development of all such techniques will inevitably improve through training in what is already understood about the evolution of life.

Mutation and selection of somatic cells and organelles within multicelled individuals are now seen as a normal part of development, the immune response, senescence, and pathologies such as neoplasms. Evolutionary considerations have virtually revolutionized studies of the development of the nervous systems and the brain. Thus, in immunology, oncology and brain sciences training in evolutionary thinking is needed.

As we have intimated, evolutionary biology makes important contributions not only to basic sciences such as developmental biology and ecology, but also to human needs. Researchers trained in evolution are helping to locate and analyze genes responsible for inherited diseases and other human variations, to trace the origin and spread of infectious agents, such as HIV, and to combat the evolution of drug resistance in pathogenic microbes. (Likewise, crop pests evolve resistance to pesticides and cancers can evolve

resistance to chemotherapeutic agents.) Evolutionary principles and methods contribute to developing pesticide resistance, drought resistance, and other important traits in crop plants, and to finding organisms that can be used for the biological control of pests. Studies of adaptations and phylogenetic analyses of species relationships can help to determine which species are likely to yield useful natural products. Studies of evolution of plants in polluted soils have helped in reclamation of severely degraded land. Conservation of endangered biodiversity depends on knowing the genetic effects of low population size, as well as on systematic and biogeographic studies of biodiversity.

Throughout the industrialized world, from the United States to the European nations to Japan, evolutionary biology has grown vigorously in the last twenty years. Almost all major universities have either established departments with names like "Ecology, Systematics, and Evolution", or have developed strong sections of evolution within their biology departments. Molecular biologists, developmental biologists, and physiologists have increasingly supported these structural changes, as they have come to see the importance of evolution for their disciplines. Ph.D. students with some training in evolution are prominent researchers in fisheries, pest management, human genetics, and even in fields such as evolutionary computation. Evolutionary biologists are being hired by universities in those countries, not only because the scope and importance of the field has grown, but also because teachers are needed to provide a background in evolution to students who will pursue careers in biomedical fields, biotechnology, agriculture, and environmental science.

Because evolution is so fundamental to all the biological sciences, it is clear that explicit training in evolutionary biology is an essential component of any curriculum in biology. Any student who obtains a first degree in biology should have had a course that was at least partly, and preferably wholly, devoted to the fundamental principles of evolution. It should not be assumed that students will learn evolution by osmosis from other courses, for the subject is as challenging and difficult as any of the other fields of biology, and cannot be learned except by explicit application. A student who has been well trained in biology should understand not only the fundamentals of evolution, but also why it is relevant to other areas in biology.

Perceived problems and suggestions

The. Demography of Evolutionary Biologists

It was our impression that the greatest single problem with the future of evolutionary biology in Israel is demographic. Within the next five years, a substantial fraction of the major evolutionary biologists at Hebrew University, Tel Aviv University and Haifa University will be retiring. While there are some very able younger people already in faculty positions, their numbers are not sufficient to meet the research, teaching and administrative requirements of this area of biology. We can anticipate a gap in the leadership in evolutionary biology within each of these universities and in the country at large. This problem should be recognized and measures should be taken to deal with it with all deliberate haste. We have three suggestions:

Develop programs to encourage and train current graduate students in Israeli universities to take faculty positions in Israel. One way of doing this is to identify particularly promising senior graduate students and provide them with contracts for tenure track positions following postdoctoral training with prominent evolutionary biologists in other countries.

Recruit exceptionally able early- and mid-career evolutionary biologists from other

countries for positions in Israeli universities. Towards this end, it may be necessary to allow these people a period of grace to learn Hebrew sufficiently to teach in this language and, within that grace period, to teach in English.

Coordinate current training of graduate students in the different Israeli universities to improve the quality and diversity of their educational experience in evolutionary biology. One way of doing this is to organize 4-6 week intensive, all-Israel "summer" courses in specific areas of evolutionary biology. For these courses, foreign evolutionary biologists can be invited to teach areas for which there are no Israeli evolutionary biologists with the appropriate background. These courses could be designed to attract foreign students in evolutionary biology as well, which would facilitate intellectual cross-fertilization and the establishment of future collaborations and could provide a source of revenue for these courses. Another way of doing this is to provide support for particularly able Israeli graduate students to either participate in such courses in other countries, e.g. the Molecular Evolution course at Woods Hole. Alternatively, they can spend 3 or so months in the laboratories of evolutionary biologists in these countries.

The Fragmentation of Evolutionary Biology in Israel.

We were struck (appalled is also accurate) by the dearth of opportunities for evolutionary biology graduate students, postdoctoral fellows and faculty from different universities (as well as departments and research groups from the same universities) to get together to share ideas, results, other information and enthusiasm.

We suggest that informal (and inexpensive), frequent, regular one-day meetings in evolutionary biology should be organized on a national basis. These meetings should encompass all areas in which evolutionary considerations are important or can be employed, including ecology, anthropology, palaeontology, population biology, epidemiology, mathematical modeling, computer science, molecular biology, developmental biology, agriculture, and medicine.

