

## Free Executive Summary

### Review of NASA's Biomedical Research Program



Committee on Space Biology and Medicine, Space  
Studies Board, National Research Council

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## Executive Summary

The 1998 Committee on Space Biology and Medicine (CSBM) report *A Strategy for Research in Space Biology and Medicine in the New Century* (NRC, 1998) assessed the known and potential effects of spaceflight on biological systems in general and on human physiology, behavior, and performance in particular, and recommended directions for research sponsored over the next decade by the National Aeronautics and Space Administration (NASA). **The present follow-up report reviews specifically the overall content of the biomedical research programs supported by NASA in order to assess the extent to which current programs are consistent with recommendations of the *Strategy* report for biomedical research activities.** In general, NASA programs concerned with fundamental gravitational biology are not considered here. The committee also notes that this report does not include an evaluation of NASA's response to the *Strategy* report, which had only recently been released at the initiation of this study.

Summarized below are the committee's findings from its review of (1) NASA's biomedical research and (2) programmatic issues described in the *Strategy* report that are relevant to NASA's ability to implement research recommendations.

### NASA BIOMEDICAL RESEARCH

Most of the biomedical research funded by NASA is carried out through (1) a program of NASA Research Announcements that funds proposals by individual investigators, (2) research conducted in scientific or clinical programs at either the Johnson Space Center (JSC) or the Ames Research Center (ARC), and (3) focused research projects managed by the National Space Biomedical Research Institute (NSBRI). The committee considered all NASA biomedical research projects, irrespective of their origin, under the following disciplinary categories:

- Sensorimotor integration,
- Bone physiology,

- Muscle physiology,
- Cardiovascular and pulmonary systems,
- Endocrinology and nutrition,
- Immunology and microbiology,
- Radiation biology, and
- Behavior and performance.

In order to assess the degree to which NASA's research programs will meet the agency's needs for biomedical knowledge in the next 10 years, the committee compared current and planned research to the recommendations made in the *Strategy* report. Within this context, the committee attempted to answer the following questions.

### **What Is the Balance of Discipline Areas in NASA's Biomedical Research Program?**

The *Strategy* report gave the highest overall priority to specific research questions dealing with bone and muscle loss, changes in the function of the vestibular and sensorimotor systems, orthostatic intolerance, radiation hazards, and the physiological and psychological effects of stress. Although the committee found the balance of NASA research between the various biomedical disciplines to be generally consistent with the relative emphasis given to them in the *Strategy* report, many of the specific research topics given the highest overall priority are still to be addressed. Noted below is the degree to which these research topics appear in the current program. It should be kept in mind that many of the *Strategy* report recommendations called for specific microgravity investigations that cannot be carried out until appropriate flight opportunities again become available.

As recommended, mechanistic studies and the use of ground-based animal models to understand changes in bone and muscle during and after spaceflight are being emphasized in NASA's current program. Preliminary ground studies of the relationship between exercise activity and protein-energy balance have also been started. Implementation of recommendations to collect in-flight astronaut data on bone loss and hormonal profiles must await flight opportunities.

Some preliminary investigations have been carried out that are relevant to the recommendation for in-flight recordings of signal processing following otolith afferent stimulation. However, the recommendation to study the basis for compensatory vestibulomotor mechanisms on Earth and in space has not yet been addressed. The performance of the recommended microgravity studies on neural space maps and pattern learning in the vestibulo-oculomotor system will depend on the availability of flight opportunities.

Mechanistic studies of total peripheral resistance responses during postflight orthostatic stress have been conducted on the recent Neurolab mission and in the cardiovascular laboratory at JSC. The Mir cardiovascular experiments were relevant to the recommendation to examine cardiovascular changes on long-duration missions. However, inadequate plans exist to monitor these changes on the International Space Station. Current pulmonary studies focus on the issue of decompression sickness but do not address aerosol deposition and respiratory muscle function.

