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"GENOMICS AND THE BIOECONOMY"

Symposium Report and Policy Considerations

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"GENOMICS AND THE BIOECONOMY"

Montpellier, France – 17-18 May 2010

Symposium Report and Policy Considerations

Introduction

1. On 17 May 2010, the Organisation for Economic Co-operation and Development (OECD), the Human Genome Organisation (HUGO), the McLaughlin-Rotman Centre for Global Health of the University of Toronto and the Mexican Health Foundation (FUNSALUD) jointly organised a one-day symposium in Montpellier, France entitled "Genomics and the Bioeconomy." Financial support from the Government of Japan also helped to facilitate the Symposium, which took place in conjunction with HUGO's annual meeting.

2. The Symposium was a follow-on activity to "The Bioeconomy to 2030," a report published by the OECD in 2009. This report makes the case for the numerous ways in which the scientific tools of modern biology, especially tools linked to genetics and genomics, will impact future global economic growth and the political imperative to tackle societal challenges in human health and the environment for the coming generation.

3. The Symposium provided a forum for expert presenters representing a wide range of disciplines in the life sciences. The agenda included discussions relevant to human health, animal breeding, food security, industrial and environmental biotechnology and climate change. The audience was equally accomplished and diverse. Together, the presenters and audience members undertook a highly interactive conversation about both the opportunities and the challenges inherent in achieving the potential of the bioeconomy.

4. On 18 May 2010, many of the Symposium attendees re-convened to discuss how best to prioritize the issues raised during the previous day and to determine what possible policy recommendations could be made by the group. They also considered work areas that might involve efforts by HUGO in conjunction with the OECD and other potential partners.

5. This paper discuses many of the points raised during the Symposium as well as the ensuing discussion of areas in which further policy analysis may be required.

Key themes

6. Throughout the course of the Symposium, five key themes were recurrent in presentations and discussions:

i. An appreciation for the depth and breadth of modern genomics and the historic achievement in human health in the ten years since the first draft sequence of the human genome.

ii. The importance to the next phase of the bioeconomy of emerging technologies (like synthetic biology, nanotechnology, genomic sequencing, *etc.*) and converging technologies (*e.g.* the marriage of the concepts of biology with engineering) and the numerous issues that surround this trend.

iii. The importance of the financial underpinnings of the bioeconomy, both in the form of continued funding for basic life science research from governments, and a robust private sector in venture capital, which is essential to seed and grow the bioeconomy at all phases in the creation of new products and services.

iv. The relevance of the tools of modern biology to meeting global challenges in the environment, including climate change, food security, resource depletion and achieving sustainable green growth in a post-recession world.

v. The global nature of the bioeconomy and the particularly important role to be played by developing countries, not just as a source for "problems" to be solved, but as a source of opportunities to be offered in terms of entrepreneurial institutions, people and approaches.

1. The Human Genome at 10: A decade of advances in human health

The science

7. In June 2000, President Bill Clinton and Prime Minister Tony Blair joined together via satellite link between Washington and London to unveil the first draft sequence of the three billion base pairs of the human genome. While it was a moment of profound scientific achievement, it was also cause for no small amount of hyperbole. Mr. Clinton himself said at the time, "One day, we will know cancer only as a constellation of stars," a prediction which, while poetic, has certainly not yet been achieved.

8. Nonetheless, there is ample evidence that the shift in our understanding of the human condition from a phenotypic to a molecular level is producing historic changes in the ways in which research is done and in which health care is delivered. Most research efforts in diseases such as cancer, diabetes, cardiovascular disease and other high mortality conditions are now rooted in the discovery of genetic and genomic information. True, the search for the genetic basis for many of these diseases is more arduous than had once been hoped. A decade ago, scientists sought "the gene for …" a given condition; now they search for "the genes for …" in recognition that a single gene is rarely the sole cause for a complex disease. Now the search is for *patterns* of genes and their interactions with one another and with their greater epigenomic environment.

9. Technology is the great enabler of this search. In many respects, the research tools are as impressive as the biological insights they provide. Tools such as microarrays borrow much from the semiconductor industry, and like their computer chip brethren, microarrays have been doubling their

information content while halving their costs every 12-18 months, if not sooner. This embodiment of Moore's Law has had a particularly strong impact in the area of genome wide association studies (GWAS) that scan across a large population to link a particular condition with its genetic root. The OECD "Bioeconomy to 2030" report shows an almost exponential increase in GWAS studies beginning in about 2005, when both the content of arrays had reached a critical mass and their price had dropped to make them affordable to more of the research community.

10. More powerful GWAS studies, powerful in the sense that the sample populations can be much larger and thus the genetics involved can be much more informative (as an example, consider the difference in resolution between a photograph made with a 3-megapixel digital camera and one made with a 12-megapixel camera) are resulting in dramatically faster research paradigms. Beyond advances in microarrays have come advances in so-called "next generation" genomic sequencing, the practical impact of which is that rather than working with a composite map of the human genome such as the one Messrs. Clinton and Blair introduced in 2000, scientists are now able to sequence an individual's genome for USD 10000, with a sequencing cost of as little as USD 100 per genome on the horizon. (By comparison, the Human Genome Project itself cost approximately USD 2.7 billion over a decade.)

