

## Proteasome play C4 debuts

Start-up C4 Therapeutics of Cambridge, Massachusetts, in January raised \$73 million in series A funding to develop therapeutics that target disease-causing proteins and facilitate their degradation through the ubiquitin/proteasome system. C4 was founded by a group from Boston's Dana-Farber Cancer Institute, including Jay Bradner, whose laboratory invented C4's targeted protein degradation (TPD) platform, which links drug-like small molecules to the cellular ubiquitin/proteasome system to eliminate designated proteins by tagging them with ubiquitin for destruction by the proteasome. Announcement of the funding coincided with news that C4 has entered into a strategic collaboration with the Basel-based pharma Roche to identify TPD drugs against a set of prespecified protein targets. Celgene, in Summit, New Jersey, has also inked proteasome-oriented collaborations with startups, including San Francisco's Nurix and Forma Therapeutics in Watertown, Massachusetts. Cleave Biosciences in Burlingame, California is currently in a phase 1 trial for myeloma with CB-5083, an inhibitor of p97, a AAA ATPase that regulates the ubiquitin/proteasome system. Proteasome inhibition is a core strategy in treating multiple myeloma: sales of the leading myeloma drug, Celgene's proteasome inhibitor Revlimid (lenalidomide), are projected to rise above \$6 billion in 2016. In November, the US Food and Drug Administration approved Ninlaro, a proteasome inhibitor directed at the subunit beta type-5, from Takeda Pharma in Osaka, Japan (p. 126).

**“I don't know of anyone who has thought this through as a realistic policy innovation because it has never been even close to happening”** John McDonough, a former aide to Senator Edward M. Kennedy and professor at the Harvard T.H. Chan School of Public Health. McDonough feels the prospects of the US government negotiating drug prices are slim, despite lip service given to it by some politicians. (*STAT*, 6 January 2016)

**“Your genetics don't determine your destiny, rather just your potential.”** #ISB100K <http://ow.ly/WBTi7> Leroy Hood comments on genetic reductionism. @ISBLeeHood

**“Doctors get the data and often don't know what to do with it. [But in the future,] we'll be able to find utility in that data.”** Teresa Wang, senior research manager at the digital health investment firm Rock Health, in San Francisco, commenting on the new health apps rolled out at this year's Consumer Electronics Show in Las Vegas. Among them are an app that confirms that you snore (EmfitQS), one that responds to mood swings by playing music or talking you down (Sensaura), and one that maps out dry facial skin (MAPO mask). (*STAT*, 6 January 2016)

## Direct Genomics revives Helicos sequencing system for China's hospitals

Direct Genomics, a Shenzhen, China-based sequencing company, is mounting a challenge to San Diego-based Illumina and other sequencing giants with a low-cost sequencer for clinical use. Last October, the company launched its GenoCare analyzer, a single-molecule genome sequencer specifically for clinical applications. Since then, competition in the genomic sequencing spaces has continued to heat up. In January, at the JP Morgan Healthcare conference in San Francisco, Illumina launched the MiniSeq System, an integrated benchtop analyser designed for clinical diagnosis, which will begin shipping this quarter. And Human Longevity, the San Diego-based company co-founded by J. Craig Venter unveiled its oncology program, a set of products still in development for whole germline, tumor genome and whole cancer exome analysis.

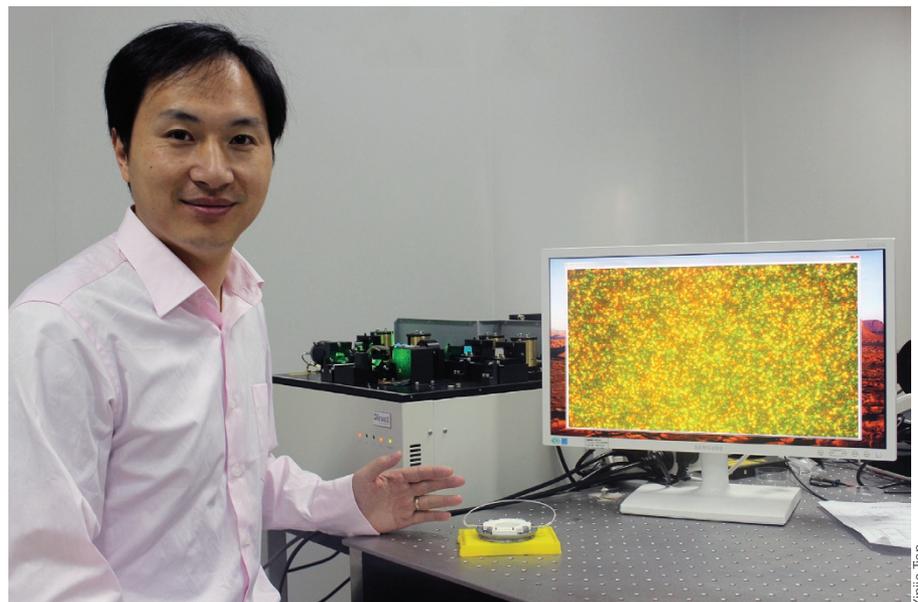
For now, Direct Genomics has set its sights on China. The company is taking advantage of patents licensed from Caltech, using a sequencing method first brought to market by Helicos Biosciences of Cambridge, Massachusetts. Helicos was founded in 2004 by Stephen Quake, who came up with the idea of single-molecule sequencing, though Helicos eventually went bankrupt in 2012. A postdoc in Quake's laboratory, He Jiankui, now Direct Genomics CEO and a biophysicist and genomics researcher at South University of Science

and Technology of China, returned to China and set up his company to build a sequencer geared towards diagnostics. Quake now leads the scientific advisory board for this new company.

Direct Genomics' instrument is meant only for the clinical market. The GenoCare analyzer enables 'direct' reading of raw, unmodified DNA in single molecules. Whereas conventional sequencers require amplification of DNA with PCR and several other steps, the GenoCare analyzer is an amplification-free technology. It intensely focuses light on DNA molecules and prevents illumination of contaminants to allow detection of the tiny signal from a single strand of DNA. Though it cannot match Illumina or Thermo Fisher sequencing platforms on volume in whole-genome sequencing, the technology promises fast and cheap sequencing of critical areas of patient genomes so that doctors can tune in on particular mutations and tailor treatment to patients.

“I really like it. It takes advantage of sort of 'traditional' sequence by synthesis methods like 454 and Ion and Illumina, but gets to single-molecule detection,” says Michael Weiner, a sequencing expert and biotech entrepreneur at the life sciences tools provider AxioMx, in Branford, Connecticut.

As whole human genome sequencing descends into the \$1,000 range, Direct Genomics intends to offer \$100 clinical



Jiankui He, president and CEO, Direct Genomics, pictured with GenoCare sequencer. The green, red and yellow spots represent a single fluorescence dye labeling a nucleotide. Each spot is a single molecule.

Xinjie Tian