In September 2015, APSA Policy chair Jennifer M. Kwan, MD, PhD visited the J. Craig Venter Institute (JCVI) in La Jolla, CA to learn more about some of the latest biomedical research projects at the JCVI including insights on human and environmental microbiomes, updates on the hot topic of synthetic biology and its potential applications, and outlook and opportunities for physician scientists. A leader in genomics research and biomedical science, the campus is also a model of green design. The research facility collects and recycles all rain water and uses rooftop solar panels as its major energy source, achieving LEED-Platinum certification and a net-zero energy footprint [1].

To learn more about cutting edge research at JCVI, Dr. Kwan met with Nobel laureate and synthetic biology pioneer, Hamilton Smith, MD. His Nobel prize winning work on restriction enzymes initiated the era of recombinant DNA in the mid-1970s and led to gene cloning and genetic engineering, thus enabling scientists to introduce and remove genes from microbes to explore their functions and roles. She learned about JCVI’s work in synthetic biology starting with the total synthesis of the PhiX174 viral genome in 2003, to the first cell entirely controlled by a chemically synthesized genome in 2010 [2], and finally to the design and complete chemical synthesis of a minimal bacterial genome, Syn3.0 [4].

Although Dr. Smith acknowledged how exciting the potential positive applications could be for synthetic biology, including new pharmaceutica, biologically produced “green” fuels, and the possibility of rapidly generating vaccines against emerging microbial diseases, e.g. Zika virus, Dr. Smith is a basic scientist at heart and focused on the basic science questions and significance thereof. Right before the publication of Syn3.0, he discussed the journey in exploring this minimal cell: it has only 473 genes, the fewest of any freely living organism. This fast growing new cell was created by transplanting the genome of Mycoplasma mycoides, with all the non-essential genes removed, into Mycoplasma capricolum, which had been emptied of its own DNA. Surprisingly, 149 genes that are essential to life/viability of Mycoplasma do not have precisely defined functions, suggesting that there is more to be learned if we are to understand the minimal genetic requirements for life. Dr. Smith says that there is a strong need to support fundamental research that does not lead to immediate applications. The functions of the 149 genes with unknown or poorly defined functions can tell us about essential life processes. This could perhaps lead to new insights into the role of microbial genes in survival and replication; insights which will be important when it comes to tackling pathogenic microbes. However, it has been challenging to try to obtain funding to study the functions of these essential genes. From Dr. Smith’s experience, there is a need for more robust basic and translational science funding and a need to help the public understand...

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**By Jennifer M. Kwan**

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**Considering Science Policy as a Career?**

One-year fellowships, offered by many scientific societies, provide experience in guiding and developing national policy

**Role:** get in front of cutting edge research, assess societal implications, and patch holes in the regulatory framework

**Goal:** make sure technology is used responsibly and that society can capture benefits from new science and technology

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Career Pearls for Physician-Scientists from Dr. Smith

1) It is an exciting time in science and technology. We have powerful tools today which will only continue to get better that will enable great science to be done: For example, I believe tools like synthetic sequencing will be able to truly enable personalized medicine.

2) Do something you like! Learn the importance of how it may impact society and the role of policy in shaping its implementation. Importantly, do what you are passionate about and learn by doing.

3) There’s a bright future in medicine and biomedical research; persistence and luck have helped me in my career; keep at it!

that clinical applications come from such fundamental knowledge and insight.

Given the importance of public policy in influencing applications and the safety of biomedical innovations, we also met scientist and policy scholar Bob Friedman, PhD, who is the Vice President for Policy and University Relations at JCVI. Dr. Friedman gave us a personal tour of the JCVI, provided some history and inspiration for JCVI’s research, and described ongoing collaborative, cutting edge initiatives that may increase wellness and lifespan for humans. One integral part of these efforts is biomedical research policy: the JCVI had the foresight to recognize the importance of policy in shaping use of new biomedical insights and applications. Dr. Friedman and his team were tasked with coming up with policy options for addressing the societal implications of next-generation biotechnologies. Their work was done in collaboration with the Center for Strategic and International Studies (CSIS), an influential American think tank based in Washington, D.C. to create a biosafety/biosecurity report in 2007 that included options to both enhance biosafety and biosecurity. One mechanism was to screen orders from companies that make synthetic dsDNA. In doing so, this helps to make sure the companies know the identity of their customers and to ensure that the synthesized DNA did not come from known human bioterror pathogens [5].

It is a well-recognized phenomenon that there is often a lag of government regulations behind cutting edge science. While there is a necessity to moving science forward, there is also a need to ensure safety moving forward. One instance of the intersection of government regulations and cutting edge science was the Supreme Court case of Diamond vs Chakrabarty in the early 1980s. This case concerned a microbiologist and General Electric genetic engineer Ananda Chakrabarty, who genetically engineered a bacterium capable of breaking down crude oil which he proposed to use in treating oil spills and for which very similar strains are still released on oil spills today [6]. The Supreme Court ruled that there was a right to patent the living organisms in that case, with Chief Justice Warren Burger noting “the relevant distinction is not between living and inanimate things,” but rather between naturally existing and human-made inventions. The ruling of this case has created precedent for patenting living organisms, setting up the premise for patenting genetically modified microbes, plants, and animals. The ruling on this case opened the floodgates to the biotech industry and startups quickly took advantage. In 1986, the Office of Science and Technology Policy (OSTP) issued the Coordinated Framework for the Regulation of Biotechnology (CF) [7], which describes the comprehensive Federal regulatory policy for ensuring the safety of biotechnology products by three regulatory agencies: EPA, USDA, and FDA. It provided a framework for using primarily existing legislation in the US to handle anticipated products of biotech.

OSTP has undertaken several reviews of the 1986 assessment including one in 1992 [7], 2011, and one currently underway. In July 2015, the Executive Office of the President issued a memorandum directing the EPA, FDA, and USDA to update the CF for the Regulation of Biotechnology and 1) clarify current roles and responsibilities, 2) commission an expert analysis of the future landscape of biotechnology products to support this effort, and 3) develop a long-term strategy to ensure that the Federal biotechnology regulatory system is prepared for the future products of biotechnology. The objectives of the effort are “to ensure public confidence in the regulatory system and to prevent unnecessary barriers to future innovation and competitiveness by improving the transparency, coordination, predictability, and efficiency of the regulation of biotechnology products while continuing to protect health and the environment.” [9]

In 2012, in anticipation of the ongoing review of the Coordinated Framework, JCVI’s Policy Center undertook a comprehensive review of the adequacy of the CF for regulating the anticipated products engineered using synthetic biology. The JCVI released its report in 2014 [10] and continues to work closely with these regulatory bodies to ensure safety as the technology moves forward.

Acknowledgments

Thanks to APSA and JCVI for making this educational piece possible, Alex Adami for article design, and Bilwaj Gaonkar and Ronnie Knowlton for their feedback and photos for this article.

References


