THE AMERICAN SOCIETY FOR CELL BIOLOGY

Request for Information: Building A 21st Century Bioeconomy
Reply by The American Society for Cell Biology

1) Identify one or more grand challenges for the bioeconomy in areas such as health, energy, the environment, and agriculture, and suggest concrete steps that would need to be taken by the Federal government, companies, non-profit organizations, foundations, and other stakeholders to achieve this goal.

One of the biggest challenges to the health sciences will be maintaining a long-term vision of impact of the biological research on human health. Leveraging the tremendous advances in biology has already led to remarkable progress in diagnosis. However, the translation from a diagnostic phase to a successful treatment will be slower. It is important that the government stay the course to realize the gains of biomedical research.

With the costs of health care skyrocketing, a challenge to the biomedical research community is how we can make an impact on stabilizing these costs and avoiding the 'valley of death' that comes between progress in research and diagnosis, and subsequent translation of these findings to successful treatments.

One of the greatest challenges facing the American bioeconomy and general economy is research into the diseases of the brain. Three examples are: 1) The health care and emotional impact of diseases such as Alzheimer's disease in older people when they would otherwise be functional; 2) The impact of traumatic brain injury on soldiers returning from war and the increased susceptibility of these soldiers to Alzheimer's disease because of traumatic brain injury; 3) The psychiatric consequences of war oneven physically healthy soldiers. Collectively these problems have trillions of dollars of healthcare and economic impact while the Federal government barely invests $1-2 billion a year to fight them. We are still farther than we want to be from solutions. But an increased effort to understand how all cells function, to understand how basic cellular functions are used in neurons, and to understand how these functions fail in all of these disease conditions (and many others) is essential.

2) Constrained Federal budgets require a focus on high-impact research and innovation opportunities. With this in mind, what should be the Federal funding priorities in research, technologies, and infrastructure to provide the foundation for the bioeconomy?

The foundation for the bioeconomy will depend upon sustainable, dependable growth

in biomedical research. The last decade has seen boom and bust funding cycles that have led to irresponsible growth in infrastructure followed by underfunding of the science and technological technologies, ultimately undermining the investment in infrastructure.

The federal government should immediately double its portfolio of basic research ranging from basic cell biology to neural network formation and function in brain biology and disease. It should then commit to inflation +2% growth in the coming years for funding of this vital research until the problems are solved.

3) What are the critical technical challenges that prevent high throughput approaches from accelerating bioeconomy-related research? What specific research priorities could address those challenges? Are there particular goals that the research community and industry could rally behind (e.g., NIH $1,000 genome initiative1)?

High throughput technology generates massive amounts of data. However, the usefulness of this data is extremely dependent upon validation of its accuracy and validity. We are overrun with data at the moment, and it's been very difficult to sort out what it all means. Better statistical and combinatorial approaches are necessary to help find meaning and identify the rare mutations etc within all the noise of the datasets.

Reducing sequencing costs to the amounts similar to the cost to sequence the human genome will have tremendous impact directly on human research. This reduction in cost per base pair would also revolutionize the utility of model systems from which we derive most of our molecular knowledge of human. The ability to change as well as to assess DNA sequence would also revolutionize biology. With this in mind, the development of technology to allow high throughput DNA assembly of Kbs of DNA (currently 100 bps) should be emphasized.

Federal priorities should also focus on encouraging teams of interdisciplinary investigators to work together on important problems. While it is imperative to maintain investigator initiated projects, incentivizing collaborative interdisciplinary research will yield the greatest impact in the coming years scientifically and economically.

4) The speed of DNA sequencing has outstripped advances in the ability to extract information from genomes given the large number of genes of unknown function in genomes; as many as 70% of genes in a genome have poorly or unknown functions. All areas of scientific inquiry that utilize genome information could benefit from advances in this area. What new multidisciplinary funding efforts could revolutionize predictions of protein function for genes?

