The background of the entire page is a topographic map with white contour lines on a solid orange-red background. The lines are irregular and wavy, representing elevation changes across a landscape.

Burroughs Wellcome Fund Programs

PAST, PRESENT AND FUTURE

The potential of biomedical research to advance human well-being has never been greater.

More than treating disease, disease prevention strategies and efforts to enhance human accomplishment and longevity have gained greater centrality. The National Institutes of Health in the United States has promoted this culture beginning in the Vietnam war era, and they remain the primary support system for most academically oriented institutions. In this manuscript, we will highlight how a non-profit, non-governmental organization, the Burroughs Wellcome Fund, has thought about optimizing its impact given the resources it has available to invest, in the past, and what efforts are currently underway to continue this disproportionately high impact given the scale of the funding it controls in comparison to other funders, by prioritizing its targets.

Biomedical Research, Broadly

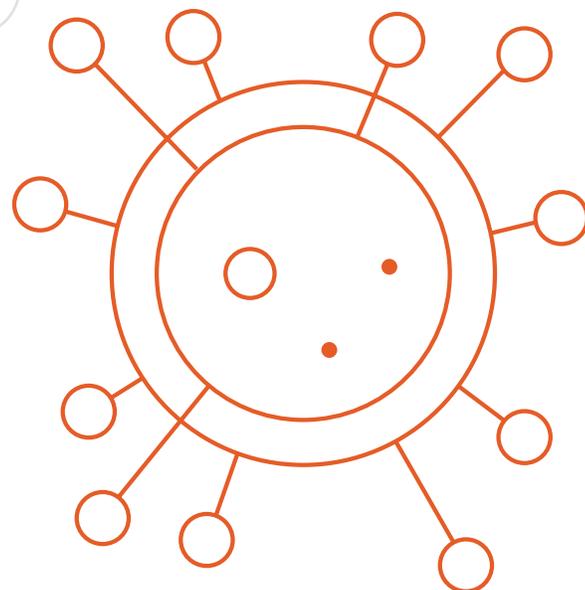
Since becoming an independent foundation in the mid-1990s, the Burroughs Wellcome Fund has distinguished itself as a funder by focusing on the human capital of the research enterprise, in particular, the individual researcher. Such a focus began with the Career Awards in the Biomedical Sciences (1995-2006), which served as a bridging award for postdocs focused on basic biomedical questions and provided risk funding into the early years of independent research. Aided by a distinguished Board of Directors and Advisory Committee, the prestige associated acquiring these awards inspired many early stage investigators to apply. The success of this approach contributed to the NIH instituting the K99/R00

awards which addressed a similar demographic. As a consequence, the Fund reconfigured the CABS award into the Career Awards for Medical Scientists (CAMS) award to further enhance its ongoing impact.

The Career Award for Medical Scientists (CAMS) focused on the transition of physician-scientists from postdocs/fellows into an independent research position. This program hoped to address the shortage of physicians entering the research workforce. To date, the program has funded 148 physician-scientists to go on to become independent researchers.

In spite of the successes of the CAMS program, it became apparent to the Board (and a large number of people)

that we were not training enough physician-scientists, especially MD's-only. In 2017 the Fund's Board of Directors approved a \$25 million initiative aimed at encouraging medical schools to offer research-training programs to MD-only students. Ten programs were funded with the goal of keeping this group closely networked to share best practices in the hopes of inspiring other medical schools to offer similar programs. This mechanism tests divergent strategies to achieve the enhancement of the MD physician-scientist pool given constraints in clinical training requirement, physician debt, and protected research time during training.



The Investigators in the Pathogenesis of Infectious Disease program has funded 177 assistant professors with **\$500,000 grants** throughout the years.