Another solution to the problem of fragmentation might be the formation of an Israeli society of the evolutionary sciences. Such a society could unite researchers in the diverse disciplines concerned with evolution and its applications, could hold annual meetings, formulate recommendations for the development and application of evolutionary research in Israel, and serve as a much needed voice for evolutionary biology. (We noted that many of the scientists we spoke with advocate the formation of such a society.)

Molecular/Developmental Biology and Evolution

Both molecular and, more recently, developmental biology are making major contributions to evolutionary biology. At the same time, studies of molecular evolution and developmental evolution are contributing to fundamental knowledge of molecular genetics and developmental biology. Molecular tools are also being used to address a vast variety of questions about evolution at the organismal level. Studies in areas such as phylogenetic systematics, population genetics, speciation, evolutionary physiology and behavioral evolution commonly use molecular data. Thus, there is no conflict between organismal studies and molecular methods. Symbiosis of molecular biologists and evolutionary biologists in research teams has become increasingly common and effective.

Although the tools of molecular biology are used by a number of evolutionary biologists in Israel, these applications to organismal evolutionary studies warrant expansion. The committee did not see any studies in the developmental aspects of evolution, the so-called evo-devo approach. In order to stay abreast of modern studies of

evolution and to be on the forefront in evolutionary studies worldwide, we suggest that Israel would benefit by increasing its efforts in molecular evolution and initiating studies in evo-devo. The integration of molecular and developmental biology into organismal studies will add a necessary ingredient for the vitality of evolutionary studies in Israel. It is likely that the introduction of courses in these subjects and the creation of a focus on evolutionary biology in Israel would serve to attract individuals to these subjects, especially Ph.D. students and postdoctoral fellows. Molecular and developmental approaches to evolution can also be encouraged by the creation of a National Plan in Evolution as described below.

A National Plan

One approach that has been used by some Institutes at the US National Institutes of Health to guide researchers in certain areas is to produce a strategic document called the National Plan that is generated by experts in the field under consideration. For example, the most recent National Plan written by the National Eye Institute of the US National Institutes of Health can be found on the internet at **http://www.nei.nih.gov.** An Israeli National Plan in Evolution instigated by the Israel National Academy of Sciences could summarize the state of the field and state priorities for further work, pointing out especially windows of opportunity. While this document would not "ear-mark" subjects that would be necessarily supported, it would define areas to be given priority for support. A National Plan for Evolution would place a clear focus on evolutionary studies in Israel, encourage students to pursue a career in evolution and guide future studies into areas that would be important to encourage in this country.

A Need for Shared National Facilities

Natural history collections in Israel are excellent and provide a central resource for the study of all aspects of evolutionary biology. These collections suffer from a lack of funding and recognition of their importance. The pool of trained systematicists to manage these collections is rapidly dwindling to the extent that Israel will soon lack the expertise to cover even the major taxa of the country. It is essential that these collections be maintained and that research based on them be encouraged for international as well as by Israeli scientists.

We consider the development and maintenance of a national facility to house these collections as well that of the gene banks of indigenous wild relatives of crop plants as an important priority. Funding for such a facility should include support for the curation of these collections and training of future systematists. This facility might not be associated with a specific university. However associated, it should be fully national in character and availability. In addition to its mission of research and scholarship this facility should include public exhibition areas to educate children and the general public about evolution as well as ecology and biodiversity.

Preparation of Biology Teachers

Because of the phenomenal advances in biology and in its applications, it is increasingly important that educated citizens have some understanding of biological principles - including evolution. However, it appears that the great majority of students in Israel receive little if any education about evolution, either in high school or in university. Among the many reasons for this distressing state of affairs is that most high-school teachers of biology themselves have not been educated on the subject. Very possibly, fundamentalist antipathy to evolutionary theory also plays a part in this. We suggest that evolution be included as an integral part of the university education of all biology

students, including those who intend to become teachers.

Evolution, Science, and Society:

a "white paper" on behalf of the field of evolutionary biology

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Evolution, Science, and Society:

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At the invitation of their respective Society Presidents, representatives from the **American Society of** Naturalists, the Society for the Study of Evolution, the Society for Molecular Biology and Evolution, the Ecological Society of America, the Society of Systematic Biologists, the Genetics Society of America, the Animal Behavior Society), and the Paleontological Society met in Indianapolis on April 22-23, 1995, to discuss the need for preparation of a "White Paper" defining the challenges and opportunities facing the study of evolution. At that workshop, co-chairs D. Futuyma (editorial) and T. Meagher (organizing) were elected to seek funding to support workshops to develop the White Paper as well as an associated Executive Summary and to coordinate and oversee their writing and publication. A Working Group representing major disciplines in evolutionary biology was convened to draft these documents with support from the Alfred P. Sloan Foundation and NSF. Announcements of the existence of this Working Group and its charges were made in **The American** Naturalist, Ecology, Evolution, Genetics, Molecular Biology and Evolution, and Science.

The final documents (presented here in draft form) will be addressed to decision-makers responsible for guiding basic and applied scientific research and for developing educational curricula. They will also be addressed to anyone interested in understanding the current and potential accomplishments of evolutionary biology. Their major goals are:

- to describe our present understanding of evolution and the major intellectual accomplishments of evolutionary biology,
- to identify major questions and challenges in which progress in evolutionary science can be expected in the near future;
- to describe past and expected contributions of evolutionary biology both to other sciences and to social needs in areas such as health science, agriculture, and environmental science; and
- to suggest ways in which progress can be facilitated in basic research, in applications of evolutionary biology to social needs, and in biological science education.

