THE AUTHOR FILE

Shankar Balasubramanian

A chemist intrigued by DNA and RNA structure and two-wheeled mountainous ascents.

University of Cambridge

Shankar Balasubramanian

Cambridge is a thought-provoking, beautiful environment with a close-knit community across all disciplines, says Shankar Balasubramanian, a researcher at the University of Cambridge who has appointments in the chemistry department and at the university's Cancer Research UK Cambridge Institute. In this issue he publishes two papers, one of which describes a technique to capture and sequence double-strand DNA breaks (DSBs) more robustly, sensitively and with greater precision, he says.

DSBCapture simplifies the preparation of sequencing libraries used by researchers to study various types of DNA damage. The method will also help clarify the role of G-quadruplexes (G4s), which are four-stranded structures that can form in DNA. His interest in G4s led him to DSBCapture, says Balasubramanian. G4s appear to be located at sites where DSBs can occur, but these sites have been tough to map. Now G4s can be characterized at higher resolution and in different cell states.

Balasubramanian and his team have also developed RNA G4 sequencing (rG4-seq) to profile these structural motifs across the transcriptome. He hopes that rG4-seq will help scientists interrogate any collection of input RNAs to identify stable rG4s. "When applied across the transcriptomes of many organisms this will help us see whether there is generality in some of the proposed roles of rG4s across species," he says. The scientists also believe that the regulation of some transcripts may be modulated by the presence of rG4s in microRNA target sites.

Balasubramanian completed his PhD in chemistry at the University of Cambridge and his postdoctoral fellowship at Pennsylvania State University. He returned to Cambridge as a fellow, then became a reader and ultimately was appointed professor in 2007. His interests in the structure and function of DNA and RNA are those of a "card-carrying chemist," he says. Over time his work expanded beyond the chemistry and molecular biophysics of nucleic acids to molecular biology, genomics and bioinformatics, also in relation to cancer biology.

On occasion "something unexpected" with commercial potential happens in the lab, says Balasubramanian. With his colleague, chemist David Klenerman, he developed 'sequencing by synthesis' with fluorescently labeled nucleotides and in 1998 formed the company Solexa, which was acquired by Illumina in 2007. The technique is at the heart of Illumina's high-throughput sequencing. It has been gratifying to see population-scale whole-genome sequencing emerge. "Nearly 20 years on, that big vision is now playing out," says Balasubramanian. He also cofounded the epigenetics tools company Cambridge Epigenetix.

"I love doing science," says Balasubramanian. "Still, as a scientist it is essential to have a life." Doing things outside of the lab keeps him balanced; it enhances reflection and stimulates creativity, he says. His wife and children are central to his life, and they all go on hiking and cycling trips together. As a teenager he played many sports, and he has recently taken on endurance running and cycling. It keeps him fit and is a form of meditation that helps him think. He has cycled to the top of Mont Ventoux, a challenging ascent even for Tour de France cyclists. Chemists in Cambridge are known to meet in a pub called The Panton Arms, which, says Balasubramanian, has the right environment for relaxed, open and enjoyable conversation. "At a time when the culture of research is sometimes dominated by deadlines, paperwork, short-term measurables and competition, it is important to foster open discussion and a creative culture of ideas generation," he says.

"I love doing science."

Balasubramanian says it's good to consider many ideas and reject most, even all of them, on thinking them through. Wolf Reik, a collaborator at the Babraham Institute, says he loves discussions with his friend and kindred spirit about new science ideas, especially multidisciplinary approaches involving chemistry, molecular biology, and cutting-edge biology and medicine problems. "I think of Shankar as a mentor-musician," says his former postdoctoral fellow Yamuna Krishnan, now a University of Chicago professor. He reminds her of a former neighbor learning to play the recorder: one day the cacophony had become music. Balasubramanian did the same in the lab—"without us noticing he transformed the scientific cacophony in our minds into music," she says. Conversations led to deep questions. Krishnan still struggles with his latest one: given infinite money, what would be the one problem you would solve? "His questions get tougher by the year," she says.

Vivien Marx

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