THE SELECT COMMITTEE ON SCIENCE & TECHNOLOGY

(SUB-COMMITTEE II)

GENOMIC MEDICINE
WEDNESDAY 5 NOVEMBER 2008

Written Evidence Submitted by Kevin McKernan
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Introduction:
"*The empires of the future will be empires of the mind*". ***Winston Churchill***

In these turbulent economic times we must recognize the world is not only flat but that it is now also flat broke. "Bail outs" are Tourna kits and only those nations which deftly reinforce their high growth economic sectors will ambulate out of these troubled times. As many countries face both poor demographics with rising health care costs the discussion of the genomics of medicine could not be more relevant.

Background:
My career in Genomics began in 1996 at the Whitehead Institute Center for Genome Research. In 1997 I began managing the Technology Development Team for the Human Genome Project at the Whitehead Institute/MIT. I invented several magnetic bead based DNA purification tools which enabled the streamlined automation of the sequencing process. As I enrolled in a PhD program with Leroy Hood, a race ensued which I could not sit on the sidelines for. This was a race initiated by Craig Venter and his association with Applied Biosystems. I deferred my enrollment and gave everything I had to the public genome project to ensure faith in public science was not destroyed by the media's misinterpretation of the value of both public and private projects. After an ulcer and many other sacrifices, the human genome project completed ahead of schedule and humanity had access to two genomes; one from Celera and one from the Public Centers. Welcome Trust Funding was critical in the race.

At this point I moved on to found Agencourt Bioscience Corporation, which became the leading private DNA sequencing center in the world as Celera began to divest from the sequencing business. We became profitable in our 1st year of business and received over $35Million in NIH grants in 2002-2005. We were anointed an NHGRI genome sequencing facility receiving $27M in funding starting in 2003 for the investigation of structural variation in human genomes and the sequencing of 10 fruit fly genomes. In 2005 Beckman Coulter and Qiagen began negotiating for the acquisition of our business based predominantly their mutual interest in our magnetic bead based DNA purification technology. Beckman agreed to purchase the company for $140M. Their prime interest was in coupling our DNA purification tools to their Blood analyzers thus enabling more affordable DNA testing. At this time we spun out a division of Agencourt devoted to next generation sequencing; Agencourt Personal Genomics. This company invented and developed SOLiD sequencing and was acquired by Applied Biosystems in 2006 for $120M. Today, several hundred of these SOLiD sequencers exist in the market place and

contribute to the 1000 genome project. With 4 of these sequencers in 8 weeks of the summer of 2008, we generated over 250Gb of sequence; more data than existed in all of Genbank at the time. At the time these sequencers were generating 17Gb of sequence per run and we see a clean path to 10 fold more sequence per run in the next 18 months.

In summary, my background has been intensely focused on DNA sequencing in the most competitive NIH funded environments as well as entrepreneurial implications of genomics and private sector DNA sequencing. I have a balanced perspective of government funded science, entrepreneurial innovation, and multi-billion dollar public companies required to capitalize on genomic technologies at the interface of diagnostic testing.

Discussion:
Ironically, I now work for the very company that drove my ulcerating work ethic in 1998. As I accepted this business relationship I began to realize that the scars of this public-private genome project race continue to bleed in the industry. Many colleagues were angered by my decision to sell an NHGRI funded technology to what they termed “the evil empire” of Applied Biosystems. I bring this history to your attention as I believe scientists in the UK may still be as challenged with this bias as we witness here in the United States as the Sanger Centre was a substantial contributor to the Human Genome Project and intimately involved in this race. The Applied Biosystems/Celera genome race challenged and unfortunately at times insulted my efforts and the Sanger Centre efforts. The Sanger Centre stood strong, accelerated and delivered a stunning genome for all human kind to view free of restrictions. I was their teammate in this endeavor at the Whitehead Institute and I still believe these actions will be retrospectively remembered as a historical contribution to mankind.

The Applied Biosystems of 1998 does not exist anymore. Celera has been sold off. The BOD, CEO, CSO, and most executive staff no longer work at the company and most of the people responsible for the Celera decisions now work at Illumina, Helicos and Pacific Biosystems. The Company was recently acquired by Invitrogen and as of December is now jointly named Life Technologies.

Since the “Pre-Genome” era of 1998, the world has changed and many manufacturers of DNA sequencers now exist. Any bias against Applied Biosystems may cost the UK competitive positioning in genomics if not brought to the table. The competition that exists today needs to be capitalistically exploited by the sequencing centers to get the most competitive price on sequencers.

In the Pre-Genome past, the field of genomics suffered from too few competitive suppliers of DNA sequencing tools (2 at most). This lack of competition led most genome centers to find economies of scale by selecting a single platform and building highly efficient production operations around sole sourced sequencers.