The draft documents are presently under review by the Executive Councils of the eight scientific societies named above for endorsement prior to final editing and printing. At the same time, the text is being reworked by a professional editor with a mandate to address the issue of accessibility to the intended readership. The Executive Summary [html format][pdf format], which will ultimately appear as a high impact document complete with color illustrations, is targeted to a broad audience, including policymakers at government agencies, private foundations, college and university administrations, corporations, scientific and educational societies, and the scientific community itself. The full document [html format][pdf format], which will appear as a supplement to the **The American** Naturalist as well as a stand alone booklet, is intended to serve as background material targeted to a more dedicated, implementation oriented readership whose interest has been captured by the Executive Summary.

In order for these documents to have maximal impact at the policy level, it is important that they be made available to the broader scientific community for review and comment. Consequently, we are making the text of these documents available through this web page. Please feel free to read and review these documents and to pass along comments and suggestions to the Working Group by email (ecolevol@rci.rutgers.edu). We will attempt to integrate comments made before 15 September 1997 into the final edit of the documents.

EVOLUTION, SCIENCE AND SOCIETY:

Evolutionary Biology and the National Research Agenda

[working draft - last updated 23 December 1998]

[EXECUTIVE SUMMARY]

Evolutionary biology is the study of the history of life and the processes that lead to its diversity. Based on principles of adaptation, chance, and history, it seeks to explain all the characteristics of organisms, and therefore occupies a central position in the biological sciences.

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American Institute of Biological Sciences

American Society of Naturalists

Animal Behavior Society

Ecological Society of America

Genetics Society of America

Paleontological Society

Society for Molecular Biology and Evolution

Society of Systematic Biologists

Society for the Study of Evolution

RELEVANCE OF EVOLUTIONARY BIOLOGY TO THE NATIONAL RESEARCH AGENDA

The undisputed emerging prominence of biological sciences in the next century will be driven by accelerating public concern over threats to environmental quality, increasing need for improvements in food production due to population pressures, demands for new approaches in human health prompted by the emergence of antibiotic resistance and novel diseases, and the explosion of new technologies in biotechnology and computation. Evolutionary biology in particular is poised to make very significant contributions in the coming "Century of Biology;" it will contribute directly to pressing societal challenges as well as inform and accelerate other biological disciplines.

Evolutionary Biology has unequivocally established that all organisms evolved from a common ancestor over the last 3.5 billion years; it has documented many specific events in evolutionary history; and it has developed a well-valued theory of the genetic, developmental, and ecological mechanisms of evolutionary change. The methods, concepts, and perspectives of evolutionary biology have made and will continue to make important contributions to other biological disciplines, such as molecular and developmental biology, physiology, and ecology, as well as to other basic sciences such as psychology, anthropology, and computer science.

In order for evolutionary biology to realize its full potential, biologists must integrate the methods and results of evolutionary research with those of other disciplines both within and outside of biology. We must apply evolutionary research to societal problems, and we must include the implications of that research in the education of a scientifically informed citizenry.

To further such goals, delegates from eight major professional scientific societies in the United States whose subject matter includes evolution have prepared this document. It includes contributions by other specialists in various topics and feedback on earlier drafts elicited from the community of evolutionary biologists in the United States and by making the draft public on the World Wide Web. In summary, the delegates arrived at a series of recommendations addressed towards the following.

ADVANCING UNDERSTANDING THROUGH COMMUNICATION

We urge the following roles for evolutionary biologists:

- communicating to federal agencies, and to other institutions that support basic or applied research, the relevance of evolutionary biology to the missions of these organizations

- training the next generation of evolutionary biologists to be aware of the relevance of their field to societal needs

ADVANCING UNDERSTANDING THROUGH RESEARCH

To capitalize on evolutionary biology as an organizing and integrating principle, we urge that:

- evolutionary perspectives be incorporated as a foundation for interdisciplinary research to address complex scientific problems
- evolutionary biologists work towards building meaningful links between basic research and practical application
- evolutionary biology play a more explicit role in the overall mission of federal agencies that could benefit from contributions made by this field

ADVANCING UNDERSTANDING THROUGH EDUCATION

We encourage major efforts to strengthen curricula in primary and secondary schools, as well as in colleges and universities, including:

- support of mid-career training of science teachers in evolutionary biology
- greater emphasis on evolution in undergraduate college curricula for biology majors and premedical students, with accessible alternative courses for non-majors
- integration of relevant evolutionary concepts into the post-baccalaureate training of all biologists and of professionals in areas such as medicine, law, agriculture, and environmental sciences

WHAT IS EVOLUTION?

Biological evolution consists of change in the hereditary characteristics of groups of organisms over the course of generations. From a long-term perspective, evolution is the descent with modification of different lineages from common ancestors. From a short-term perspective, evolution is the ongoing adaptation of organisms to environmental challenges and changes. Thus evolution has two major components: the branching of lineages and changes within lineages.

WHAT ARE THE GOALS OF EVOLUTIONARY BIOLOGY?