Studies to examine the space radiation-induced risks of cancer and central nervous system damage are being carried out by NSBRI investigators at new facilities at Loma Linda University for proton studies and at Brookhaven for heavy ions. These will provide greatly improved access to investigators for relevant studies. Flights are not yet available for the recommended study of the combined effects of radiation and stress on the immune system, and no preliminary ground studies on this issue appear to be planned.

The majority of NASA-supported psychosocial research is currently directed toward the recommended studies of neurobiological mechanisms involved in circadian rhythm and sleep disturbances, and there are strong indications that NASA also plans to give explicit emphasis to the recommended studies on psychosocial mechanisms in the future. However, the work recommended on counter-measure evaluation and development has so far received little attention, with the exception of circadian and neurovestibular system studies.

### **What Is the Balance Between Ground and Flight Investigations?**

The majority of NASA's current and planned biomedical studies are ground based due to the limitation in flight opportunities over the next several years. Some notable exceptions include behavioral research and sensorimotor integration, which have a significant percentage of experiments in the flight program. As for radiation biology, its program focus on ground-based research is consistent with the recommendations of the *Strategy* report. However, the *Strategy* report recommended a major flight component for most discipline research programs, and the current lack of appropriate flight opportunities may lead to delays in the development of needed countermeasures for physiological changes such as orthostatic intolerance and muscle loss. Although it is possible, and even necessary, to perform much of the preliminary work on the ground, many of the critical research questions cannot be resolved without in-flight studies.

### **To What Degree Are Studies of Fundamental Cellular and Physiological Mechanisms Addressed in Research Programs?**

In general, there is a strong and very appropriate degree of emphasis on mechanistic studies across the various biomedical disciplines, as recommended in the *Strategy* report. In the area of bone physiology, for example, an independent program of basic cellular and molecular biology has been initiated at ARC, while an NSBRI laboratory is taking pharmacologic approaches to the study of biochemical pathways. Some of the specific mechanistic studies recommended in the *Strategy* report remain to be addressed, however, with studies of psychosocial mechanisms being particularly sparse.

### **What Are the Plans for Validation of Animal Models?**

In most of the disciplines for which a need for animal research was cited in the *Strategy* report, NASA is making significant use of animal models. However, their use in sensorimotor integration studies is thus far limited to only a few of the recommended research topics. One widely utilized animal model is hindlimb unloading in rodents, which is being used to study muscle atrophy, bone loss, and immunological changes.

The extent to which the various animal models are being tested to confirm that they duplicate certain physiological changes seen in space-bound humans was more difficult for the committee to determine. However, it is known that attempts have been made, or are planned, to validate aspects of the models used in bone and immunology studies. It was noted that evaluation is needed of the models used in studies of cardiovascular adaptation and endocrine changes.

### **What Are the Plans for the Development and Validation of Physiological and Psychological Countermeasures?**

Although NASA has countermeasures in place for a number of the adverse effects of spaceflight on humans, many have not been rigorously tested for efficacy and side effects. However, the development of future countermeasures is the primary focus of NSBRI research, and JSC is developing an administrative mechanism for soliciting and testing countermeasures. Issues related to implementing this process are discussed under programmatic issues below.

Most of NASA's discipline programs include some level of research activity directed at adverse effects, such as bone and muscle loss, for which no effective countermeasure exists. Studies include investigation of the respective effects of pharmacologic intervention, nutrition, and centrifugation on bone loss, renal stone formation, and sensorimotor impairment. However, there is considerable variation in the organization and scope of these activities. Although studies on respiratory tract infections appear likely to meet countermeasure goals, planning appears to be very limited for developing and testing countermeasures for orthostatic intolerance, psychosocial deficits, and radiation effects.

### **What Are the Plans to Perform Epidemiology and Monitoring?**

Plans exist to monitor indicators for a number of physiological changes in International Space Station (ISS) astronauts. These include measurements of bone density change, radiation exposure, orthostatic intolerance, and cardiac atrophy after missions longer than 30 days. Muscle atrophy will be monitored as part of a program of countermeasure testing, and the capability for in-flight monitoring of psychological status is planned. There are, however, a number of factors that may limit the usefulness of the collected data. Much of the data is collected for medical operations purposes and will not be accessible to the scientific community, nor in many cases do there appear to be plans even within the clinical program to systematically analyze and interpret the data. In addition, it is not clear that in every discipline the techniques best suited to the measurement, such as the use of magnetic resonance imaging (MRI) to measure cardiac mass, will be used on a routine basis.

