Hayden Metsky

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EDUCATION

Massachusetts Institute of Technology 2014–2020
Ph.D. in Computer Science

Massachusetts Institute of Technology 2013–2014
M.Eng. in Computer Science

Massachusetts Institute of Technology 2009–2013
S.B. in Computer Science and in Physics

INDUSTRY AND ACADEMIC EXPERIENCE

Stealth startup Oct. 2024–present
Leading research at an early-stage startup, based in NYC, that builds infrastructure for real-time biosecurity threat detection and response by learning from biological sequence data.

Project Lead • Inceptive Feb. 2023–Oct. 2024

- Led projects advancing design of mRNA-based medicines using machine learning and high-throughput experiments.
- Co-developed and co-led Apprenticeship Program, which hires early-career individuals and provides year-long training in machine learning and biology.
- Co-led company-wide structure for non-technical management of nearly all employees as part of a matrix structure, complementing technical project leads.

Group Leader and postdoctoral fellow • Broad Institute of MIT & Harvard 2020–Feb. 2023

- Raised and managed $1.1 million in independent funding as Principal Investigator. (Relinquished this funding, as well as three tenure-track faculty offers, to join a start-up.)
- Mentored and supervised staff scientists, graduate students, and undergraduate students.
- Developed a machine learning approach to designing viral diagnostics. Published in *Nature Biotechnology*, this study marked the first application of machine learning to that problem and established its effectiveness on CRISPR-based diagnostics. The approach entailed creating: (i) a large-scale training dataset on guide sensitivity for viral detection; (ii) a deep learning algorithm to devise maximally sensitive diagnostic sequences; and (iii) ADAPT, a system to rapidly design diagnostics for any virus factoring in all public genome data. Designs for 1,900 vertebrate-associated viruses are publicly available. In experimental testing, ADAPT outperforms existing diagnostic design paradigms.

Graduate student researcher • Broad Institute of MIT & Harvard 2015–2020
Pardis Sabeti's lab (infectious disease genomics and evolution; computational biology).

- Led a global team to generate the largest and most diverse dataset of Zika virus genomes during the 2015–16 epidemic, and to map Zika's spread across the Americas using these genomes. Published as the cover article in *Nature*, the findings: (i) demonstrated that Zika spread undetected for months, underscoring the need for viral surveillance; (ii) informed Zika virology and public health; and (iii) established viral genome sequencing as a crucial tool for subsequent outbreaks, including COVID-19.

- Developed CATCH, an algorithm that enables sensitive sequencing of highly diverse genomic targets by designing comprehensive, scalable enrichment probes. Applied CATCH to design probes that enrich whole genomes of all human-associated viruses, including all their known variation. In patient and environmental samples, CATCH's probes recover genomes and improve hypothesis-free detection of infections. Published in *Nature Biotechnology*, CATCH has been adopted by US government agencies (e.g., CDC, NBACC) for viral and bacterial pathogen surveillance; by labs for microbe and cancer identification; and by Twist Bioscience for designing target enrichment panels.

Undergraduate and graduate student researcher • MIT Computer Science & AI Lab 2012–2014
Manolis Kellis's lab (gene regulation and epigenomics; computational biology).

Teaching Assistant • MIT 2013–2014
MIT's Design and Analysis of Algorithms (6.046).

- Spring 2014 — Taught sections to 70 students. Student rating: 6.8/7.
- Fall 2013 — Taught sections to 50 students. Student rating: 6.4/7.

Internship in software engineering • Google Summer, 2011

Undergraduate researcher • Broad Institute of MIT & Harvard 2010–2011
Aviv Regev's lab (gene regulation; computational biology).

SELECTED PAPERS

Model-directed generation of artificial CRISPR-Cas13a guide RNA sequences improves nucleic acid detection.

S Mantena, PP Pillai, BA Petros, NL Welch, C Myhrvold, PC Sabeti, **HC Metsky**.

Nature Biotechnology. Oct. 2024. doi:10.1038/s41587-024-02422-w.

Designing sensitive viral diagnostics with machine learning.

HC Metsky, NL Welch, PP Pillai, NJ Haradhvala, L Rumker, S Mantena, YB Zhang, DK Yang, CM Ackerman, J Weller, PC Blainey, C Myhrvold, M Mitzenmacher, PC Sabeti.

Nature Biotechnology. July 2022. v. 40, p. 1123–1131. doi:10.1038/s41587-022-01213-5.

Massively multiplexed nucleic acid detection with Cas13.