Today, market conditions are much different with up to 5 suppliers of competitive sequencers (AB, Illumina-Solexa, 454, Danaher, Helicos). This fierce competition is being heavily leveraged in North American and Asia as most genome center have multi-platform centers (Baylor, Broad, OICR, RIKEN, Genome Institute of Singapore). The

Sanger Centre has taken a more historical approach and selected a single platform scale up with Solexa/Illumina.

The platform they have selected was developed locally with many of the scientists at Sanger being intimately involved in its development. David Bentley, a former PI at the Sanger Centre is now the acting CSO for Illumina/Solexa. Harold Swerdlow, the former technology development lead at Solexa now works in a similar capacity at the Sanger Centre. As Richard Durbin pointed out, he was formally on the Solexa Scientific Advisory Board. We have interactions with many genome centers and few have left this competition as unexploited as the Sanger Centre.

I think very highly of Richard Durbin and the Sanger Centre scientific team and doubt this bias is the true reasoning for their decision but often the perception of such a bias can be more damaging than the reality. Even at Applied Biosystems, we questioned whether we'd get a fair evaluation at the Sanger Centre and thus prioritized our efforts at centers, which appeared more neutral.

In summary, I believe my oral comments delivered as evidence properly focused on the dire need for digital medical records. Although immediate diagnostic use of these records is still years away, their availability will drastically accelerate research and intellectual property for the nations which properly focus on them. Key to any countries technological competitiveness in a given field is the requirement to take a global view and avoid patriotic localisms. Cross border competition should be exploited. This week we witnessed a press release showcasing the Sanger Centre's decision to remove 5 Applied Biosystems SOLiD sequencers from their laboratory. This is coming on the heels of most other centers buying more of them and may signal to other technology providers to avoid the Sanger Centre as its unlikely any relationship will be met with truly open and collaborative spirits given the history with the Sanger Centre and Solexa. At Life Technologies, we not only see the SOLiD platform expanding to 10 fold more throughput per dollar than what the Sanger Center experienced with SOLiD 2.0, we have another program in place to deliver 2-5Kb reads from real time single molecule sequencers. We are not only the largest molecular biology reagent and tool provider, we are the only provider which has DNA sequencing equipment and research programs which spans capillary electrophoresis, short read next generation sequencing (SOLiD) to single molecule real time sequencing and our relationship with your leading genomics institution is distant compared to other competitive countries like the US, Canada, Japan, Singapore, and China. I can only hope this distance is unburdened by the past history just explained as I know we can surmount any technological concerns the Sanger Centre may have and our simple presence in their lab will ensure Illumina is always providing a competitive price.

With sincere respect and gratitude,

Kevin McKernan
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Applied Biosystems
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By Julia Karow *Editor, In Sequence*

NEW YORK (GenomeWeb News) - The Wellcome Trust Sanger Institute has returned five SOLiD sequencing systems that Applied Biosystems had placed at the institute a year ago, *GenomeWeb Daily News* has learned. The systems were returned to Life Technologies, the new firm formed by the recent merger of ABI and Invitrogen.

Jason Liu, senior director of SOLiD Commercial Operations at Life Technologies, told *GWDN*'s sister publication *In Sequence* last week that the instruments were "sales demonstration units" that ABI had placed at the Sanger Institute for a scientific collaboration on small cell lung cancer in December 2007.

In May of this year, ABI said that scientists were using the five instruments to sequence the genomes of a small cell lung cancer cell line and a non-cancerous cell line to comprehensively cover genomic variations in both cell lines.

The return of its SOLiD sequencers comes about a month after the Sanger Institute said that it had purchased 11 additional Illumina Genome Analyzer sequencers, adding to 26 Illumina units already on site.

At the time, Julian Parkhill, director of sequencing at the Sanger Institute, told *In Sequence* that it was easier and less costly to add Illumina sequencers to the institute's existing pipeline, and that the decision was not a verdict on the merit of the SOLiD or the Genome Analyzer.

"The Sanger Institute looked carefully at all available machines for its recent sequencing expansion and how they might fit with its pipelines for sequence production," Parkhill told *In Sequence* via e-mail today. "For these purposes, the Institute sought the minimal additional commitment in molecular biology and informatics over its existing large-scale capillary platforms."

He added that the institute will continue to review next-gen sequencing platforms.

During a conference call in October, an ABI official revealed that the company has been using the placement of SOLiD instruments with potential customers as a sales strategy.

The SOLiD units returned from the Sanger Institute "will be re-deployed into other strategic accounts within the European region," according to Liu.