11. Ed Liu, the president of HUGO and the chief executive officer of the Genome Institute of Singapore, cited his own career in working with the HER2 gene in breast cancer; in the course of that career, research that had once taken 9 years to complete can now be done in 1 month. He also spoke of the downstream aspects of this accelerated pace of research, and cited as an example the development of three new therapeutics for breast cancer in the last four years.

The impact on patient treatment

12. These advances go beyond the lab bench and are having a tangible impact at the patient bedside. The field of pharmacogenetics (PGx) is one of the first important outgrowths of the Human Genome Project. Pharmacogenetics focuses on how an individual's genetic profile correlates to the variable ways in which people respond to pharmaceuticals. At the Symposium, Y.T. Chen of Academia Sinica in Taiwan spoke of the advances in pharmacogenetics. PGx data is now part of more than 10% of the labels for drugs approved by the US Food and Drug Administration (FDA). He gave the example of work being done in Taiwan on Stevens – Johnson syndrome, a life threatening drug reaction which afflicts the Han Chinese population who take a certain therapeutic for epilepsy. Being able to identify those patients who have the genetic marker for this adverse reaction will both save lives and ultimately save money for health care systems as adverse drug reactions can be a very high cost medical problem to treat.

13. Dr. Chen also spoke about the use of PGx tools in developing a treatment for Pompe's disease. When approved by the FDA in 2006, this enzyme replacement therapy became the first such treatment for any genetic muscle disease.

The rise of personalised medicine

14. Pharmacogenetics has given rise to a new approach to health care known as personalized medicine, which is essentially the use of targeted therapeutics, often with companion diagnostic tests that determine if a drug is paired with the right patient in the right dosage based on that patient's genetic profile. Personalized medicine presents both a new scientific/clinical approach to healthcare as well as a new economic model for its delivery. By abandoning the traditional one-size-fits-all model for drug development, personalized medicine is a disruptive force to the traditional "blockbuster" model of drug development in the pharmaceutical industry. Success in the traditional model calls for a drug to be successful with a large share of a large market; the personalised medicine model goes in the opposite direction and defines success as a large share of what is, by definition, a much smaller market, *i.e.* one

more restricted to those who are, by dent of their genetic makeup, more likely to respond favourably to a given drug.

15. Howard McLeod of the University of North Carolina School of Pharmacy spoke about the significant potential of personalised approaches to medical care. Currently, a physician has many drugs from which to choose and no certain way to understand which ones will work best in an individual patient. Responses are variable and toxicity can be a significant problem. Drugs are typically prescribed on the basis of familiarity and cost, and the physician and patient engage in what amounts to an educated practice of trial and error to gauge the optimal dosage. Modern genomic approaches change this practice by basing drug decisions on each patient's genetic profile, including his/her drug metabolism, thereby allowing a physician to make a more accurate decision in determining which drug to prescribe and how much a patient should take.

16. While the scientific and clinical case for PGx/personalized medicine is advancing, the business model is still evolving. More and more pharmaceutical companies in the ranks of "big pharma" are willing to stake their futures on a personalised medicine approach, in part because they are genuinely committed to it, in part because they have declining drug development pipelines and the blockbusters they have in the market today will be off-patent in the near to medium term thus making them available at lower cost as generics and, in part, because they are under pressure from the financial markets to cut development costs and from regulators to minimise adverse events in patients taking their drugs.

17. Most biotechnology companies, the bulk of which are SMEs, endorse wholeheartedly the personalised medicine model. Their challenge is to raise enough capital in a difficult economy to bring products to market. This is especially true for the development of diagnostics which typically command a low price point and are less of interest to investors because of those lower returns. Nevertheless, many see diagnostics as a critical lynchpin in the commercial expansion of personalised medicine.

Beyond humans; other areas of important genomic discovery

18. While many of the better known advances in genomics in the last ten years have been in the field of human health, it would be incorrect to look at the last decade and conclude that it has been exclusively one of progress in improving the understanding of human beings. Every living organism has a genome. Plants, animals, bacteria and viruses all have genomic structure to them and there have been significant steps forward in better understanding those structures.

19. Henry Yang gave Symposium attendees an overview of the work ongoing at the Beijing Genomics Institute (BGI), the world's largest genomic sequencing facility. BGI currently operates 128 high throughput sequencing machines. In addition to BGI's contributions to the Human Genome Project and the International HapMap effort, BGI has sequenced the rice, chicken, cucumber and panda genomes, to name a few. BGI has plans to sequence more than 1000 other plants and animals as well as 10000 microbial genomes.

20. Much of the plant, animal and microbial genomic information being generated by BGI and other institutions will have direct impacts in fields such as agriculture, environmental and industrial biotechnology, areas that are prominent in the expansion of the bioeconomy and in meeting global challenges in green growth.

Summary

21. In the summer of 2010, on the 10th anniversary of the first draft sequence of the human genome, there were a number of media articles questioning the overall significance of the Human Genome Project and its current impact on health. Predictably, there was backlash against some of the enthusiasm of 2000 and it was openly asked if the Human Genome Project had been such a profound moment in science after all. "A Decade Later, Genetic Map Yields Few New Clues," read a headline in the *New York Times*.

22. But if the early acolytes of the genome were a little overly enthusiastic, today's skeptics under appreciate the importance of the Human Genome Project, both its scientific impact and its "real world" applicability to human health. In the case of medicine, genomics was never intended to be a binary switch between an old era of health care and a new one. Closer reflection suggests that as groundbreaking as genomics is, it is still an evolutionary process over many years to fully integrate genetic discoveries into the practice of medicine. Personalised medicine does not, indeed cannot, exist in a separate vortex from medicine as it has been historically practiced. That being said, evolutionary change is often no less profound in its impact.

