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Laudation for Dr. Randall Platt[1]

Assistant Professor of Biological Engineering, ETH Zurich;
Assistant Professor, University of Basel;
Investigator, NCCR Molecular Systems Engineering;
Investigator, Botnar Research Centre for Child Health

Winner of the Eppendorf Award for Young European Investigators 2020

by Prof. Laura Machesky, Beatson Institute, University of Glasgow, Member of the independent Eppendorf Award Jury[2]

Have you ever felt like you have "information overload" after going online just to look up the answer to a simple question? Or have you ever re-discovered a dusty old device, such as a big clunky computer or music player and realised just how much capacity and demand for storing data, songs, videos have changed in the past 5 years, 10 years, or even longer for some of us? We live in an information age, where data generation and storage are rapidly becoming limiting factors for our budgets and our energy consumption. Wouldn't it be wonderful if we could develop even more efficient ways to record experiences and store information for the future?

Perhaps we should look to nature for some inspiration here, as often the problems that we struggle with now have also been grappled with during the past 3-4 billion or so years while life was evolving here on Earth. This is where Randall, or as he prefers, Randy Platt's exciting work on CRISPR recording of biological data into the genomes of microbes comes into the picture. His future vision includes using microbes or other living organisms as cheap and efficient biocomputers and biorecorders, changing the way we interact with our environment and harnessing friendly microbes to report on our well-being.

It has been known for decades that microbe genomes harbour hypervariable regions of short repeats, termed “clustered regularly interspaced short palindromic repeats” or CRISPR for short. Between 2005-2007, groups in Spain, France, Canada and the US proposed that these repeats might represent an adaptive immune function and it was published in 2007 that these short palindromic repeats were in fact due to the bacteria writing into their own genomes a memory of an infection by a bacteriophage. By taking a little snip of DNA from the phage and pasting it into a storage cassette in their own genome, the bacteria were able to remember having been previously infected and mount an immune response against the invader if it attacked a second time. This would also give the bacteria an inheritable immunity against bacteriophages that had infected their ancestors, which is quite different from how our immune system normally functions.

While at first glance, the presence of a novel immune system in bacteria might seem like just a curiosity, it soon became apparent to some very clever scientists that this system for genome editing could be harnessed to make powerful tools. Laboratories such as that of Feng Zhang, Randy’s PhD supervisor, soon modified the CRISPR-Cas9 systems of microorganisms to allow precise gene editing by CRISPR in eukaryotic organisms. This enabled creation of CRISPR modified cells, offering the chance to knock out genes and knock in mutations or changes in the genomes of virtually any organism in a precise and controlled manner. The CRISPR revolution had begun!

One of Randy’s notable early contributions was to create the first CRISPR-Cas9 knock-in mouse system, allowing the use of CRISPR gene editing to create mice predisposed to cancer by precision modification of oncogenes and tumour suppressors. Randy’s paper developing this mouse has been cited nearly 1,000 times since 2014 when it was first published and CRISPR mice are now revolutionising the way we use mouse models for all sorts of diseases.

But Randy wasn’t contented to use CRISPR technology just to create tools for laboratory science. He pushed the boundaries even further when he started his own laboratory group at the ETH Zurich in Basel. There, he developed a tool called "Record-seq" where, by repurposing the elements of CRISPR that enable it to remember viral invaders, the experiences of cells can be recorded into cassettes in their genomes. Thus, each cell can write its own molecular history, which can later be deciphered by sequencing the DNA in the storage cassettes. This method allows monitoring of the experiences that a particular group of cells have over time. For example, cells were exposed to different concentrations of a herbicide, causing a stress response, and later Record-seq was used to determine which treatments different cells had received and how the cells changed to survive the insult.

Imagine if doctors could obtain a record of your body's experiences from the millions of friendly microbes living in your gut. You might be given a yogurt drink in the days before your test and microbes passing through your gut could be sequenced at different time points to report on stresses, diseases, cancer or other events. This is just one of many possible uses which Randy is currently actively pursuing for Record-seq and which may transform the future of medical monitoring.

He has further highlighted that by developing these microbial bio-computers, complete with read and write capabilities, this might allow extremely efficient storage of all sorts of information. DNA is one of the most efficient of known media for information storage – much more than your old computers, DVDs or even magnetic tapes. DNA is so efficient, that it has been estimated that all of the information currently stored around the world would fit into a 1m x 1m cube of DNA.

This explosion of technological advance has set our imaginations racing – and nobody more so than Randy Platt, the winner of the Eppendorf Young Investigator Award for 2020.

Randy grew up in Utah in America and attended the University of Utah for his undergraduate studies as a pre-medical student in biomedical engineering and chemistry. An experience with a benign osteochondroma on his shoulder as a child left Randy with a respect for the powers of medicine and a desire to pursue a biomedical career. Randy worked as a medical assistant, gaining clinical experience, alongside his studies. But it was during this early part of his career that Randy also become switched on to the impact that basic science could have on medicine. He cited a strong influence of his undergraduate research with neurotoxic venoms from the cone snail under the mentorship of Prof. Baldomero Olivera. Olivera, originally from the Philippines, has dedicated his life's research to understanding how these toxins target ion channels and how the snail uses these toxins to hunt fish. As an undergraduate, Platt was given freedom to conduct independent research projects in Olivera's lab and this resulted in Randy's first two first author publications, something almost unheard of for an undergraduate. But even more importantly, this experience gave Randy a taste of scientific discovery and turned him on to the idea of bio-hacking – or harnessing the ingenious inventions of nature – to solve problems or develop innovative tools.

In Randy's own words, these early experiences gave him an appreciation for the "fundamental need for basic life sciences research," which is still at the heart of his philosophy. He had a short postgraduate fellowship in London, working on bioengineering with Molly Stevens before he went on to do his PhD with Feng Zhang at MIT. Following on from this, he took the rather unconventional and bold step of applying for faculty positions directly from his PhD, where he ultimately accepted a tenure track position at the ETH Zurich. He managed to squeeze a short but productive 7-month postdoc during the transition phase, where he was co-advised by Feng Zhang and Paola Arlotta at Harvard. There, he started a collaborative project with Paola's group, still ongoing today, which involves applying in utero genome editing in mice to identify and characterising genes important for the specification of projection neuron subtypes (i.e. master regulators) during neocortical development. While this transition has been highly productive and Randy's lab at the ETH have already been very successful, he admits that even he would currently be a bit wary of hiring someone basically straight out of their PhD into a faculty position. But the ETH must have sensed his innovative and highly collaborative and productive research and his future potential.

Finally, on a personal note, he mentioned that he has a young family, which he and his wife started during his PhD. When I asked him how parenthood has been, combined with his and his wife's full-time careers, he replied very modestly "I like to work hard." It is often said that if you want to find the most successful people, look for the busiest ones. Randy is no exception to this. A proud young father and highly successful bio-hacker, we very much look forward to many more years of creative and impactful science from Randy's lab, harnessing nature's toolbox and impacting on many areas from medical monitoring to information technology.

[1]https://bsse.ethz.ch/platt/
[2]http://www.beatson.gla.ac.uk/

In response to the Corona virus outbreak (COVID-19), the official Award ceremony at the EMBL Advanced Training Centre in Heidelberg, which was planned for June 25, 2020, within the Young European Investigators Conference, has been postponed to June 24, 2021.

More about the Eppendorf Award for Young European Investigators at **www.eppendorf.com/award**

More about the Young European Investigators Conference at **www.eppendorf.com/award/25years**