Evolutionary biology seeks to explain the diversity of life: the variety of organisms and their characteristics, and their changes over time. Evolutionary biology also seeks to interpret and understand organismal adaptation to environmental conditions. The two encompassing goals of evolutionary biology are to discover the history of life on earth and to understand the causal processes of evolution. Insights achieved through efforts to meet these goals greatly enhance our understanding of biological systems.

Evolutionary biologists often work at the interface of many sub-disciplines of biology, leading to the development of subject areas such as behavioral evolution, evolutionary developmental biology, evolutionary ecology, evolutionary genetics, evolutionary systematics, and molecular evolution. The sub-disciplines of evolutionary biology also have formed direct links with fields such as statistics, economics, geology, anthropology, and psychology.

HOW IS EVOLUTION STUDIED?

Evolutionary biology draws on a wide range of methodologies and conceptual approaches.

Methods for understanding the history of evolution include observations of the fossil record and categorization and classification of variation among living organisms. Differences and similarities among species in anatomy, genes, and other features can be analyzed by statistical methods that enable us to estimate historical relationships among species and the sequence in which their characteristics evolved.

Studies of ongoing evolutionary change employ observation and experimentation. Analysis of genetic variation enables us to characterize mutation, genetic drift, natural selection, and other processes of evolution. The "comparative method" contrasts features of species that have adapted to different environments. Finally, mathematical models and other analytical tools are frequently brought to bear.

WHY IS EVOLUTIONARY BIOLOGY IMPORTANT?

Evolutionary biology provides the key to understanding the principles governing the origin and extinction of species. It provides causal explanations, based on history and on processes of genetic change and adaptation, for the full sweep of biological phenomena, ranging from the molecular to the ecological. Thus, evolutionary biology allows us to determine not only how and why organisms have become the way they are, but also what processes are currently acting to modify or change them.

Response to change is a feature of evolution that is becoming increasingly important in terms of scientific input into societal issues. We live in a world that is undergoing constant change on many levels, and much of that change is a direct consequence of human activity. Evolutionary biology can contribute explicitly to enhanced awareness and prediction of mid and long term consequences of environmental disturbances, whether they be deforestation, application of pesticides, or global warming.

Distinctive perspectives on biology offered by evolutionary biology include emphasis on the interplay between chance and adaptation as conflicting agents of biological change, on variation as an inherent feature of biological systems, and on the importance of biological diversity. Variation is a key concept, since evolutionary change ultimately depends on the differential success of competing genetic lineages. The ultimate consequence of variation and evolutionary divergence is biological diversity.

Biological species are not fixed entities, but rather are subject to ongoing modification through chance or adaptation. Understanding why and how some species are able to change apace with new environmental challenges is critical to the sustainability of human endeavor.

HOW DOES EVOLUTIONARY BIOLOGY CONTRIBUTE TO SOCIETY?

In addition to the historical dimension, evolution is an important feature in our everyday lives. Evolution is happening all around us: in our digestive tracts, in our lawns, in woodland lots, in ponds and streams, in agricultural fields and hospitals. For short lived organisms, such as bacteria and insects, evolution can happen on a very short time scale. This immediacy brings evolutionary biology directly into the applied realm. Indeed, evolutionary biology has a long history and a bright future in terms of its ability to address pressing societal needs (L. R. Meagher & T. R. Meagher (eds.). 1994. *Workshop Report: The Emerging Relevance of Evolutionary Biology to Applied to Problems and Opportunities.* Rutgers University, New Brunswick, NJ). Evolutionary biology has already made particularly strong contributions in the following areas:

Environment and conservation. Evolutionary insights are important in both conservation and management of renewable resources. Population genetic methods are frequently used to assess the genetic structure of rare or endangered species as a means of determining appropriate conservation measures. Studies of the genetic composition of wild relatives of crop species can be used to discover potentially useful new genes that might be transferred into cultivated species. Studies of wild plants' adaptations to polluted or degraded soils contribute to the reclamation of damaged land.

Agriculture and natural resources. The principles of plant and animal breeding strongly parallel natural evolutionary mechanisms, and there is a rich history of interplay between evolutionary biology and agricultural science. Evolutionary insights play a clear role in understanding the ongoing evolution of various crop pathogens and insect pests, including the evolution of resistance to pest-control measures. The methods of evolutionary genetics can be used to identify different gene pools of commercially important fish and other organisms, their migration routes, and differences in their physiology, growth, and reproduction.

Finding useful natural products. Many thousands of natural products are used in medicine, food production and processing, cosmetics, biotechnology, pest control, and industry, but millions of other potentially useful natural products have yet to be screened or even discovered. Evolutionary principles allow a targeted search by predicting adaptations to environmental selection pressures and by identifying organisms related to those that have already yielded useful natural products. Exploration of related species has also made it possible to develop natural products from more accessible relatives of rare species in which natural products have been found, as occurred when the rare and endangered Pacific yew was found to contain a substance (taxol) useful in treating breast cancer.