2. The bioeconomy and converging technologies

23. The modern bioeconomy is being built not on one scientific platform, but upon many. Biology and chemistry, the building blocks of the first phase of genomic advances, are being joined by computational science, physics, engineering and many other disciplines. The next generation of genomic science will be driven by convergence of many fields, and labs will have biologists partnering with engineers, chemists working alongside physicists and computer scientists/bioinformaticians working alongside everyone else, so great will be the demand to manage the unprecedented amount of data generated by their colleagues using powerful research platforms.

24. A few weeks after the symposium in Montpellier, the Bureau (in effect, the executive committee) of the OECD Working Party on Biotechnology (WPB) met in Boston, MA for a planning retreat. On the campus of the Massachusetts Institute of Technology (MIT), bureau members saw first-hand the impact the trend of convergence is having on life sciences. Claude Canizares, MIT Dean for Research, described how the university has made technology convergence – in this case, the convergence of biology and engineering – a cornerstone for MIT's future, cutting across all schools and curriculum on the campus. WPB Bureau members then met with Robert Urban, Executive Director of the Koch Center for Integrated Cancer Research, who described the center's mission to pair cancer researchers with engineers to create new tools to fight cancer. He specifically described how these teams are drawing from biology, chemistry and engineering to create new types of cells that are capable of attacking and killing cancerous cells in the body.

25. In Montpellier, Drew Endy of Stanford University's Department of Bioengineering and the BioBricks Foundation, talked about the dynamic field of synthetic biology, which involves the synthesis and manipulation of DNA to create novel organisms. In many ways, synthetic biology is the embodiment of convergence and, as such, it is giving a "stress test" to traditional frameworks of thinking in everything from research funding to academic career advancement to mechanisms for collaboration between researchers and the sharing of knowledge to governance and oversight to precepts of intellectual property to public engagement.

Changing research and academic models

26. As Dr. Canizares stated, while convergence is the combination of many disciplines, research funding models still seem stuck in stovepipes. Cancer research funding goes toward projects that are specifically targeted to cancer; physics research funding goes for projects that are clearly related to physics, and so forth. But in the era of scientific convergence, many of the most important research efforts are caught between the traditional well-delineated boundaries of public funding agencies. They are not in a grey zone, fish nor fowl, as the saying goes. And yet these are the very areas, ones like synthetic biology, that borrow from many disciplines and that are critical to advancing the goals of the bioeconomy.

27. Beyond questions of funding, convergence means that biologists will be publishing papers in physics journals and chemists will be teaching classes in schools of engineering. For the bioeconomy, that's a positive development and underscores the whole notion of convergence. But university leadership must recognise, embrace and encourage this change. Scientists should be recognised academically and rewarded financially for publishing and teaching outside the comfort zone of their core careers.

An evolution in the concepts of sharing knowledge and intellectual property

28. Technology convergence is also forcing many stakeholders to take a serious look at existing intellectual property (IP) regimes, especially the patent system, and determine if this framework is consistent with achieving the goals of the bioeconomy. This is not to say that the undergirding of intellectual property is any less important, rather to state that numerous commentators have suggested that the current IP system as it is administered and adjudicated must evolve and keep pace with advances in science so that it can foster the very innovation that it is designed to protect.

29. At the Symposium, Dr. Endy gave concrete examples of this conflict: If he and his team were to take a patent on every "invention" to come from his lab at Stanford, at a cost of approximately USD 25000 per patent, the total cost would be USD 37 million, more than ten times the annual operating budget of the lab itself. He also cited examples of both university and industry labs where, even if cost were not an issue, IP attorneys simply cannot keep pace with the volume of discoveries coming from the labs.

30. Increasingly, intellectual property is moving from a model of "own and protect" to one of "own and share", that is, how one protects the rights of those who truly invent something new while encouraging the spread of and use of the knowledge to come from that invention as a means to spur innovation.

31. In a sense, the bioeconomy is a well-prepared staging ground for this debate. For more than a decade, this issue has been brewing as stakeholders have weighed the merits of allowing patents on naturally occurring gene sequences. Recent decisions by a US federal court to disallow patents on the BRCA 1 and 2 genes closely related to breast cancer, and by the Obama Administration to cast a skeptical eye on gene patents as a matter of public policy, have reignited the discussion but, in many ways, the question of patentability is less important than the need to explore other mechanisms, such as patent pools and clearinghouses, and alternative business structures, to allow freer access to a wider base of precompetitive knowledge, for these are really the building blocks in new fields like synthetic biology that will drive the bioeconomy.

Support for innovative governance and public engagement

32. Advances in fields like synthetic biology have been scientifically dramatic but have also caught the attention of the public and the regulators and other officials whose job it is to protect them. A key question for this age of converging technologies is what level of oversight and governance is appropriate? Do new technologies like synthetic biology require new regulatory regimes or can the existing frameworks grow with the technologies and be flexible and inclusive enough to encompass them?