### **To What Extent Are Programs Supporting New, Advanced Technologies and Methodologies?**

Considerable attention is being paid to the development of new technologies and methodologies that can be used in basic research, monitoring of in-flight physiological changes, and countermeasures. This seems to be true across nearly all discipline programs and in all components of the program. It is a particular focus of work at NSBRI. Some of the more innovative approaches under development include a portable bone densitometer, virtual environments to study human perception and navigation, and advanced telemetric-based sensor systems.

## **PROGRAMMATIC ISSUES**

The 1998 *Strategy* report raised a number of concerns in the program and policy arena, including issues relating to strategic planning, conduct of space-based research, and utilization of the ISS; mechanisms for promoting integrated and interdisciplinary research; and collection of and access to human flight data. The committee looked at both the current program and what was known regarding future plans in order to evaluate the congruence with *Strategy* report recommendations. Additional

overarching issues having to do with countermeasure testing and validation, and with the role of the Office of Medical Operations in human research, came to the committee's attention during the course of the present study. Some of the most significant issues that remain to be addressed follow.

### **International Space Station: Utilization and Facilities**

The adequacy of the life sciences research facilities that will actually be in place on the ISS at its final build-out remains an issue of serious concern. Possible design changes, the mounting delays in utilization timetables, and the perceived potential for downgrading of research facilities and budgets have continued to erode the confidence of the user scientific community. Important questions also remain about the availability of Russian cosmonauts for long-term follow-up in the conduct of biomedical research, especially in the early phases of ISS utilization.

### **Countermeasure Testing and Validation**

The need for effective countermeasures against the deleterious effects of spaceflight on astronaut health and performance will become increasingly critical as longer-duration flights become the norm on the ISS and beyond. The development of effective, mechanism-based countermeasures requires three well-integrated phases: (1) basic research to identify and understand mechanisms of spaceflight effects; (2) testing and evaluation of proposed countermeasures to determine their efficacy; and (3) validation of promising countermeasures by well-designed clinical studies. Recently, NASA has begun to develop a standard procedure for testing and evaluating countermeasures, but this has not yet been implemented. It is essential that the process, once in place, be readily accessible to all investigators, extramural as well as intramural, and that criteria for acceptance into the testing program be clearly defined.

### **Operational and Research Use of Biomedical Data**

Access to in-flight biomedical data, as well as to longitudinal data collected during postflight longitudinal monitoring of astronaut health, is limited, and the partial and incomplete availability of human data to qualified investigators was highlighted as a major concern in the *Strategy* report and continues to be an issue. The committee urges that NASA explore ways in which these data and samples, collected in the past and future, can be made available to investigators. Additionally, steps are needed to ensure that future data collection includes measurements and sampling that have been optimized to give the most useful information on in-flight development of problems and postflight recovery of normal physiological function. The role played by the crew surgeon is especially critical to collection of these data, and rigorous training in clinical research and basic research is recommended as a requirement for the position.

## **POLICY ISSUES**

### **International Cooperation**

The era of ISS construction and utilization, with increased emphasis on international crews and operations, raises important issues with respect to acquisition and management of human data. Mechanisms are needed to ensure that protocols and facilities for pre- and postflight monitoring and testing are

consistent across national boundaries. There must be common criteria for evaluation and utilization of countermeasures and international cooperation in their development.

### **Integration of Research Activities**

NASA funding for biomedical research is increasingly distributed among a diverse set of organizations and programs. These include the program of NASA Research Announcements (NRAs), intramural investigators in NASA center science programs, the NSBRI, and the NASA Specialized Centers of Research and Training. NASA science benefits from the unique strengths of each of these program constituents, but careful planning is required to delineate the roles, responsibilities, and appropriate funding levels for each; to ensure effective collaborations; and to integrate research findings. In particular, NASA should maintain a healthy NRA program as the primary mode for support of space-related biomedical research because it remains the best method of accessing the entire investigator community and exploring novel ideas and approaches.