Infectious Disease

Throughout the years of the Fund's association with the pharmaceutical company, the organization offered scholar programs in various fields of infectious disease. As an independent foundation in the mid-90s, the Fund decided to switch gears and focus on the infectious disease researcher at the assistant professor level. Funding at this level provides flexible risk capital for the investigator to explore novel approaches that have come to light during their independent research career. The program, Investigators in the Pathogenesis of Infectious Disease (PATH), is especially looking for the connection between the host and pathogen. Throughout the years the Fund has funded 177 assistant professors with \$500,000 grants.

The infectious disease program has also tried to build networks throughout the field, exploring areas to facilitate collaborations. Nearly two decades ago, the Fund provided support around the Eukaryotic Pathogen Genomics Database (EuPathDB.org), which is a collection of resources for analyzing large-scale datasets associated with microbial pathogens.

Pathogenesis has also been actively involved in a variety of meetings and funding for other efforts in areas such as mycology and malaria. The Fund provided significant funding for sequencing the *Plasmodium falciparum* genome, which was published in *Nature* in 2002.

Since 1999, BWF has supported a program of the American Society of Tropical Medicine and Hygiene that

sends junior M.D.'s to conduct research in areas of the world where tropical diseases are prevalent. As of 2019, 53 fellows have been funded.

Scientific Interfaces

By the mid-1990's, the Burroughs Wellcome Fund identified the interface of biology and the physical and quantitative sciences as an area in need of funding. It quickly became apparent that there was little formal training for individuals with a quantitative or physical science background interested in tackling biomedical questions. So rather than follow its pattern of funding individual investigators directly, the Fund created a program (Institutional Awards at the Scientific Interface - IASI) that funded 10 institutions from 1996-2000, which supported 367 trainees.

The Career Awards at the Scientific Interface program began in 2001, and a total of 167 awards have been granted for an investment of **\$81.4 million**.

The success of the IASI program led to the creation of the Career Awards at the Scientific Interface (CASI) program that was modeled closely on BWF's Career Awards in the Biomedical Sciences (CABS) program. CASI is distinguished by the requirement that applicants have doctoral level training or evidence of significant expertise in a computational, theoretical, or physical science discipline outside of biology. The CASI program began in 2001, and a total of 167 awards have been granted for an investment of \$81.4 million.

Importantly, this institutional program and CASI have been one of the few private sources of funding for foreign nationals—a vital source of biomedical intellectual capital in North America. Following the success of funding foreign nationals in this program, the other career awards programs at the Fund opened their application process to such individuals.

Reproductive Sciences

A core goal of the Fund is to provide funding for important, yet undervalued and underfunded areas. Reproductive sciences are seen as one of these areas. BWF has provided longstanding support for the Frontiers in Reproduction course at the Marine Biological Laboratories

(MBL) in Woods Hole, MA and the Reproductive Scientist Development (RSDP) award program.

Recognizing a particular need for more research into understanding the mechanisms of preterm birth, the Fund established its Preterm Birth Initiative. The program currently funds six awards of \$500,000. Since its full inception in 2011 (in 2009 10 planning grants were made) 31 grants have been made for an investment of more than \$15 million dollars. Meeting collaborations with the March of Dimes have also been a core part of support for Preterm Birth, although they have recently evolved to smaller, interactive across disciplines meetings supported exclusively by the BWF. Adverse pregnancy outcomes of other types, such as growth restriction, stillbirth, and preeclampsia will be considered as well.

Regulatory Sciences

The Fund identified regulatory science as an underfunded field in 2012. The program created focuses on support for academic researchers developing new methodologies or innovative approaches in regulatory science that will ultimately inform the regulatory decisions the FDA and others make. This field too relies on

the interdisciplinary talents of researchers.

Following the approach for preterm birth, the Innovation in Regulatory Science Awards funds five research proposals at \$500,000. Since the first funding cycle in 2013, the Fund has provided 32 grants for an approximately \$16 million investment. This program is distinguished by a requirement that the applicant show clearly how the research is intended to impact regulations.