33. The advent of pharmacogenetics and personalized medicine has put these governance questions squarely on the table because approval of many PGx-based products will require new and different approaches from those used with traditional drug approvals for the last 30 years. Some countries, like Singapore, have been able to take a more "white board" approach, fashioning new systems that are, by design, more flexible and intended to rely more heavily on post-market surveillance mechanisms. Other countries, like the United States and in European countries, are looking to retrofit their existing systems to the task. [To address these issues, the OECD, in co-operation with the governments of Germany and Canada, held a workshop in Berlin in September 2010 entitled "Better Health through Biomedicine: Innovative Governance." A report from that workshop will be forthcoming in 2011.]

34. As complex as these tasks are in the world of personalised medicine and pharmacogenetics, they will be far more challenging when products based on nanotechnology and synthetic biology start to come to the market in significant numbers. And not just in the area of drugs and diagnostics, but in areas that are more in line with the portfolios traditionally held by agricultural and environmental regulators.

35. Throughout the Symposium and in the discussions the following day, various speakers and attendees discussed the importance of public engagement and consultation in the bioeconomy. Truthfully, it could be included in almost any section of this paper, but the topic was given special emphasis in the context of emerging and converging technologies. Indeed the days immediately after the Symposium saw a great deal of media attention given to the work by US scientist J. Craig Venter and his team, who used the techniques of synthetic biology to create the genome of a bacterium, resulting in headlines about "creating life" and "God 2.0".

36. The oft-cited example of genetically modified organisms (GMOs) in Europe and the backlash against them was repeatedly held out as an example of what *not* to do, *i.e.* for scientists and industry to proceed without effective public engagement. Another specific set of concerns revolved around the need for ensuring privacy and security, especially in the use of personal genetic data, how it is accessed, used and shared.

37. Public engagement means many things to many people and given the variety of emerging and converging technologies on the landscape, there will be no ubiquitous approach. But in the view of many Symposium participants, it must be at the forefront of the bioeconomy, not an afterthought.

3. Financial support for the bioeconomy

Determining a value proposition for the bioeconomy

38. Over the course of the Symposium, there was considerable discussion of the financial models that will empower the bioeconomy. Both public and private investments have significant roles to play, often together in the form of innovative public-private partnerships. Public funding typically provides a baseline of support that is beyond the ability of the private sector. For example, it was public funding that covered the costs of the Human Genome Project. The private sector typically takes the lead in commercializing products.

39. Participants discussed and debated how one calibrates the true value of the bioeconomy. This is not an academic matter as elements of the bioeconomy, such as personalised medicine, require significant upfront investment by either the public or private sectors, or both. In tumultuous economic times, government appropriators, health care payers and investors are understandably questioning the value proposition when many look at health care, for example, as principally a cost containment challenge. Symposium participants cited the need to find the appropriate metrics to demonstrate that investments in

these next-generation approaches to health care and other major societal challenges are not a one-way street; that they are, in fact, generating payback in the form of better health outcomes or more diverse energy sources.

How should governments make sound infrastructure investments to support the bioeconomy?

40. Even in the current flagging global economy, countries are still keen to be part of the bioeconomy. Symposium participants discussed how best to launch that investment. The traditional model for many has been to build a flagship genomics institute (like the Genome Institute of Singapore or INMEGEN in Mexico) and to use that institute as a launch pad for genomics in the country. But is that the wisest approach today? Or, is a more decentralised, distributive approach better, with resources spread out among institutions as opposed to concentrated in one place? For that matter, is there a need for "bricks and mortar" at all? Can all of this simply be done on the Internet?

41. One school of thought holds that large centralised genomics facilities are well worth the investment. They have clearly been a key to the US leadership in many aspects of the bioeconomy as they have been innovation incubators on campuses and within communities. They offer the chance to pool resources and to serve as training centers for researchers who can then move across a region or country. They also offer a place to house the large computing facilities that are essential to data management and interpretation. And while foregoing the creation of a centralized genomics center may seem to be a cost saver, the decentralised approach can quickly escalate in cost as various health centres start to duplicate their respective efforts. There can also be additional costs associated with standardising many disparate platforms if that is not done up-front.

42. Other participants argued that this was essentially an elite, highly specialised model, and that a broader model was preferable, especially for developing countries. They suggested multiple regional resource centers that could share data in open source frameworks. As for computational needs, many of those can now be accessed via the web through innovations like cloud computing. One model cited was India, where large numbers of individuals are trained to share in open sourcing thus to enable large-scale education of young people who can contribute to data mining and analysis.

43. Ultimately there is no perfect solution that works in all scenarios. Different platforms are needed to fit the needs of different economies. The challenge for each region or country will be to determine which platform or mix of platforms works best and makes the most sense from a national investment perspective.

An investment view from the private sector

44. At a more practical, hands-on level, Sue Siegel of Mohr Davidow Ventures (MDV) gave an overview of the bioeconomy from the investor perspective, most notably that of venture capital (VC), which is critical to fund companies hoping to bring new genomic technologies to market. She spoke of the current environment as being one where science has made powerful technological advances, and of the impact those are having on the marketplace. As an example, sequencing costs have decreased x10(4) in the last decade; VC firms are funding most of the companies driving toward the USD 1000 genome. She also spoke of how those advances are, to some degree, currently offset by the continuing lag in the global economy and how the sluggish economy is dampening the appetite for investment by the large sovereign wealth and pension funds that are more risk averse and thus pulling back from the VC market as a result.

45. Investors looking at the bioeconomy see multiple market opportunities, including personalised medicine and pharmacogenetics; clean technology and green chemicals, especially those that might replace fossil fuels; consumer-driven opportunities in so-called Health 2.0 that involve interaction through the

Internet; veterinary genomics; agriculture and environmental testing; and IT and biomedical platforms and tools, including cloud computing models.