Human health and medicine. Methods and principles from evolutionary biology have contributed to understanding the links between genes and human genetic diseases, such as Alzheimer's disease. Evolutionary methods help to trace the origins and epidemiology of infectious diseases, and to analyze the evolution of antibiotic resistance in pathogenic microorganisms. Evolutionary principles are used to interpret human physiological functions and dietary needs. Methods developed by evolutionary geneticists are playing an important role in mapping defective human genes, in genetic counseling, and in identifying genetic variants that alter risks for common systemic diseases and responses to medical treatments.

Biotechnology. The interplay between biotechnology and evolutionary biology holds great promise for application to important societal needs. As genetic engineering has reached the field implementation stage, evolutionary biologists have been prominently involved in risk assessment as well as interpretation of phenotypic consequences of transgene insertion. Finally, the automation of DNA sequencing has made it possible to reconstruct the precise genealogical relationship among specific genes, such as those of the human immunodeficiency virus (HIV).

Understanding humanity. Evolutionary biology has contributed greatly to human understanding of ourselves by describing our origins, our relationships to other living things, and the history and significance of variation within and among different groups of people. Evolutionary anthropologists, psychologists, and biologists have advanced hypotheses on the biological bases of human culture and behavior. In addition, the evolutionary framework for understanding humanity has had a profound impact on literature, the arts, philosophy, and other areas of the humanities.

HOW DOES EVOLUTIONARY BIOLOGY CONTRIBUTE TO BASIC SCIENCE?

Accomplishments in the Study of Evolution

Among their accomplishments in studying the history and processes of evolution, evolutionary biologists have

- established that all organisms have evolved from a common ancestor over more than 3.5 billion years of earth's history
- developed methods of inferring phylogenetic, or genealogical, relationships among organisms
- described patterns of diversification and extinction in the fossil record
- developed and tested general theories that account for the evolution of phenotypic traits, including complex characters such as cooperative behavior and senescence
- made substantial progress in understanding evolution at the molecular level
- elucidated many aspects of human evolution

Contributions to Other Biological Disciplines

Evolution is widely viewed as central to biological understanding in general (NAS. 1998. *Teaching about Evolution and the Nature of Science.* National Academy Press, Washington, D.C.). Many biologists in diverse fields regard at least a portion of what they do as evolutionary. Recent accomplishments to which evolutionary biology has contributed include the following:

Molecular biology. Evolutionary approaches have contributed insight into the function and structure of molecular processes within cells. Examples include reconstruction and functional analysis of ancestral protein sequences, and elucidation of the significance of different types of DNA. Evolutionary research thus points the way to research on fundamental molecular mechanisms.

Developmental biology. A resurgence in interaction between developmental biology and evolutionary biology is now under way, in part through comparisons among families of genes that play critical roles in development. For example, the same genes in organisms as different as insects and mammals play similar developmental roles in some instances, and surprisingly different roles in other cases. Such studies help to identify the developmental functions of genes and lead to a deeper understanding of the processes that transform a fertilized egg into a complex adult.

Physiology and anatomy. Evolutionary biology has long influenced the study of physiology and anatomy in animals and plants, and has the potential to make many other contributions that are only now being developed. Some of these contributions will affect the study of human physiology, including related areas such as clinical psychology. The logical perspectives, methods, and comparative data of evolutionary biology can advance our understanding of functional anatomy and physiological mechanisms, and can be applied to areas such as medicine, agriculture, and veterinary science.

Neurobiology and behavior. From its inception, the field of animal behavior has had a strong evolutionary base, for its goals have included understanding the evolutionary origin of behavioral traits and their adaptiveness. The evolutionary study of animal behavior has Joined with comparative psychology in several areas of research, such as the study of learning and the search for adaptive mechanisms in human cognitive processes.

Applications beyond biology. There have long been rewarding interactions between evolutionary biology and other analytical fields, notably statistics and economics. Some of the basic tools in statistics, including analysis of

variance and path analysis, were originally developed by evolutionary biologists. Along the same lines, evolutionary algorithms that mimic natural selection in biological systems are currently being used in computer and systems applications.

WHAT DOES THE FUTURE HOLD FOR EVOLUTIONARY BIOLOGY?

Researchers in molecular and developmental biology, physiology, ecology, animal behavior, psychology, anthropology, and other disciplines continue to adopt the methods, principles, and concepts of evolutionary biology as a framework. Likewise, applied research in forestry, agriculture, fisheries, human genetics, medicine, and other areas has increasingly attracted scientists trained in evolutionary biology. Evolutionary biologists have expanded their vision, addressing both basic questions throughout the biological disciplines and problems posed by society's needs. As a result of both the rapid growth of this "evolutionary work force" and technological advances in areas such as molecular methodology, computing, and information processing, progress in evolutionary biology and related areas is more rapid now than ever before. With the appropriate and necessary support in education and research, the evolutionary disciplines will make ever greater contributions to applied and basic knowledge.

Applied Science

In the applied realm, evolutionary biologists are embracing their social responsibilities. There are many ways in which their discipline can help humanity

- to understand and combat genetic, systemic, and infectious disease
- to understand human physiological adaptations to stresses, pathogens, and other causes of ill health
- to improve crops and mitigate damage by pathogens, insects, and weeds
- to develop tools for analyzing human genetic diversity as it applies to health, law, and the understanding of human behavior
- to use and develop biological resources in a responsible manner
- to remedy damage to the environment
- to predict the consequences of global and regional environmental change, and
- to conserve biodiversity and discover its uses.

