



November 24, 2009

Dear Mr. President and Members of Congress:

On behalf of Harvard Medical School, I want to extend my heartfelt appreciation to you and the American taxpayers for the unprecedented boost in support for biomedical and health care research and training included in the American Recovery and Reinvestment Act (ARRA).

Through a critical infusion of funding to agencies such as the National Institutes of Health (NIH) and the National Science Foundation, the ARRA awards are helping to advance a wave of scientific inquiry that will foster new understanding and spur future innovation. Support of highly-rated scientific ideas at HMS and elsewhere is sustaining jobs in laboratories where some of the world's most vital biomedical research is being conducted. In the future, this investment will help fuel the country's economic engine as resulting discoveries translate into public policy and developments that will enable the delivery of therapies that can directly improve health.

While you invested billions in renovation of our country's physical infrastructure, it was visionary to invest as well in scientific innovation, so that we simultaneously create jobs today and lay the groundwork for the future developments that will be carried on the new roads, bridges, networks and grids.

Coming after years of flat funding and inflation erosion of research support, the Recovery Act has rescued a backlog of high-quality proposals put forth by established researchers and young scientists who are struggling to move forward in exciting directions.

As of mid-November, Harvard Medical School-based researchers have received 96 awards totaling \$76.7 million over two years. The awards include five NIH Grand Opportunities, or "GO," grants totaling more than \$8 million to launch bold, creative studies whose success is far from guaranteed but which have the potential to dramatically transform key scientific fields.

At least 10 other research teams at Harvard Medical School received about \$21 million over two years in NIH Challenge Grants to jumpstart ambitious, multidisciplinary projects anticipated to have a high impact in biomedicine and public health. At Harvard, the creative excitement about these grants generated more than 100 proposals, which is further evidence of the potential progress funding can make possible.

Other GO and Challenge grants as well as supplemental funding to affiliates and other institutions have enabled additional important collaborations among HMS faculty and their colleagues at many other institutions who are working together to advance biomedical research and human health.

The largest award to HMS sponsors a collaboration between Harvard Catalyst (the Harvard Clinical and Translational Science Center) and eight other research institutions across the country, from Alaska to Mississippi, Puerto Rico, Hawaii and New Hampshire. The project, known as the eagle-i Consortium, received \$15 million to help connect biomedical scientists with hard-to-find but highly valuable research resources. The project eventually aims to include dozens of other sites and to accelerate the pace of research and avoid unnecessary duplication of efforts.

ARRA funding supports the most important things we do at Harvard Medical School: generating medical discoveries, translating them into improved public health, and training the next generation of scientists and clinicians.

At Harvard Medical School, many of the projects funded by the Recovery Act fall into several key areas where today's science is best poised to become tomorrow's medicine: human genetics, neuroscience, systems biology, engineering and therapeutics, all arising from the revolution in molecular and cell biology. Here is a small sample of the impressive array of science funded by the Recovery Act.

Education and training

- At least five proposals awarded to HMS incorporate either high school students, college students, or local secondary school science, technology, engineering and mathematics teachers in the studies. This will provide invaluable experience and training for aspiring researchers as well as for those who will inspire the next generation of students in the high school classroom to pursue a career in science.
- Another award provided scholarship money to seven medical school students who came from disadvantaged backgrounds. With starting salaries in medicine lagging behind increases in educational debt, such support extends important financial aid to remarkable students who overcame substantial obstacles to pursue their dreams of helping society through medicine. We have high expectations for these young trainees and their future impact on the world.

Scientific and medical innovation

- Several ARRA projects in basic cell and molecular biology provide fundamental insights into normal human biology and disease processes, including cancer, immune responses, and infectious and metabolic diseases.
- The Immunology Genome Project, a consortium of researchers coordinated by several HMS investigators, aims to draw a roadmap of the genetic pathways that define the way the 200 types of immune cells in a mouse function through all developmental stages and under various conditions of immune challenge. The information gained from this work will inform our understanding of immune response and point to new solutions for infectious diseases and disease caused by chronic inflammation.
- In parallel, a human roadmap of immunological gene expression is underway in another ARRA-supported project. The collaborative effort based at HMS aims to explore a broad range of gene expression in human blood cells and how that differs in groups of different ancestry.
- In another lab, researchers are teasing out the fine components of potential drug targets to combat the human herpes viruses.
- In the first ARRA award at HMS this spring, a young investigator is working to develop a much-needed mouse model of hepatitis C. Efforts to create a cure or a protective vaccine have been hindered in the absence of research models that permit the study of the virus in the liver, its natural setting. The funding of this project could accelerate our ability to create new approaches to tackle this debilitating disease.
- In neurobiology, the Recovery Act is supporting the development of new tools likely to result in transformative technologies in the field. The funds will expand one "plug-and-play" molecular delivery system that allows neuroscientists to tease out functions served by virtually any neuron subtype. Another grant will allow researchers to improve a new prototype microscope that provides unprecedented resolution of brain activity, including the power to monitor synaptic terminals, conformational changes in DNA and molecular markers in brain tissues.
- Another ARRA project uses electrical stimulation to understand how neuronal genes respond during development to control the normal remodeling of circuits necessary for learning and adapting to situations. Mutations in components of the transcriptional program in the study are known to cause profound defects in human cognitive function.