46. MDV sees its investments in terms of market opportunities, the people behind a company and the technology. MDV looks for products that can be commercialised in three to five years, capital efficiency, limited regulatory risk, strong IP positioning and a clear path to reimbursement for health care products.

47. From an investor perspective, there are several hurdles to be overcome in order to realise greater expansion of the bioeconomy. These include the need for regulatory and governance modernisation, a better rate of reimbursement for health-related products, a greater assurance of privacy and security in safeguarding an individual's genetic data; the need to update intellectual property regimes. Ms. Siegel also spoke about a lack of harmonisation and standards in various areas and the need to address this in a global context. Finally, along with many speakers and attendees, she shared a concern about the paucity of formal genomics education in the medical community and, in particular, in medical school curricula.

48. It should be noted that the economic drivers that relate to health genomics are different from those that apply to industrial and environmental biotechnology. Whereas health genomics developed along much the same regulatory and economic paradigm as the pharmaceutical industry, industrial biotechnology draws much of its history from the chemicals industry, which has very different regulatory and economic drivers.

4. The bioeconomy as a tool to meet challenges in the environment and to promote green growth

49. Governments around the world have prioritised the need to emerge from the current recession with economic platforms for environmentally sustainable "green growth" for the next generation. This has become a widely held political imperative, embraced by the developed and developing worlds alike, and by a wide range of multilateral institutions such as the G-20. Indeed as part of many national economic stimulus plans over the last two years, there have been significant outlays of funding for research, development and deployment of new environmental technologies. Many of these new technologies may be considered part of the bioeconomy as they embody genomic or other biotechnological approaches to everything from developing biofuels to food safety to bioremediation as a method of cleaning up oil spills.

50. The significance of the bioeconomy in this sphere goes well beyond current political fashion. One of the "Bioeconomy to 2030" report's principle policy recommendations is for countries to increase their support of agriculture and industrial biotechnologies. As the report shows, approximately 75% of the future economic contributions of biotechnology as well as large environmental benefits are likely to come from these two areas. Yet, over 80% of research investments in biotechnology by the private and public sectors alike go to new health applications.

Genetics and alternative energy production

51. At the Symposium, several speakers described various ways in which future energy, environmental and food needs would shape the bioeconomy. Edward Rubin of the US Department of Energy's Joint Genome Institute talked about "energy genomics," that is, the use of genomics to increase the production of biofuels which are an important alternative to fossil fuels like petroleum. While biofuels offer an attractive energy alternative, there are significant bottlenecks to its widespread adoption. The biomass used to produce them has not been optimised and technologies that break down biomass need more investment. And there is a need for technologies to convert sugars into biofuels. Dr. Rubin spoke about the use of cellulosic crops, that is, crops that can contribute to the production of biofuels. In particular he mentioned poplar as a plant that can be genetically modified to grow in a manner that is both

beneficial to produce biofuels while limiting environmental degradation, *i.e.* it can grow on a limited amount of land with limited water and no fertilizers.

Genetics and human sustainability

52. Jean-Christophe Glaszmann of the Department of Biological Sciences in CIRAD in France spoke of using genetic diversity in crops to enhance the supply of rice. With over 1 billion people living in poverty (< USD 1 per day), increasing the yield of rice, the planet's most prolific crop, is an imperative. There is a need to produce an additional 50 million tons of rice per year.

53. Among all crops, rice is exceptionally well constructed with the molecular tools that make it a model genetic system. Significant work has already been done to better understand rice at a molecular level. The rice genome was sequenced almost six years ago. Current efforts are directed at making rice more stress resistant, *i.e.* resistant to salinity, drought and flood conditions. Current varieties that are more flood resistant are being deployed now, but drought resistance is a tougher challenge.

54. Dr. Glaszmann also spoke of efforts to increase the genetic diversity in rice. The International Rice Genebank Collection currently has more than 118000 genetic varietals of rice and this resource is being used to create even more new varietals. He concluded by saying that food security is essential and that sustained investment is needed not only in the genetic science of improving crops, but also in training a new generation of scientists who can work in the converging areas of agriculture and genomics.

55. Martin A.M. Groenen gave a corresponding perspective with respect to animal breeding and genomics and how they are impacted by new technologies like genetic sequencing and other platforms. He showed the similarities between efforts to advance human genomics and those with animals. The chicken, horse and pig genomes have been sequenced using the same chips that have been used to map the human genome; sequences for the duck and several species of fish are on the way. He highlighted the importance of innovative animal breeding practices to human sustainability.

56. Lastly, Dirk Radzinski from Algernol spoke about the company's novel technology based on engineering algae as tiny "cell factories," directly producing fuels and green chemicals, and showing the contribution the process makes toward green growth. The process itself is environmentally sustainable as it does not require the use of fresh water, fertilizers, feed stocks or farmland.

Summary

57. To one degree or another, all the presenters gave an account of how the tools from human genetics are having a powerful spillover effect on areas relevant to the environment, food and agriculture. Clearly scientists in these fields are able to build on the work in human genomics that has been done over the last decade and, in many cases, they can work more quickly using the lessons and skills learned from the Human Genome Project. One can envision the bioeconomy as being a strong contributor toward building a cleaner, greener, and more sustainable world. But the speakers all cautioned that in order to achieve this vision, there is a need to repair the inequity in investment between genomics for health and genomics for green growth.

