The Mount Sinai Postdoc Periodical
Monthly newsletter, October 2015

Revolution of genetic engineering: Alternative CRISPR/Cas9 system could improve genome editing
By Mar Gacias-Monserrat

Molecular biologists have been able to edit genomes for decades; however, problems with accuracy, engineering and high costs have often jeopardized its success. In 2012, a new technology called CRISPR/Cas9 became a real game-changer in the field of DNA editing and might even be considered one of the most revolutionary discoveries to hit molecular biology since PCR.

The CRISPR/Cas9 system is part of the microbial adaptive immune system used by bacteria and archaea to defend themselves against foreign genetic elements. The CRISPR/Cas9 system uses RNA-guided nucleases to recognize and cleave target DNA (or in some cases, RNA) in a site-specific way. Researchers have been able to turn this microbial system into a powerful molecular biology tool to edit almost any genome by disrupting selected genes or inserting desired sequences (Figure 1). Unlike other gene editing methods, this new system is cheap, quick and easy to use and allows researchers to modify the DNA of nearly any organism, including humans.

Even though CRISPR/Cas9 has rapidly become one of the most used tools for genetic engineering it seems that there still might be room for improvement. In September 2015, a team led by one of the technique’s pioneers, Dr. Feng Zhang of the Broad Institute in Cambridge (Massachusetts), might have found a way to improve CRISPR/Cas9 and make it even simpler and more precise. Dr. Zhang’s lab has discovered a new RNA-endonuclease, called Cpf1, that should make it easier to edit genes by replacing one DNA sequence for another1.

The RNA-endonuclease Cpf1 differs from Cas9 in terms of structure and function. On one hand, the CRISPR/Cpf1 system uses a shorter single guide-RNA to hone in its target DNA whereas Cas9 requires two RNA molecules. In addition, Cpf1 cuts DNA at different sites than Cas9, expanding the targeting range of RNA-guided nucleases. This would not only cut down the costs but would also simplify the design and delivery of these new DNA engineering tools. Another different and important feature of Cpf1 is the way in which it cuts the DNA. Cas9 cuts both DNA strands at the same position leaving behind “blunt ends”, whereas Cpf1 leaves one strand longer than the other, generating “sticky ends”. This feature is important because sticky ends carry information that can be used to direct the integration of the DNA insert and allow its proper orientation into the genome. Moreover, this structure of the cleavage product could not only increase the frequency of insertion but also be advantageous for overcoming some of the challenges of non-homologous end joining (NHEJ)-based gene insertion into the mammalian genome and improve the efficiency of gene editing in non-dividing cells.

While is still too early to tell whether this new system will surpass the popularity of CRISPR/Cas9, there is no doubt that these findings are an exciting step forward in the field of genetic engineering. The CRISPR field is still young and, despite the huge potential and prompted excitement, it could be years before we are able to unravel whether these new tools will ultimately have a role in human therapeutics, particularly with the concomitant ethical concerns.

REFERENCES:

Figure 1: Schematic representation of gene silencing and editing using CRISPR-Cas systems. From “Pak E.: Science in the News, Harvard University”.

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How to Create a Compelling LinkedIn Profile: Tips and Tricks from a Career Coach
By Delaine Ceholski

In September, the Mount Sinai Postdoc Writing Group hosted a workshop by Barbara Frankel, a career coach with Coaching Initiatives LLC. With years of human resource and management development experience at companies like Amex and JP Morgan Chase, Barbara joined LinkedIn at its onset and advocates for a discernible online presence, especially when involved in the job search.

I always viewed LinkedIn as simply a way to present your CV online. However, Barbara explained that LinkedIn uses a search algorithm to look for key words in specific areas, allowing companies to find the ideal employee and linking you to jobs that would be a good fit. Using her advice, you will be able to maximize your online presence on LinkedIn, hopefully allowing for a more visible profile and increased attention from headhunters and companies looking for people just like you! Here are some of her tips:

1. In your heading, don’t simply put “post-doctoral research fellow”. Elaborate to include what you actually DO. For example, if you are a specialist in stem cell biology and gene editing, you can change your heading to “Post-Doctoral Research Fellow, Stem Cell Biologist, Gene Editing Specialist”. This is a far more striking heading and will draw attention to your profile.

2. The 2000 word summary is your opportunity to brand yourself. This is where LinkedIn searches for keywords so this is your chance to sell yourself and what you can do.

3. For each position you’ve held, try to get at least 2 recommendations. You can ask co-workers or employers to write these for you and, in exchange, you should write them back! When a potential employer is looking to hire, it pays to see that someone was willing to openly recommend you.

4. In the skills section, list your top 5 skills first. Why? When LinkedIn searches for and identifies people for a position, the top 5 skills are sent out to the company so this is all they initially see. Don’t list your skills in chronological or alphabetical order - list them in their order of importance. Also, get past co-workers or collaborators to endorse your skills to add even more credibility.