### **REFERENCE**

National Research Council (NRC), Space Studies Board. 1998. *A Strategy for Research in Space Biology and Medicine in the New Century*. Washington, D.C.: National Academy Press.

# Review of NASA's Biomedical Research Program

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## Preface

In 1998, the Committee on Space Biology and Medicine (CSBM) completed a comprehensive report, *A Strategy for Research in Space Biology and Medicine in the New Century* (National Academy Press, Washington, D.C., 1998), that reviewed the status of space life sciences research in all of the disciplines funded by the National Aeronautics and Space Administration's (NASA's) life sciences program and laid out a detailed strategy for research during the International Space Station era. In that report, numerous biomedical research questions related to astronaut health and safety were identified as critical to NASA's long-duration flight program. Shortly after the report's publication, NASA requested that CSBM assess the agency's entire current program in biomedical research, both intramural and extramural, in light of the recommendations of the *Strategy* report.

After a series of discussions with NASA's Life Sciences Division, the committee began reviewing NASA's entire biomedical research program in December 1998 in order to assess the degree to which the program seemed likely to meet research needs over the next 10 years. The research priorities given in the 1998 *Strategy* report were to be used as a point of departure when considering future needs and priorities. Specifically, the committee agreed to examine the relationship between intramural and extramural biomedical research activities sponsored by the agency and to review the content and program organization of both. The roles of the NASA Specialized Centers of Research and Training and the National Space Biomedical Research Institute, in the biomedical program, were also to be examined. The review was to cover all NASA biomedical research activities, including those currently conducted in conjunction with operational medical and aerospace medicine programs.

Some of the specific points the committee considered in developing its recommendations were the following:

- The balance of discipline areas emphasized in the current program;
- The degree to which studies of fundamental cellular and physiological mechanisms are addressed in each discipline program;
- The balance between ground and flight investigations;

- NASA plans for the development and validation of physiological and psychological countermeasures;
- Plans for epidemiology and monitoring;
- Plans for validation of animal models; and
- The extent to which programs are supporting new, advanced technologies and methodologies.

The committee made use of a variety of sources in gathering information for this study. Documents available to the committee included FY 1998 and FY 1999 life sciences budget information, the 1998 and 1999 Life Sciences Task Book, the first annual report of the National Space Biomedical Research Institute (NSBRI) and 1998 and 1999 program budget information, the Countermeasure Evaluation and Validation Project Plan, the International Space Station Medical Operations Requirements Document and relevant sections of the Astronaut Medical Evaluation Requirements Document, and NASA Research Announcements for 1998 and 1999. In addition, the *Proceedings of the First Biennial Biomedical Investigators' Workshop*, held in January 1999, provided valuable current information. In addition to receiving briefings from NASA and NSBRI spokespersons, the committee as a whole held one meeting at Johnson Space Center, and a subgroup visited Ames Research Center to learn about the activities at that site relevant to biomedical research. These visits provided a vast amount of useful information, and the committee wishes to express its considerable appreciation of the hard work that went into the centers' preparation for the visits and the thoroughness and candor of the briefings and discussions.

## Acknowledgment of Reviewers

This report has been reviewed by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council's (NRC's) Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the authors and the NRC in making the published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The contents of the review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. The committee wishes to thank the following individuals for their participation in the review of this report:

James Bagian, Environmental Protection Agency,  
Norman Bell, Medical University of South Carolina,  
Robert A. Greenes, Harvard Medical School,  
Robert Langer, Massachusetts Institute of Technology,  
Robert Nerem, Georgia Institute of Technology,  
Gary Paige, University of Rochester, and  
Edward Schultz, University of Wisconsin Medical School.

Although the individuals listed above have provided many constructive comments and suggestions, responsibility for the final content of this report rests solely with the authoring committee and the NRC.



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