Basic Science

In basic science, we stand at the threshold

- of fully documenting biodiversity and describing the phylogenetic relationships among all organisms
- of more completely understanding of the causes of major changes in the history of life
- of discovering and explaining processes of evolution at the molecular level
- of understanding how developmental mechanisms evolve and give rise to new anatomical structures
- of elucidating the processes that both cause and constrain adaptations in physiology, endocrinology, and anatomy
- of deriving a deeper understanding of the adaptive meaning and mechanisms of behavior, and
- of developing a predictive theory of coevolution between species, such as pathogens, parasites, and their hosts, and of the effects of coevolution on populations and ecological communities.

CONCLUSION

Evolutionary biology can play a central role in advancing many dimensions of basic and applied biology. Therefore, the continued and enhanced support of this field is critical to maximizing the nation's research progress in both basic and applied arenas. In terms of societal needs for the next century, the time to make the investment in evolutionary biology is now, while there is still time either to change current trends or to better prepare us to deal with their

consequences. Current and projected population levels will result in increasing environmental impacts, increasing pressure on food production, ever greater challenges to biological diversity, and enhanced opportunities for the emergence of new diseases. A healthy scientific base in evolutionary biology is an essential element in preparing us to meet these issues. Evolutionary biology must be at the heart of the nation's research agenda in biology, just as it is at the heart of the field of biology.

EVOLUTION OF INFECTIOUS DISEASES

Release Date: December 18, 1998

RFA NUMBER: GM-99-005 P. T.

National Institute of General Medical Sciences National
Institute of Allergy and Infectious Diseases

Letter of Intent Receipt Date: February 01, 1999
Application Receipt Date: March 17, 1999

PURPOSE

The goal of this joint NIGMS/NIAID Request for Applications (RFA) is to encourage development of a predictive science of infectious diseases by applying the perspectives, theories, and methods of population and evolutionary biology to important issues of disease emergence, prevention and treatment. To achieve this goal, this RFA seeks collaborations between two major groups of scientists: (1) those with expertise in population and evolutionary biology and molecular phylogenetics, including mathematical modeling and complexity theory; (2) infectious disease experts such as clinicians, epidemiologists, immunologists, microbiologists, veterinarians, or plant pathologists. NIGMS and NIAID anticipate that this RFA will be released again within a year.

HEALTHY PEOPLE 2000

The Public Health Service (PKS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Evolution of Infectious Diseases, is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2000" at http://www.crisny.org/health/us/health7.html.

ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal Government. Racial/ethnic minority individuals, women, and persons with disabilities are encouraged to apply as principal investigators.

MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) research project grant (R01) and program project grant (P01). Foreign institutions are not eligible for program projects. Supplements to existing NIH grants will also be considered. Responsibility for the planning, direction, and execution of the proposed project will be solelv that of the applicant. The anticipated award date is September 1, 1999.

FUNDS AVAILABLE

The NIGMS and NIAID intend to commit approximately $5 million in FY 99 to fund 16-20 new grants in response to this RFA. An applicant may request a project period of up to 5 years and a budget for direct costs of up to $1 million for 5 years, excluding indirect costs on consortium arrangements. Because the nature and scope of the research proposed may vary, it is anticipated that the size of each award will also vary. Although the financial plans of the NIGMS and NIAID provide support for this program, awards pursuant to this RFA are contingent upon the availability of funds and the receipt of a sufficient number of applications of outstanding scientific and technical merit.

RESEARCH OBJECTIVES

Background

Population dynamics and evolutionary processes are fundamental to virtually all

aspects of infectious diseases, including their emergence or re-emergence as public health threats, their prevention and their treatment. The ability of an infectious species to colonize plant or animal hosts, to proliferate, to cause disease, and to spread depends on a variety of factors, such as its genetic characteristics, its life history, and its mode of transmission, all of which can be modified by evolutionary forces. Ecological and environmental factors also play an important role in the development of infectious diseases. The ability of a host species to prevent and control infections similarly depends on its innate defense system (including immune defenses), its behavior, its environment, and human intervention. Population dynamics, including population density, migration, population subdivision, and competition for resources, affect the evolution of both pathogens and hosts, including humans.

Evolutionary biology, in combination with molecular biology, genetics, systematics, immunology, mathematics, and other disciplines, will contribute significantly to our ability to develop a predictive science of infectious diseases. For example, identifying the origins and host ranges of infectious agents requires a variety of molecular, genetic, mathematical, and evolutionary tools. Intervention to prevent or treat infections by behavior modification, control of vectors, vaccination, chemotherapy or other means influences a variety of dynamic evolutionary processes in individual hosts, communities of hosts, and communities of pathogenic organisms. Understanding the conditions under which interventions fail (e.g., antibiotic resistance or live vaccines' reversion to virulence) and designing protocols to prevent these failures requires application of evolutionary and ecological principles. Multidisciplinary approaches, including evolution and ecology, are also essential for anticipating the conditions under which new infectious diseases will emerge and old ones will re-emerge .