5. The bioeconomy in the context of the developing world

58. Developing countries are often discussed in terms of the profound societal challenges they face, and there is no question as to the formidable nature of those challenges such as widespread poverty, persistent hunger, combating disease and environmental degradation. The Symposium focused, in part, on how to better use the tools of the bioeconomy to help countries meet these challenges. But speakers and attendees did not see this as a one-way street of resources flowing into the developing world in the

traditional manner of aid to developing countries; rather, they engaged in a robust discussion about the significant contributions the developing world can make to the global bioeconomy, how the bioeconomy can become an engine of innovation in developing countries, to power economic growth and societal progress, and the resources and policies needed to make this vision a reality.

59. Iain Gillespie of the OECD provided two salient facts. One, that China now accounts for 30% of the world's R&D expenditures. And two, in 2010, Brazil, China, India and South Africa will produce half as many Ph.D.'s as the 34 countries in the OECD. The OECD is making a priority to reach out to these countries and to work co-operatively with them. Indeed, in recent years, the OECD has created a special category for these countries known as "Enhanced Engagement" to invite Brazil, China, India, Indonesia and South Africa to more formally and substantively participate in the Organisation's deliberations.

60. In terms of meeting needs of the developing world, Howard McLeod of the University of North Carolina described how the tools of personalized medicine – which in the United States and Europe have historically been targeted to the well-funded realm of diseases like cancer – can be made to work in a public health context in the developing world. Specifically, he talked about the Pharmacogenetics for Every Nation Initiative (PGENI) which involves helping countries develop the education, guidelines and infrastructure necessary to make the precepts of personalised medicine available to a wider range of countries and to integrate genetic information into public health decision making.

61. These measures take on added importance because, as some speakers pointed out, various genetic maps assembled in the developed world – the International Hap Map is a good example – do not sufficiently incorporate the genetic diversity of the developing world. A programme like PGENI also has real-world applicability in that it can help public health officials survey the population and prioritise treatment for a condition like malaria, selecting drugs by looking at both the genetic makeup of the virus and the genetics of the population. This helps avoid drugs that will incur a greater burden to the health system in terms of toxicity, a significant problem for already-overtaxed health care providers.

62. Abdallah Daar from the McLaughlin-Rotman Centre for Global Health spoke of the increasingly global nature of the bioeconomy. A report from the World Health Organisation in 2002 stated that all nations should pursue biotechnology to ensure global health equities. Indeed, developing countries have many reasons for wanting to ramp up their participation on the bioeconomy such as harnessing genetics to improve health, reduce development costs, stimulate their bioeconomies and uncover more genetic diversity, which is particularly beneficial to the population, as previously discussed.

63. In presenting a roadmap for the bioeconomy for developing countries, Dr. Daar offered several necessary conditions: Political will, which comes from scientists and others who can communicate the benefits of the bioeconomy to political leaders; institutional leadership and the willingness of institutions to take risks; a clear demonstration of local health benefits; genomic sovereignty, the notions that countries have control over the genomic resources within their borders; and the advancement of the knowledge-based economy. In looking at local challenges to developing the bioeconomy, Dr. Daar cited the need for skilled human resources, funding and political will, the development of a healthcare infrastructure and better mechanisms for collaboration among scientists and others in the research community. Internationally, Dr. Daar saw a need for more creative means of data and sample sharing and a need to build research capacity. He concluded by saying that the products of the bioeconomy should be accessible to a larger portion of the world'spopulation, which means a break from traditional business models for drug and diagnostic development.

64. Dr. Daar gave a positive assessment about the ability of the developing world to contribute to the bioeconomy. Certainly this aligns with what the OECD is experiencing in working with the Organisation's Enhanced Engagement countries. As an example, South Africa has one of the most well-articulated

national strategies on nanotechnology of any country, developing or developed. The OECD is also seeing innovative products in industrial biotechnology come from Brazil and China, and Brazil is especially engaged – from both the private and public sectors -- in many discussions about how to optimise biofuels to meet the demands of climate change.

65. While Dr. Daar gave an overview of the bioeconomy in the developing world, Dr. Gerardo Jimenez-Sanchez gave a country-specific view of the founding of INMEGEN, Mexico's national institute of genomic medicine, part of the overall Mexican National Institute of Health. INMEGEN was launched by the Mexican Health Foundation and is a key component of developing the bioeconomy in Mexico. Dr. Jimenez-Sanchez spoke about the reasons to develop genomic medicine in Mexico, including the epidemiological and demographic transition in the country as it experiences more instances of chronic disease in an aging population, the need to implement more preventive measures in public health, the desire to develop pharmacogenetic products for the Mexican market (and the very large and growing Latino population in the United States), and the desire to serve as a springboard for the knowledge based economy in Mexico.

66. INMEGEN was launched in 2004 as an alliance of the government and private sectors, with Dr. Jimenez-Sanchez as its founding director. Today, in addition to its core technology labs, INMEGEN also has a centre for the study of economic, legal and social issues (ELSI) associated with genomics, an intellectual property unit and a business centre, all contributing to the institute's role in going beyond research to stimulate the Mexican bioeconomy.