5. Join groups and share content. Through LinkedIn, you can join various groups (e.g. Mount Sinai Postdocs and Postdoc Alumni, Publishing and Editing Professionals, PhD Careers Outside of Academia, Academia PhD Network). Through these groups, you can have discussions, make new connections and potentially find job opportunities. You should also take the opportunity to share articles or something of interest to you by posting it on your LinkedIn page or in a group discussion. This activity gets you more views and increases your profile strength!

6. Lastly, many might be tempted to join LinkedIn premium. For $29.99 per month, you can directly contact recruiters, see who’s viewed your profile, and be a featured applicant on recruiters’ applicant lists. However, Barbara says that a strong profile will do more for your job search than LinkedIn premium will.

Co-Chair Corner
Greetings postdocs,

On behalf of the Postdoc Executive Committee (PEC), we would like to thank you for your attendance and enthusiasm during the 6th Annual Postdoctoral Symposium! Registration numbers were up from last year, which is a reflection of the desire of postdocs to participate in the community here at Mount Sinai. The PEC works extremely hard to organize the symposium and several other events for the postdocs. We are always looking for ways to improve these events to meet your needs. That said, if you have not done so already please send us your feedback through this short survey so that we can better plan for next year’s symposium. Even if you did not attend this time, your input is still valued!

Speaking of surveys, we are in the process of collating all the data from the annual Postdoc Survey and will be sending out a summary soon, so please be on the lookout for those findings! Again, survey participation in 2015 increased from previous years - thank you for your feedback! Two ongoing programs that were created to address comments from previous surveys include the Leadership / Conflict Resolution Course and the Future Leaders in Science Education and Communication Training Program. Also a result of last year’s survey is the Postdoc Secondary Mentoring Program, designed to align postdocs with faculty mentors who share or have had similar career aspirations. Lastly, we use data from the survey to advocate for positive changes for all postdocs when we meet with the senior leadership. Let’s see what comes out of this year’s survey!

Best,
Ryan

Ryan J. Cummings and Merina Varghese are your PEC co-chairs

Postdoc Day Follow-up Survey:
https://www.surveymonkey.com/r/GTDKYZQ

Postdoc Secondary Mentoring Program:
http://librarycf.mssm.edu/postdoctoralmentorship/portal.cfm
The future of Adam – Richard Dawkins at the 92Y
By Olivia Engmann

Every cathedral contains a symbol of its time. The observant eye can deduce, independent from its composition, in what environment the building was erected. It can also spot how architects and artists have been influenced by the evolution of a style. The same holds true for fossils: the remains of a random organism can tell a paleontologist in what surroundings it lived and who its precursors were. To go one step further, a scientist may infer from the fossil’s phenotype what genome the animal possessed and how its DNA was shaped epigenetically by the environment.

Richard Dawkins, one of the world’s most famous public science writers, is a master in explaining the art history of life. He integrates evolutionary theory, culture and religion to tackle bigger-than-life questions. Looking back on decades of science writing, he recently published the memoir *Brief Candle in the Dark*, which he introduced to New York at the 92Y on September 30, 2015.

“Most of what is unusual about man can be summed up in one word ‘culture’”, he writes in *The Selfish Gene* (Oxford University Press, 1976). How man can be original despite relying on genes like every other living being has occupied the mind of Richard Dawkins for most of his career. At the 92Y he explained to his interviewer, Robert Krulwich, how architecture of simpler animals is based on genes. Dawkins calls this the extended genotype. He gives the example of a wasp, the mud-dauber, that builds a series of small tubes, placing a paralyzed spider and an egg into each partition. Dawkins considers these tubes vital organs, similar to legs and wings, as they are essential to its survival. Building them correctly is a matter of natural selection and the behavior for nest-making is genetically determined with the nest-tube being the extended phenotype. Dawkins also applies this mechanism to other animals such as beavers. He even admits that beavers’ dams may be so individual that one may recognize which beaver has built it, albeit the individuality is based on the beaver’s genomic variability.

Krulwich then asked Dawkins about the architect of the Chrysler Building – a virile design that may reflect the superiority of the male designer’s genome that, akin to a peacock’s tail, may give him a reproductive advantage. When asked if the Chrysler Building is the extended phenotype of its designer, Dawkins says no. He thinks that while architectural talent perhaps may be genetic, the style in itself isn’t. Here is where Dawkins’ idea of the meme comes in. A meme is a rapidly evolving, culturally transferred element of knowledge – a good idea that sticks around. Examples are beliefs, styles, and songs. While a person’s genome is diluted after a few generations, an important idea can persist for thousand of years – see religion. Hence, cathedrals or the Chrysler building may not only reflect the extended phenotype of the architects but also their cultural meme pool. Krulwich wistfully avoided any topic of religion at the 92Y, a Jewish institution (“I don’t want you to go anywhere near the bible tonight”), knowing that Dawkins is famous for defending atheism, articulated in depth in his bestseller, *The God Delusion* (Houghton Mifflin Harcourt, 2008). Dawkins needs no fairies in the grass to believe in a garden’s beauty. We would not admire a cathedral less, if we knew about its history.

