

BroadCast for August 26 – 30, 2019

Dear Broad colleagues,

Labor Day weekend is peak season for Storrowing: the local phenomenon of overheight vehicles losing their tops, sardine-can style, when they scrape Storrow Drive's low bridges and overpasses. Storrowing happens all year round to all manner of motor vehicle over ten feet tall, but the most commonly Storrowed vehicles are rental trucks crossing the city around September 1, when most of Boston's residential leases begin. Neither sign nor social media mantra nor any other 21st century technology has solved the Storrowing: in the first eight months of 2019, there have been no fewer than eight Storrowings or near-Storrowings.

Readers, it's high time we Broadies applied ourselves to this urgent problem. We proudly present The Atlas of Rental Truck Storrowings (TARTS), our map of the most spectacular Storrowings and near misses by box trucks since 2015, as recorded by Universal Hub. Our hope is that our exercise in data visualization will move you to hackathons, expressway-wide association studies, and all manner of Broadie ingenuity. Together, we can surely make Storrowing a thing of the past.

Alternatively, we can crack open a refreshing beverage, post up at the vantage point of our choosing (we'll be at the Fenway/Kenmore exit, ourselves), and scroll through the week's Broad news while we wait for the unmistakable crunch of metal on concrete:

The complex genetics of same-sex sexual behavior

In a study published in *Science*, an international team led in part by Andrea Ganna and Ben Neale examined existing data from nearly 500,000 UK Biobank and 23andMe participants to look for genetic variants associated with same-sex sexual behavior. They found evidence that there are likely thousands of genetic variants contributing to same-sex sexual behavior, but each has a small influence (similar to what is seen for many other complex traits); that it's not possible to predict same-sex behavior through genetics; and that same-sex sexual behavior is a natural part of our overall diversity as people. Learn more about the study in a Broad resource page and on the study website. Because the research raises important social, ethical, and scientific issues that are worth considering, the Broad invited members of our community to provide their thoughts on the study, the process, the implications, and lessons we might learn in a series of perspective pieces. Follow coverage of the study and these discussions in *The New York Times*, NPR, *The Washington Post*, and elsewhere. On Thursday, September 5 at 10am, join Out@Broad in Serengeti for a discussion about the study and lessons we can learn; share your questions and thoughts ahead of time.

## A quiet genome speaks up

Some cancers, including pediatric rhabdoid tumors (RTs), have “quiet” genomes lacking recurrent, targetable mutations. To find potential targets, Stuart Schreiber, Charles Roberts (now at St. Jude), Elaine Oberlick, Matthew Rees, Jake Bieber, and colleagues in the Cancer Program, Chemical Biology and Therapeutics Sciences, and the Pediatric Dependencies working group performed a high-throughput small-molecule screen and a genome-scale CRISPR-Cas9 screen in RT and control cell lines. Described in *Cell Reports*, the work points to receptor tyrosine kinases as potential targets and demonstrates that large-scale perturbational screening can uncover vulnerabilities in quiet genomes.

## A better predictor of antibiotic lethality

Researchers have thought that antibiotics are better at killing bacteria that are fast-growing versus slow-growing ones. But Allison Lopatkin, Jim Collins, and their colleagues have found that bacterial metabolic state at the time of treatment better predicts antibiotic lethality than growth rate. The team measured growth and metabolism in various Gram-positive and Gram-negative species, across a range of conditions including nine different antibiotics, to determine the relative contribution of growth and metabolism to antibiotic lethality. The researchers write that the findings could influence the development of new antibacterial drugs and suggest ways of boosting the efficacy of existing drugs. Read more in *Nature Microbiology*.

## Picture this

College students are on their way back to campus (we do hope those arriving in moving trucks will avoid Storrow Drive). Among them are alumni of the 2018 Broad Summer Scholars Program, who joined us as rising high school seniors last summer and matriculate as undergraduates this fall. Visit the Broad Instagram account to find out where some of them are headed.

## Now in preprint

- The Angiosarcoma Project: enabling genomic and clinical discoveries in a rare cancer through patient-partnered research (Corrie Painter, Esha Jain, Brett Tomson, Nikhil Wagle, and colleagues)
- Compressed sensing for imaging transcriptomics (Brian Cleary, Eric Lander, Fei Chen, Aviv Regev, and colleagues)
- Interactions between earliest Linearbandkeramik farmers and central European hunter gatherers at the dawn of European Neolithization (David Reich and colleagues)
- Prevalence and mutational determinants of high tumor mutation burden in breast cancer (Nikhil Wagle and colleagues)
- RNA polymerase mutations cause cephalosporin resistance in clinical *Neisseria gonorrhoeae* isolates (Yonatan Grad and colleagues)
- Multi-resolution single-cell state characterization via joint archetypal/network analysis (Shahin Mohammadi, Jose Davila-Velderrain, and Manolis Kellis)

- Optimization of AsCas12a for combinatorial genetic screens in human cells (Kendall Sanson, Peter DeWeirdt, John Doench, and colleagues)

### Who is Broad: Emily Munro-Ludders

The latest Broadie to be featured on Who is Broad is Scrum Master Emily Munro-Ludders. Visit the intranet to learn why her role at the Broad aligns with her personality and lifelong passions, why she drives north with fistfuls of flapjacks, and what foreign locales top her “must-see” list. If you'd like to nominate a Broad colleague to be featured on Who is Broad (or would like to volunteer yourself), send a note to the BroadCast team.

### What to do next week (and beyond)

 Starting to think about your application for the October NIH deadline? OSR keeps tabs on the NIH news Broadies need to know. Read their digest of NIH news from July and August, including resources for grant writing and applications, updates on gender equity and anti-sexual harassment efforts, and more.

 Attend a special seminar by 10x Genomics on Single Cell Gene Expression Assay Optimization on Wednesday, September 4, featuring presentations by the Regev Lab's Orr Ashenberg and others. Register to attend; lunch will be provided.

 Want a child who's special to you to experience the Broad firsthand? Enter them in the lottery for the October 2019 and February 2020 Take Your Little Broadie to Work Days by Friday, September 6.

 Hear eighteen emerging scientists present innovative research at the intersection of biomedical disciplines and discuss exciting new directions at the Next Generation in Biomedicine Symposium on Monday, September 9.

 Join painter Emily Eveleth and curator Deborah Davidson for a gallery talk and reception on Wednesday, September 11. Eveleth's exhibit "Results of Interpretation" is on view in the second floor connector through the end of September.

 Nominate a stellar trainee (such as yourself, if that describes you) to serve as chair or vice-chair of the NextGen association during the 2019-2020 academic year. Friday, September 13 is the deadline to submit nominations to the Office of Academic Affairs.

 Registration is now open for the September Blood Drive, taking place on Friday, September 20 in the Blood Mobile that will be parked outside 415 Main Street. If you donated in August, you are unable to participate this time around. After you've registered, visit the Intranet to read up on preparing for your appointment.

 BITS is upgrading Broad's telephone service to Dialpad, meaning you'll soon be able to make and receive calls using your Broad phone number anywhere on (almost) any device. Learn about what you can do with DialPad and when it's coming to a phone, mobile device, or computer near you.

 There's a lot more going on. See the CalendarBroad for September 3–6 for more talks, meetings, and special events.

And now let us eat cake. Have a good weekend.

-The BroadCast team

David Cameron

Allison Dougherty

Leah Eisenstadt

Amanda Dykstra Esposito

Corie Lok

Namrata Sengupta

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