67. At this point, INMEGEN is perhaps best recognised for the Mexican Genome Diversity Project, the genesis of this effort being that the initial International HapMap was based on a largely Caucasian sample and did not cover the genetics of the Mexican population. This was problematic for Mexico as there is a risk that products developed elsewhere based on genomics, but not including Mexican genetic samples, could have fewer efficacies in the Mexican population and increase the risks of toxicity. The Mexican Genome Diversity Project was launched to demonstrate the importance of building genetic databases for specific ethnicities, in this case the mestizos population that makes up most of Mexico. The results of this project have formed the backbone for a series of additional studies looking at a range of health conditions in the Mexican population. This information is also possibly a backbone for innovative new drugs and diagnostics as well.

68. Charles Rotimi of the Center for Research on Genomics and Global Health at the US National Institutes of Health addressed the challenges of developing the bioeconomy in Africa where he described both significant potential and challenge. Thirty years ago, the population of Africa was 200 million; today it is 500 million and projected to grow to 1.3 billion in the next 25 years, the highest population growth rate in the world. What is generally not appreciated by developed countries is that Africa's economies are growing, and more countries are moving toward more stable political leadership. That being said, enormous challenges abound. Per capita food production is 2 100 kilocalories per day, the lowest in the world. Most of the population remains undernourished and hungry, and there are rampant problems with diseases such as TB and malaria.

69. Dr. Rotimi asked about the true meaning of health, saying that it was not just the absence of disease but the total well-being of people. Then, in a similar vein to the views of Dr. Jimenez-Sanchez, he talked about the need to make international genomics mapping efforts more inclusive of diverse populations. The African population has been left out of the major genomic studies; in fact, there has been only one large genome study done there. And those studies that have been done in Africa tend not to have been done by African scientists, a trend he believes should change.

70. Dr. Rotimi talked about the unpredictable consequences of introducing new technology into societies. He cited the example of the introduction of cell phones into Nigeria. Skeptics had wondered why this would work. Africans were poor and could not afford cell phones, so what purpose did this serve? In fact, cell phones have changed people's lives in very fundamental ways, allowing them to do everything from moving their goods to market to managing their banking and money transfers, something that never could have happened over landlines. Just as cell phones allowed Africans to leap frog analogue technology phones, Dr. Rotimi sees the possibility that Africa could leap frog in the bioeconomy as well. He cited some early research success, one a new breakthrough in TB which involved the isolation of 44 human proteins that the TB bacterium uses to survive inside the body. He also cited the MalariaGEN project, looking at the genetics of malaria, which involves 11 countries and samples from 13000 cases. To keep these successes from happening in isolation, Dr. Rotimi called for increased capacity building in African labs.

71. He also sees an important future for agricultural biotech in utilising GMOs and talked about the success Burkina Faso has seen in using biotechnology to improve cotton production. GMOs could have a powerful impact on hunger in Africa and he urged that there not be a misdirected debate about the pros and cons of GMOs when people are starving.

72. A major theme running through the discussion of the bioeconomy and the developing world was the ability of many developing countries to bypass legacy approaches to science and to offer innovative new approaches using genomics combined with tools like the Internet to create dynamic pathways for sharing knowledge. With younger scientists, this is especially true as they explore and expand on new avenues of social networking and build new models of collaboration. Samir Brahmachari of India's Council of Scientific and Industrial Research discussed how India has launched a new and innovative open source model of drug development. In this case, the effort was to create a drug to combat tuberculosis, which kills 370000 people in India each year. India is the world's most TB-prevalent country with over 3.4 million TB patients. Progress on TB has been very slow, though it has been 10 years since the sequencing of its genome.

73. India was described as a melting pot of the world's populations and, as such, is an ideal setting for genomics. But the traditional process of drug discovery does not work for a host of logistical and economic reasons. What India has now created is an open source method of drug discovery that allows effective drug development in an affordable framework for "low value" diseases like TB. The hub is a semantic web 3.0 process that has contributors from 73 countries. The average age of a contributor was 22 years The result is Risorine, a new TB therapy which enhances the effectiveness of existing TB drugs. It is an eitrely new generation drug, less expensive than the existing regimen.

6. Policy considerations

74. Over the course of the Symposium, there was strong support from participants for the notion that modern biology will make a powerful contribution to the global economy, one which, if channelled correctly, will have a compelling and positive impact on the lives of the world's population. Indeed most felt it will be an impact that is transformational in historic terms. That being said, participants are not of the opinion that this positive impact will happen of its own accord, but that a successful architecture for the bioeconomy can only come from sound and forward looking policies in the public and private sectors.

75. While shepherding the bioeconomy to the betterment of the world's population is too large and diverse a topic for any one meeting, there were certain recommendations that were repeated by many participants in one form or another, and they bear mention here:

A substantial and sustained investment in basic life sciences research remains not only warranted but highly desirable for both scientific and economic reasons.

76. There is a temptation to look at the sequencing of the human genome as a "mission accomplished" moment, a watershed point in time after which there are other priorities and other issues that need attention and support, financial and otherwise. That would be a mistake. In part, this is because the science of genomics itself is still in its relative infancy. All we know about the human and other genomes remains greatly overshadowed by all that we have yet to learn. Understanding the fundamentals of DNA simply raises more questions than it answers and brings into play questions of proteomics, messenger RNA, the transcriptome and numerous other aspects of life found within a single cell.