Career Guidance

Throughout its history the Fund has provided guidance to biomedical scientists regarding career choices. In particular we have tried to help young scientists as they begin their careers. This has ranged from sponsorship of numerous meetings (e.g. GREAT, ABRACAMS, SACNES) as well as early support for postdoctoral associations in the US and Canada. In recent years we have run a more formal program entitled Career Guidance for Trainees (CGT). Our CGT awardees, who receive grants of up to \$50,000, have been recognized for their novel contributions to providing information and guidance to young scientists. We also provided early support for the AAAS myIDP program.

Since its inception in 1996, the Student STEM Enrichment Program has reached all 100 of North Carolina's counties and granted almost **\$40 million**.

Education

The Fund has focused its science and math education efforts in North Carolina and in grades K-12. The longest running of the programs is SSEP (Student STEM Enrichment Program). This program emphasizes informal science education outside of the classroom. Since its inception in 1996 the program has reached all 100 of North Carolina's counties and granted almost \$40 million.

Other science education programs are CASMT – Career Awards for Science and Math Teachers -which runs on alternate years and funds five outstanding teachers at \$175,000/5 years. It is based on the same idea as a Career Excellence Award (e.g. MERIT) the NIH provides – choose the best and most promising investigators and give them a substantial grant for multiple years. It remains, to the best of our knowledge, the largest financial award for K-12 teachers in the US.

PRISM – Promoting Innovations in Science and Mathematics Program, is another of our alternate year programs. It is focused on providing small grants to teachers to get equipment and supplies and, if needed, some professional development to use those materials. The application process is simple, and it

has as a goal to encourage a large number of teachers to apply and be funded to provide the confidence and expertise that will enable them to submit more and larger grants.

Other programs in education include our support of implementation of Singapore Math in several schools. For the schools that implemented and continued the curriculum the results have been positive. There has been some wider adoption in schools outside of those funded by the BWF, but there has not been the hoped-for broad implementation. The assessment of what works and doesn't is ongoing, though, and will be valuable for others who may choose to try this approach that has been so successful in Singapore.

Science, Math, and Technology Education Center

The Science, Math, and Technology Education Center (SMT) under the leadership of Dr. Sam Houston is an independent organization, but because the BWF provides most of its funding, it is often viewed as an extension of the Fund. The Center is seen as a neutral broker for education in the state and individuals and groups from a wide variety of com-

munity to political entities come to the Center to help run programs or collaborate in seeking grant funding. The most recent program that has involved the direct support of the Fund is an effort to get hands-on science kits to the largest number of students possible.

SMT recognized that a major barrier to kit implementation is the lack of funds to refurbish kits, thus many were abandoned after their first use. By establishing two refurbishment centers with the support and collaboration of the various school districts involved, the barrier to refurbishment has been removed and now, in the areas served, all the students have a chance to do hands-on science using well-vetted kits that are constantly being renewed. The SMT Center has led this effort and has worked hard to make the process sustainable, requiring that school districts help provide part of the funding and establishing an escrow account for future funding.

Diversity in Science

The Fund has long recognized that the scientific community does not reflect the diversity of the US population. To try to encourage more underrepresented minorities and women to participate in science, the



The Fund has long recognized that the scientific community does not reflect the diversity of the US population. The Post-doctoral Enrichment Program is a three-year grant, with **16 awards** made per year, and is open only to members of underrepresented groups.

Fund has encouraged applications by participation in the many minority meetings, as well as in meetings that focus on women's participation. With regards to women, the Fund does make awards in proportion to the women applying (about 35-40%) which is a number quite close to the awarding of NIH RO1's and perhaps even slightly higher.

Although awards are made to underrepresented minorities in proportion to the application rates, these numbers are extremely small. To increase this number, the Fund has worked to increase the number of underrepresented minorities in the applicant pool. The post-doctoral enrichment program (PDEP) is a direct outgrowth of this effort. This three-year grant, with 16 awards made per year, is open only to members of underrepresented groups. We have averaged around 80 applications per year and helped create a strong cadre of well-qualified individuals who are already moving

on to academic positions as well as to other BWF awards.

