Genomics is not genetics

The ACS honors the founder of Human Genome Sciences; the outgoing CEO reflects on the biotech field and his role in it.

BY ANN M. THAYER

"It's been a wonderful time," said William A. Haseltine, referring to his past 20 years working in the field of genomics. Haseltine, founder, chairman, and CEO of Human Genome Sciences (HGS, *www.hgsi.com*), was speaking at the ACS National Meeting in Anaheim, CA, where he was awarded the David Perlman Memorial Lectureship for his contributions to biotechnology.

Haseltine recently announced he would step down as CEO at HGS after 12 years at the helm. The company is also shifting its focus to concentrate resources on later-stage drug candidates that address unmet medical needs and that have the highest potential to reach the market. It plans to trim 20% of staff, or about 200 jobs, and consolidate facilities.

This combination of professional and personal milestones led Haseltine to reflect on the state of genomics research and its impact on drug R&D. "This is also a good time in terms of the field itself," he said, which has matured and nears the completion of the human genome sequence. Although many people already call today's environment "postgenomic", Haseltine prefers to call it "a world in which the understanding of multiple genomes is now able to contribute."

Plans to sequence the human genome were met with mixed reactions 20 years ago, with proponents pitted against those who opposed "big science" projects. But, by 1987, the money began to flow. At the time, the concept was not medically driven, but considered a chemical challenge, Haseltine said. And the Department of Energy, not the NIH, initially backed the project.

Although chemists saw the challenge of sequencing for sequencing's sake, a second premise slowly emerged and came to dominate thinking, Haseltine pointed out. "It's a theme you will recognize today, almost to the exclusion of any other idea, of genomics as genetics." That is, the human genome will tell us how humans differ and help us understand the causes of disease.

From this view also came the notion of personalized medicine, or drugs tailored to an individual's genes. And what tends to be called genomic medicine "is all really 'genetic' medicine," he emphasized. But the Human Genome Project, he added, is "run by geneticists, and that's their view of the world—that genetics and genomics are identical. But that's only part of the story."

PHOTO: HUMAN GENOME SCIENCES

Haseltine

From a pharmaceutical perspective, Haseltine believes genetics can be a powerful tool in understanding diseases, but it is not the first tool scientists pick up. "Genetics is usually a tool we use to verify, but very rarely to generate, hypotheses in the pharmaceutical world," he explained.

"To some extent, we've seen a massive international program overpromise what genetics can offer medicine," Haseltine said. Genetics can offer a deep understanding of some aspects of disease causality, while comparative genomics can offer insight into evolution. "Both of these are huge and worthy scientific goals, but for those of us in the pharmaceutical world, they offer too little to live up to the great promise of an immediate revolution in medicine."

Instead, Haseltine offered his alternative view, which originated in work he did in the late 1980s sequencing the human immunodeficiency virus, cloning genes, and identifying important viral proteins. "The first really systematic use of genomics was in HIV," he said. "This was a new kind of science, and it taught me how quickly you could move from genome knowledge to practical knowledge."

The idea behind what he calls "non-genetic genomics" was to get a collection of human genes that each make a protein, and focus on those with secretory signals. In that collection, Haseltine believed he would find bioactive molecules, including new protein drugs, receptors, and enzymes. To follow through on this, he founded Human Genome Sciences as a joint organization with The Institute for Genomic Research, which was based on J. Craig Venter's work at the NIH.

"It was a pretty simple idea, but diametrically opposed to the approach taken by the Human Genome Project," Haseltine said. One argument against it was that if these genes were found, no one would then pay for the rest of the sequence. Another was that patents on the genes would stop the genome work from going forward. In retrospect, these fears never amounted to much.

Haseltine's view looks at genes and proteins as reagents for drug discovery. "Why shouldn't any scientist be able to order any full-length cDNA?" Haseltine asked attendees. "We've been able to do it from [the HGS] repository since 1995."

"Something is still wrong, and it is the mind-set that genomics is genetics, not biochemical compounds," he said. With time, he believes this attitude will change. Meanwhile, he said, "It's still a wonder to me that the overarching impact of this approach has not penetrated deep into the biotechnology or pharmaceutical industry."

Still, genomics has provided powerful tools for expanding drug discovery. "We have perhaps 10 times as many validated targets—real hard data that links the role of a gene and its biochemistry," he said. "Does that mean we have drugs rolling off the pipeline? No, because genomics can't do that."

"Genomics in and of itself can't solve all the problems with drug R&D," he concluded, "but it has been successful in increasing our opportunities to solve major unmet medical needs." ■