77. The investment in genomics research has multiple "paybacks." One is obviously an increase in scientific knowledge that is the focus of human health and, increasingly, becoming the focus of green growth and the environment. But the benefits go beyond additional knowledge of genomics and genetics and encompass the invention of new research tools, platforms and processes that are gained as a result of the pursuit of a better understanding of the structure of life. This innovation has a demonstrative impact on the bioeconomy, helping to fuel economic growth in the form of new products, services and companies.

The convergence of multiple scientific disciplines and platforms is a natural evolution and a highly positive development in the bioeconomy, but it should be supported through the promotion of innovative ways of sharing precompetitive knowledge and through new methods of collaboration.

78. In many ways, the theme of convergence ran through most of the presentations and discussions at the Symposium. That convergence is happening is simply a reality. The next generation of life sciences will need to draw across a range of disciplines to achieve success. The key question then becomes how to facilitate this convergence so that it takes place in the most efficient and beneficial manner.

79. Convergence is greatly enabled by both formal and informal structures that promote the efficient flow of knowledge. Among the most prominent of these is intellectual property, especially the patent system. A fair question asked throughout the Symposium was if the patent system, as it is currently structured, is able to keep pace with the innovation and discovery occurring on a daily basis in modern life sciences. There is no serious qualm with the rights of inventors to be protected and rewarded for their efforts. But genuine questions do arise when the practical effect of the patent system might be to "wall off" too much knowledge upstream from the heart of the inventive process.

80. A further exploration of how precompetitive knowledge could be more effectively networked and shared, through licensing agreements, patent pools or clearinghouses, or through other open-source mechanisms, could be of benefit in promoting the effectiveness of research and the convergence of disciplines in the bioeconomy. More networked research efforts, like India's drug discovery in TB, should be launched using tools like Web 3.0 to engage a new generation of young scientists.

The development of innovative governance frameworks will be essential for the advancement of the bioeconomy.

81. Governance and oversight will continue to play a major role in biomedicine and in the environment. But there needs to be a concerted effort to calibrate existing regulatory frameworks with advances in life sciences and, where appropriate, to consider the creation of new frameworks. In some cases, existing regulatory systems need updating or enhanced capacity to better understand new pharmacogenetic products like those coming from personalised medicine. In other cases, regulators should experiment with how they can better use new technologies. The view of a regulator is evolving to being

both a guardian of the public interest and also an agent for innovation, encouraging new products into the marketplace with the appropriate safeguards.

82. Governance can also includes how new products are reimbursed as well as how they are regulated. Those officials who are in charge of reimbursement should actively work to include the *value* of new pharmacogenetic products in their review as well as the cost.

The bioeconomy can be a powerful source of ideas, innovation and technology to promote green growth and human sustainability, but more emphasis needs to be given to this area of genomic research.

83. As was stated by several participants in the Symposium, the bioeconomy has significant potential to promote cleaner, greener, more sustainable growth. Some of the most exciting advances are being made in sequencing and better understanding various parts of food supply or with animal genomes. Exciting new technologies are coming about in all of these areas. In addition, some areas like industrial biotechnology could prove to be some of the earliest success stories in the green growth part of the bioeconomy. But more needs to be done to allow the agricultural and environmental aspects of genomics to share the stage with the work that has been done in human health. In particular, there needs to be a better balancing of research funding into these non-human health related areas.

The developing world has much to gain from and much to contribute to the bioeconomy, and a concerted effort should be made to ensure that developing countries have the necessary capacity to realize the potential of the bioeconomy.

84. Symposium participants were highly interested in the subject of how the bioeconomy can make a stronger contribution to the developing world and, at the same time, benefit more from the people and the innovation ongoing in these countries. Many speakers touched on issues relating to capacity building, noting that there is a need to develop more of a genomics infrastructure, especially in Africa. They also noted the need to ensure that international genomic mapping efforts included greater population diversity. There also needs to be development of the human infrastructure, with more well-trained scientists and researchers working in developing countries.

Robust engagement with the public will be essential to ensuring societal support for the bioeconomy.

85. Throughout the Human Genome Project, there was and continues to be a rich history of ELSI engagement with stakeholders at all levels. Many observers feel this is one of the hallmarks of the Project and one reason that public confidence in genomics research remains high in most surveys. Certainly the public engagement during the Human Genome Project led to a more widely supported outcome in both the scientific community and in the public than did the process (or lack thereof) during the GMO debate. That engagement should continue, and as developments with synthetic biology have showed, the public will continue to have a heightened interest in advances in life sciences.

86. The recent report by President Obama's bioethics commission is one model of how that engagement can help the public understand new technologies and weigh the potential benefits and risks in a thoughtful manner. But the model of the President's commission is just one possible approach, and there needs to be a continued robust discussion of ELSI issues; one speaker even suggested adding new dimensions to the ELSI paradigm: humanitarian, economic and cultural issues.

87. One particular aspect of public engagement that deserves highlighting is a need to educate more physicians, nurses and medical students about genomics. It remains far from integrated into medical practices and few medical schools offer substantial courses in the subject.

Conclusions

"Genomics and the Bioeconomy" produced a positive and provocative conversation about the bioeconomy, its opportunities and challenges. The potential benefits are substantial and historic, but much work remains to be done to align scientific, health, environmental and investment needs with public policy. There was a sense that the Symposium participants and organisers want to continue that effort. As Dr. Liu said in his opening remarks, "…..*we live in a profound period of advancement in biology and medicine, providing the possibility for humanity to transform health, industry, agriculture, the environment as well as the economic status of mankind*".