While there is widespread understanding that population, ecological and evolutionary dynamics are central to understanding, preventing and treating infectious diseases and anticipating their emergence and re-emergence, research into these aspects of infectious diseases has been limited. With a few exceptions, the quantitative and comparative perspectives of population and evolutionary biology and mathematical modeling are rarely employed in infectious disease research or in the design of protocols to prevent and treat infections. The goal of this initiative is to remedy this situation by supporting collaborations among scientists with expertise in evolutionary and population biology, including phylogenetics; scientists with expertise in infectious disease; and scientists with expertise in mathematical modeling, computer science, and complexity theory.

Scientific Objectives

This initiative includes those areas of infectious disease research where population dynamics and evolutionary processes clearly play an important role. Proposals for research projects responsive to this announcement may address either broad evolutionary questions that may ultimately be relevant to infectious diseases or the implications of evolution and population dynamics in specific diseases. The study of model systems may be instructive in either case. Applicants must clearly explain how proposed approaches and perspectives are expected to contribute to development of a predictive science of infectious diseases.

Studies which combine theoretical and empirical approaches to investigations of the evolution of infectious diseases and their prevention and treatment are especially encouraged. Also encouraged are projects whose evolutionary focus will lead to a predictive science of the sources, prevention, and treatment of existing, emerging, or reemerging infectious diseases. Model systems, including plant systems, will be considered when they are used to address fundamental problems of the population biology and evolution of disease.

Responsive applications must employ approaches typical of population and evolutionary studies, such as mathematical modeling, phylogenetics, and cladistics, as well as in vitro and in vivo experiments that address interrelated elements an infectious system (host, pathogen, vector and environment, as appropriate). Within the areas of investigation described below, relevant applications would focus on one or more of the stated Specific aspects:

.1. Population and/or evolutionary studies related to the causes and sources of infectious diseases.

- o Genetic variation and structure of pathogen populations and the genetic relationships between commensal and pathogenic members of closely related taxa
- o Population analyses of the contributions and sources of the vertical and horizontal transfer of genes and accessory elements coding for virulence determinants, host range and specificity, and drug resistance
- o Genetic factors (pathogen, host or vector) responsible for geographic and temporal variation in disease frequency and severity

2. Population and/or evolutionary studies related to the interactions between hosts and pathogens.

- o Contribution of population dynamic and evolutionary processes to the pathogenesis and virulence of infecting organisms
- o Establishment of model systems to explore the relationship between the evolution of pathogenic organisms and factors affecting host susceptibility, including ecological, social and other environmental factors

3. Population and/or evolutionary studies related to the consequences of intervention strategies.

- o Within-host population dynamics related to intervention strategies, including reversion to virulence of live vaccines (as opposed to outgrowth of existing unattenuated organisms), as well as evolution of resistance following antimicrobial chemotherapy or vaccination
- o Establishment of model systems (either in vitro systems, or in vivo systems involving non-human pathogens and/or animal or plant hosts) to predict the ecological and evolutionary consequences of programs involving host behavior, vaccination, antimicrobial chemotherapy, and other intervention strategies on pathogen, host, and vector populations

4 . Population and/or evolutionary studies related to the factors contributing to variation in pathogen virulence and host susceptibility to infections and their consequences.

- o Establishment of model systems to explore the environmental, physiological and genetic factors responsible for generating and maintaining variation in pathogen and host populations, including co-evolutionary pressures.

5. Population and/or evolutionary studies related to the natural history of pathogenic organisms.

- o Evolutionary basis of the normal range of pathogenic organisms' habitats and hosts
- o Establishment of model systems to explore the molecular basis of host barriers that must be overcome by pathogens in order to extend their ranges
- o Establishment of model systems to explore the molecular, individual, and population dynamics of extending the niche or host range of a pathogen.

INCLUSION OF WOMEN AND MINORITIES IN RESEARCH INVOLVING HUMAN SUBJECTS

It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification is provided that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 4 92B of Public Law 103-43).

All investigators proposing research involving human subjects should read the "NIH Guidelines For Inclusion of Women and Minorities as Subjects in Clinical Research," which have been published in the Federal Register of March 28, 1994 (FR 59 14508-14513) and in the NIH Guide for Grants and Contracts, Volume 23, Number 11, March 18, 1994 available on the web at:
http://www.nih.gov/grants/guide/1994/94.03.18/notice-nih-guideline008.html

INCLUSION OF CHILDREN AS PARTICIPANTS IN RESEARCH INVOLVING HUMAN SUBJECTS

It is the policy of NIH that children (i.e., individuals under the age of 21) must be included in all human subjects research conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them. This policy applies to all initial (Type 1) applications submitted for receipt dates

after October 1, 1998.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines" on the Inclusion of Children as Participants in Research Involving Human Subjects that was published in the NIH Guide for Grants and Contracts, March 6, 1998, and is available at the following URL address: http://www.nih.gov/grants/guide/notice-files/not98-024.html

Investigators also may obtain copies of these policies from the program staff listed under INQUIRIES. Program staff may also provide additional relevant information concerning the policy.

LETTER OF INTENT

Prospective applicants are asked to submit a letter of intent that includes a descriptive title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted. Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows program staff to estimate the potential review workload and avoid conflict of interest in the review.