Improve health

- In grants directly to HMS and through collaborations based at affiliated hospitals and elsewhere, HMS faculty have obtained the largest fraction of ARRA funding to conduct exome and whole genome sequencing in thousands of individuals from phenotyped cohorts, such as the Framingham Heart Study. The widespread effort is expected to translate the rapidly expanding knowledge from the human genome into clinical tools for predicting, preventing and treating disease.
- Several projects aim to identify better cancer drugs. One collaborative project addresses a fundamental problem in translational drug development and aims to provide an information resource containing mechanistic signatures of drug response to identify those patients most likely to benefit from specific therapies.
- Another cancer project aims to develop better models for study of cancer stem cells, as well as screen for chemotherapeutics to combat this small subset of cancer cells believed to initiate tumors, resist conventional chemotherapies and promote recurrence.
- One team aims to identify and further evaluate vulnerable and effective targets in a molecular pathway in breast cancer.
- Another lab is developing research tools to generate new insights into genes, molecules and mechanisms underlying the cancers caused by infectious agents, starting with an oncogenic family of Human Papillomavirus.
- Tackling a major threat to public health, several teams are addressing drug-resistant infectious diseases from a variety of directions, including development of new antibiotics, vaccines and other interventions. One lab is exploring a new way of regulating the immune response in studies that may provide a new therapeutic approach for chronic viral infections. Another group is examining drug interactions to reduce and perhaps reverse the spread of drug resistance while providing an effective treatment paradigm.

Economic engine

- The Recovery Act funds the essential basic research necessary to understand relevant targets for drug development. Positive outcomes could yield more jobs in the pharmaceutical industry, where such findings are transformed into products to advance human health.
- The strategic and well-coordinated investment in tools and technologies in ARRA-funded grants at HMS has the potential to boost productivity in entire fields of science and form the foundation for other businesses to develop products and jobs that support the research enterprise, advance entire fields of study and enhance the clinical arena through diagnostics and patient care.
- As of the first quarterly reporting required by the Recovery Act's unprecedented effort for accountability and transparency (posted online at <http://recovery.gov>), Harvard Medical School had created or retained the equivalent of nearly 41 jobs, as of mid-September. As people fill those positions and receive their first paychecks, that number will increase to reflect the full impact of all the awards.

At Harvard Medical School, we are thrilled to participate in this public/private research partnership, and we are grateful to share in some of the extra \$21.5 billion injected into federal research funding, including \$10.4 billion in extramural funding for the National Institutes of Health.

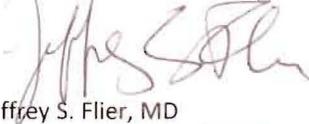
Our participation, through the submission of grant applications into a nationally competitive peer review program, assures that the national investment will result in the highest quality science possible in this exciting period of discovery.

The infusion of federal support was critically needed at a time when the national research enterprise was significantly stressed. We are convinced the science put in motion by these funds at Harvard will add to the very

substantial economic impact we have upon the local economy. Most importantly, the work here and around the country will result in meaningful therapeutic applications for patients.

We are also keenly aware that by the time the ARRA funding is exhausted, the new capacity it has helped build will need to be sustained by the normal budget and appropriations process. The Administration's request for and Congress' support of research at the major federal agencies must lead to a trajectory of regular, predictable and sustainable increases—at a level above inflation—so as to include room for new and innovative work.

Sincerely,

A handwritten signature in black ink, appearing to read "Jeffrey S. Flier". The signature is fluid and cursive, with the first name "Jeffrey" being the most prominent.

Jeffrey S. Flier, MD
Dean, Faculty of Medicine
Harvard Medical School