This memoir of Dawkins is a synthesis of his life’s “oeuvre”. It is also his second memoir in a row. This raises the question: what is the future of Dawkins? He’s certainly immortalized himself, not only by propagating his genome or leaving a carbon footprint or naming a flashy fish (*Dawkinsia exclamatio*), but he also managed to leave his mark in the philosophy of science for generations to come. In the future he will be proof for his own theory of memes.

**UPCOMING EVENTS**

- **Writing seminar**: The next seminar is Tuesday, October 20 in Annenberg 25-51 from 4-5:30pm. The speaker is Mary Mitchell who is in Professional Training and Coaching. The topic will be “Interviews: Formal and Social”. Put your best foot forward in both structured interviews and social contexts! Please RSVP to sinaipostdocwriting@gmail.com.

- **The Postdoc Writing Group** meets the 3rd Friday of each month at noon in Hess Center room 10-122 (10th floor). The next meeting is November 20. If you have writing to work on, bring a few copies of it (1-2 pages, ideally an abstract or introduction and no results or methods sections). The group will also read CVs and cover letters. Follow the ISMMS Postdoc Writing group on Twitter @PostdocWriting. To join the mailing list visit: http://mailman.mssm.edu/mailman/listinfo/postdoc-writing

- “**What can you be with a PhD?**” Register for this event at NYU on October 24-25 at http://whatcanyoubewithaphd.com/

- **Next Postdoc Social** is Friday, October 30 at 5pm in the Icahn MC Alcove. Come for food and drinks!

**The Mount Sinai Postdoc Periodical**

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**Ways to keep in touch**

- Our website: http://icahn.mssm.edu/education/postdoctoral-training
- Follow our Twitter account: @MtsinaiPostdocs
- Join our Facebook page: “Mount Sinai Postdocs”
- Follow us on LinkedIn (Mount Sinai Postdocs and Postdoc Alumni)
I am responsible for several projects. Three projects are industry-sponsored early phase clinical trials of targeted agents for treating cancer. I lead 2 phase 2 trials and 1 phase 1b. My (and my team's) responsibilities include ensuring that the hospitals and institutions where patients are treated are complying with the protocol and good clinical practices and to answer any questions that the investigators and their staff may have about treating their patients. I participate in many meetings with the investigators and their staff to discuss the safety and efficacy of the drugs being tested. I also meet with the sponsoring companies on a regular basis to discuss the progress and conduct of the study. Lastly, I work with our National Cancer Institute (NCI)-sponsored projects trying to centralize molecular characterization data that often gets erased in clinical trials.

CM: What advice would you give to people who are interested in pursuing a career like yours? What should have in their resume to make them better candidates and what are the essential qualities and skills they should have before applying for a job like yours?

ABW: Try to show that you have some understanding of how clinical trials are run and a broad understanding of good clinical practice guidelines. Display your knowledge of drug mechanisms of action. Also, showcase your non-scientific skills, including oral presentations, organization and software use.

CM: What are the pros and cons of working for a biotech company? What are the things you love about your job and what you would possibly change if you could?

AB: The pros are that my job is very family friendly. I don't work long hours and the deadlines given have very clear endpoints. Most of my work is done collaboratively in teams so I have lots of support. I also get the opportunity to attend scientific meetings so I can keep up with current research in my field. The only cons are that there is a lot riding on each project and task so it can get stressful. In addition, some travel is required.

CM: I’ve always thought that working for a company means less flexibility in terms of schedule and working hours (at least compared to the academic world). How does your job fit with your family schedule and your personal/private life?

AB: With this job, I absolutely have more flexibility. I can work from home, leave early or come in late. I was able to choose my hours (I work 7:30am-4pm most days) so I can get home in the evening and spend time with my kids.

How do we avoid becoming crazy scientists?

By Natasha Eliyahu-Shtraizent

I would like to address postdoc sanity. And no, I am neither a psychologist nor psychiatrist. I just want to bring awareness to how extreme conditions of stress, overstimulation, sleep deprivation and malnutrition affect our physical condition and ability to think clearly. I am not even referring to dealing with the nature of a career in science or questions about the global meaning of achievement in our personal lives, specifically with regards to child-rearing. Dealing with all of this pressure can drive you insane- and it does. So how do we identify the breaking point between constructive and destructive stress levels? And how do we curb excessive pressure so that we can think clearly again?

We are pressured by external factors and self-motivation to push ourselves beyond the limits of our capability. We don't even know what our limit is until we try pushing past it. Elite athletes have shown us that our bodies are capable of far more than we think. However, as with everything else in life, stress should be in moderation. Recent examples, particularly on Wall Street, have shown the extremes that people will go to in order to keep up with the seemingly forever increasing demands of the workplace- often with devastating consequences1,2. Stress is an inevitable part of life and can be harnessed to motivate us to achieve even more; however, if it becomes overwhelming, it can hinder productivity. The key could be maintenance. As with a vehicle, cleaning and oiling the parts and replacing worn out connectors will make the vehicle last longer even if it is used regularly. The same is needed for our bodies and brain- if we want to be healthy, sharp, and functional scientists, we need to exercise consistency and live a healthy lifestyle.

I will keep updating you on my progress towards finding the “golden” middle ground. For now, take a look at this article in the Harvard business review on how to turn stress into asset.