We are working to replicate this success with underrepresented minority graduate students in North Carolina and have now run a graduate enrichment program (GDEP) for two cycles. We have been pleased to get an increasing number of students applying and several of them are already qualified to be applicants for PDEP.

Other Programs

Starting in 2008 the Fund supported 10 awards of \$2.5 million each to institutions for a program unifying population and laboratory-based sciences (PUP). It was an effort to encourage population scientists to tackle biomedical questions (and vice versa). The program has had some successes, and some of the awardees are still spending out their grants. A review of the program will

be undertaken in the next several years to establish if it had a positive impact and encouraged long-term efforts in this area.

The Fund has long been interested in trying to increase the quantitative in the biological sciences. We have had numerous Board meetings devoted to how we might encourage more individuals to gain more training in this area and bring the quantitative skills to tackle "big data". The Fund decided to create such an institutional program in the most recent terrain mapping exercise, but the physician-scientist initiative was viewed as a more pressing area where the Fund could make a difference. A small program Quantitative Institutional Program (QUIP) was created and 3 schools were funded to develop curriculum that would better prepare students for what will certainly be a need for a more quantitative approach to biology in the future.



The Next Five Years at BWF

As we enter 2020, BWF is initiating its regular “terrain mapping exercise” to both evaluate existing programs for continuing research and education investment, as well as to imagine new areas emerging for substantial impact. Data and ideas gathered from the program officers and associates, advisory committees and the Board of Directors will be assembled and considered, and ultimately approved by the Board of Directors. Questions regarding current programs to be considered for ongoing resource allocation include:

- 1. Did the program attract the interest and applications desired?**
- 2. Was the quality of the applications at the high level expected by BWF?**

3. What impact did the award have on the recipient? This metric can often be difficult to assess, especially as a differentiator from those that did not receive the award. Career advancement, high impact publications, health impact, diversity development, success in acquisition of ongoing research support are all components of the evaluation.

4. Is there a strong sense the program should continue to exist? This view could be shaped by not achieving the above points, but also by whether or not the problem has been “solved” or more commonly, such as with the CABS awards, other funders are now significantly represented in this space.

One New Adventure: Climate Change and Human Health

BWF in collaboration with the National Academies of Sciences plans to embark upon scoping activities around the many consequences of climate change for human well-being. This effort will be initiated with a two-day meeting of experts to explore and articulate emerging issues that could provide critical new approaches to mitigating this critical concern. The areas of discussion will include:

- 1. Disease transmission in changing climates:** How is vector function, geographic range, and frequency of exposure being modified?
- 2. Extreme weather conditions and a consequence of climate change:**



“ As we enter 2020, BWF is initiating its regular “terrain mapping exercise” to both evaluate existing programs for continuing research and education investment, as well as to imagine new areas emerging for substantial impact. ”

weather-related disasters, hurricanes, extreme heat or cold, flooding, air quality will all have consequences acutely and chronically for human health.

3. Social dynamics and climate change:

How will climate change consequences differentially impact those in poverty, different geographies, and mentally or physically disadvantaged groups?

4. Climate change effect on nutrition:

crop quality, nutrient content, crop production.

As an initial pilot investment, the Fund will contribute \$200,000 to encourage and promote activities building upon this meeting at the National Academies. We anticipate

this will allow up to eight scoping projects that the Academies will develop collaboratively with research communities. These scoping projects will serve as a platform for BWF, as well as the Academies, to consider next steps in the vast climate change area as to which themes or approaches seem most relevant and aligned with BWF priorities.

We, at BWF, provide this framework to not only to provide our history and perspective, but also to utilize to seek your ideas as a scientific community for our incorporation in terrain mapping and program implementation in our next phase. Please send your comments to: news@bwfund.org

John Burris, PhD

President, BWF 2008 - 2019

Louis Muglia, MD, PhD

President, BWF 2020 -