Investigator initiated research is probably the most important because each problem will actually be different and requires focus and insight to solve. Critical technical

challenges are quality control and curation of large high throughput data sets.

Almost all our knowledge of human gene function has come from basic research analyzing orthologs of human genes in model systems. These model systems have tremendous experimental advantages both technically and ethically. Indeed the function of the 70% will undoubtedly only be discovered through model systems. Government should spend a significant portion of its budget on basic research of human orthologs in existing model systems and in the development of new model systems.

5) What are the barriers preventing biological research discoveries from moving from the lab to commercial markets? What specific steps can Federal agencies take to address these shortcomings? Please specify whether these changes apply to academic labs, government labs, or both.

More interactions and successful collaborations are necessary to help bridge the divide between the lab and the marketplace. There is a difference in the mindsets of the academic world verses companies, as the goals are often very different. Companies won't put efforts into drug discovery until the knowledge of potential drug targets is already quite far along and developed. In addition, the academic community often thinks its job is done once a potential target is identified.

An enormous barrier is a very complicated landscape of material exchange. Material Transfer Agreements (MTAs) complicate every academic and scientific transaction, even those essential to reproduce results to find out if they are true. One recommendation would be to put statutory limits in all MTAs so that they do not outlive patents. The other issue is how to deal with risk. On the one hand, the American people want new therapies as rapidly as possible. On the other hand, they want zero risk. Legal protection for good faith and honest problems with marketed therapies would be a good first step. Getting consumers to realize that there is no substitute for their own education and ensuring availability of accurate information for all medical consumers is a good second step. Finally, all information in an Investigational New Drug (IND) Application and subsequent filings with the Food and Drug Administration (FDA) prior to and post-registration should be publicly available so that any patient can consult their physician or other experts to evaluate for themselves what the risk-benefit trade-offs might be.

9) The majority of doctorate recipients will accept jobs outside of academia. What modifications should be made to professional training programs to better prepare scientists and engineers for private-sector bioeconomy jobs?

Graduate programs need to be more open about all the different career opportunities that exist for PhDs in the biomedical community. A PhD in science is great training for so many careers (from patent law, to investment banking, to writing and publishing, to academic research administration, to big pharma, and small biotech startup, etc). Often, it is only when students are in their last year or two that they start to think about employment possibilities outside of academia.

For that reason, first hand exposure to, and experience working in, the private sector will be an essential addition to doctoral training. Priorities differ considerably between academic research labs and the private sector, so it is important for a PhD student to demonstrate that he/she has a solid understanding of what the private sector values and how projects are designed around achieving their goals. Funding for internships will be extremely important for supporting this.

In addition, more informational seminars and career panels should take place through the graduate student's education, and could even be incorporated into the yearly graduate program retreats. Perhaps even non-academic PhDs could be placed on graduate students admission committees, or even thesis committees as external advisors.

11) What role should the private sector play in training future bioeconomy scientists and engineers?

The private sector should provide paid internships. These are currently much more common in engineering than in the basic sciences, but needs to expand to include all fields of biomedicine.

12) What role might government, industry, and academia play in encouraging successful entrepreneurship by faculty, graduate students, and postdocs?

For graduate students, finding a suitable academic postdoc is often much easier than finding an industrial postdoc, because it is very difficult for many PhDstudents to make contacts in industry. While on-campus visits by academic researchers are commonplace (departmental seminars, workshops, sabbatical leave, etc.), access to working professionals is often limited to large national meetings. Thus, recruiting PhDstudents to complete industry internships will be a major improvement.

17) What are the highest impact opportunities for pre-competitive collaboration in the life sciences, and what role should the government play in developing them? What can be learned from existing models for pre-competitive collaboration both inside and outside the life-sciences sector? What are the barriers to such collaborations and how might they be removed or overcome?

Public-private partnerships that bring multiple companies and federal investment together to solve major pre-competitive problems such as better toxicology predictions, stem cell models of disease, and shared technical resources could limit duplication and maximize synergy.