The letter of intent is to be sent to the Dr. Irene Eckstrand at the address listed under INQUIRIES by the letter of intent receipt date listed in the heading of this RFA.

APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 4/98) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research and from the Division of Extramural Outreach and Information Resources, National Institutes of Health, 6701 Rockledge Drive, MSC 7910, Bethesda, MD 20892-7910, telephone 301/435-0714, email: GrantsInfo@nih.gov.

The RFA label available in the PHS 398 (rev. 4/98) application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2 of the face page of the application form and the YES box must be marked.

Submit a signed, typewritten original of the application, including the Checklist, and five signed, photocopies, in one package to:

CENTER FOR SCIENTIFIC REVIEW
NATIONAL INSTITUTES OF HEALTH
6701 ROCKLEDGE DRIVE, ROOM 1040 - MSC 7710
BETHESDA, MD 20892-7710
BETHESDA,MD 20817 (for express/courier service)

Applications must be received by the application receipt date listed in the heading of this RFA. If an application is received after that date, it will be returned to the applicant without review.

The Center for Scientific Review (CSR) will not accept any application in response to this RFA that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. The CSR will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by CSR and for responsiveness by NIGMS and NIAID staff. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to the RFA, NIH staff will contact the applicant to determine

whether to return the application to the applicant or submit it for review in competition with unsolicited applications at the next review cycle.

Applications that are complete and responsive to this RFA will be evaluated for scientific and technical merit in accordance with the criteria stated below by an appropriate initial review group of the CSR. As part of the initial merit review, applications will receive a written critique and may undergo a process in which only those applications deemed to have the highest scientific merit will be discussed and assigned a priority score. Scored applications will receive a second level of review by the appropriate National Advisory Council.

Review Criteria

The goal of this RFA is to stimulate useful collaborations among scientists from different fields focused on developing a predictive science of infectious disease. In the written review, comments on the following aspects of the application will be made in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of this goal. Each of these criteria will be addressed and considered in the assignment of the overall score.

(1) Significance: Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge be advanced? What will be the effect of these studies on the concepts or methods that drive this field?

(2) Approach: Are the conceptual framework, design, methods, and analyses adequately developed, well-integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

(3) Innovation: Does the project employ novel concepts, approaches or method? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?

(4) Investigator: Is the investigator appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers (if any)? Are the nature and quality of the collaborations appropriate for the proposed research?

(5) Environment: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

In addition to the above criteria, in accordance with NIH policy, all applications will also be reviewed with respect to 'the following:

o The adequacy of plans to include both genders, minorities and their subgroups, and children as appropriate for the scientific goals of the research. Plans for the recruitment and retention of subjects will also be evaluated.

o The reasonableness of the proposed budget and duration in relation to the proposed research

o The adequacy of the proposed protection for humans, animals or the environment, to the extent they may be adversely affected by the project proposed in the application.

The initial review group will also examine the provisions for the protection of human subjects and the safety of the research environment.

Schedule

Letter of Intent Receipt Date: February 1, 1999
Application Receipt Date: March 17, 1999
Peer Review Date: June - July 1999
Council Review: September - October 1999
Earliest Anticipated Start Date: December 1, 1999

AWARD CRITERIA

Applications will compete with all other approved applications for available funds. The following will be considered in making funding decisions:
o the quality of the proposed project as determined by peer review;
o balance among the projects in addressing a variety of experimental approaches;
o likelihood that the proposed research will lead to significant advances in our knowledge of the evolution of infectious diseases;
o promise of the proposed studies to accomplish the goals of this RFA by increasing knowledge of the evolution of infectious disease;
o adequacy of plans to make data and material developed as a result of the proposed research accessible to the biomedical research community in a timely manner; and
o availability of funds..

INQUIRIES

Inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues to:

Dr. Irene Anne Eckstrand
Division of Genetics and Developmental Biology
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45 Center Drive, MSC 6200
Bethesda, MD 20892-6200
Telephone: (301) 594-0943
FAX: (301) 480-2228
Email: Irene Eckstrand@nih.gov

Dr. Stephanie James
Parasitology and International Programs Branch
National Institute of Allergy and Infectious Diseases
Solar Building; Room 3A-10
Rockville, MD 20892
Telephone: (301) 496-2544
FAX: (301) 402-0659
Email: sjl3y@nih.gov

Direct inquiries regarding fiscal matters to:

Ms. Marcia Cohn
Grants Management Office
National Institute of General Medical Sciences
45 Center Drive, MSC 6200
Bethesda, MD 20892-6200
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FAX: (301) 480-1969
Email: cohnm@nigms.nih.gov

Ms. Mary Kirker
Grants Management Branch
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FAX:" (301) 480-3780
Email: mkirker@mercury.niaid.nih.gov

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Nos. 93.821, 93.859, 93.862, and 93.856. Awards are made under authorization of the Public Health Service Act, as amended and administered under PHS grants policies, the NIH Grants Policy.Statement (October 1, 1998)", and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental Review requirements of Executive Order 12372 or Health Systems Agency review.

The PHS strongly encourages all grant and contract recipients to provide a smoke-free workplace and promote the non-use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, and portion of a facility) in which regular or routine education, library, day care, health care or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

Return to Volume Index

Return to NIH Guide Main

Index