CM Ackerman*, C Myhrvold*, SG Thakku, CA Freije, **HC Metsky**, DK Yang, SH Ye, CK Boehm, TSF Kosoko-Thoroddsen, J Kehe, TG Nguyen, A Carter, A Kulesa, JR Barnes, VG Dugan, DT Hung, PC Blainey, PC Sabeti.

Nature. June 2020. v. 582, p. 277–282. doi:10.1038/s41586-020-2279-8.

Combining genomics and epidemiology to track mumps virus transmission in the United States.

S Wohl*, **HC Metsky***, SF Schaffner*, A Piantadosi, M Burns, JA Lewnard, B Chak, LA Krasilnikova, KJ Siddle, CB Matranga, […], P Barriera, S Fleming, S Lett, PA Rota, LC Madoff, BL MacInnis, NL Yozwiak, S Smole, YH Grad, PC Sabeti.

PLOS Biology. Feb. 2020. v. 18. doi:10.1371/journal.pbio.3000611.

Programmable inhibition and detection of RNA viruses using Cas13.

CA Freije*, C Myhrvold*, CK Boehm, AE Lin, NL Welch, A Carter, **HC Metsky**, CY Luo, OO Abudayyeh, JS Gootenberg, NL Yozwiak, F Zhang, PC Sabeti.

Molecular Cell. Dec. 2019. v. 76, p. 826–837. doi:10.1016/j.molcel.2019.09.013.

Capturing sequence diversity in metagenomes with comprehensive and scalable probe design.

HC Metsky*, KJ Siddle*, A Gladden-Young, J Qu, DK Yang, P Brehio, A Goldfarb, A Piantadosi, S Wohl, A Carter, [...], I Lorenzana, L Gehrke, I Bosch, G Ebel, DS Grant, CT Happi, DJ Park, A Gnirke, PC Sabeti, CB Matranga.

Nature Biotechnology. Feb. 2019. v. 37, p. 160–168. doi:10.1038/s41587-018-0006-x.

Field-deployable viral diagnostics using CRISPR-Cas13.

C Myhrvold*, CA Freije*, JS Gootenberg, OO Abudayyeh, **HC Metsky**, AF Durbin, MJ Kellner, AL Tan, LM Paul, LA Parham, KF Garcia, KG Barnes, B Chak, A Mondini, ML Nogueira, S Isern, SF Michael, I Lorenzana, NL Yozwiak, BL MacInnis, I Bosch, L Gehrke, F Zhang, PC Sabeti.

Science. Apr. 2018. v. 360, p. 444–448. doi:10.1126/science.aas8836.

Rapid detection of Powassan virus in a patient with encephalitis by metagenomic sequencing.

A Piantadosi, S Kanjilal, V Ganesh, A Khanna, EP Hyle, J Rosand, T Bold, **HC Metsky**, J Lemieux, MJ Leone, L Freimark, CB Matranga, G Adams, G McGrath, S Zamirpour, S Telford, 3rd, E Rosenberg, T Cho, MP Frosch, MB Goldberg, SS Mukerji, PC Sabeti.

Clinical Infectious Diseases. Feb. 2018. v. 66, p. 789–792. doi:10.1093/cid/cix792.

Zika virus evolution and spread in the Americas.

HC Metsky*, CB Matranga*, S Wohl*, SF Schaffner*, CA Freije, SM Winnicki, K West, J Qu, ML Baniecki, A Gladden-Young, [...], A Gnirke, KG Andersen, S Isern, SF Michael, FA Bozza, TML Souza, I Bosch, NL Yozwiak, BL MacInnis, PC Sabeti.

Nature. June 2017. v. 546, p. 411–415. doi:10.1038/nature22402.

* co-first

A full publication list is on Google Scholar.

SOFTWARE

ADAPT

ADAPT designs highly sensitive and specific viral diagnostics, with a focus on CRISPR-Cas13–based diagnostics. ADAPT employs a deep learning algorithm to devise diagnostic sequences with maximal sensitivity across the full spectrum of a virus's genomic variation. The approach takes into account all publicly available genome sequences for each virus. ADAPT enables a resource of highly sensitive, species-specific CRISPR-Cas13–based diagnostic designs for 1,900 viral species that stay automatically updated to reflect the latest viral variation.

`https://github.com/broadinstitute/adapt`

CATCH

CATCH designs probe sets for targeted enrichment of diverse genome sequences, enabling more sensitive and cost-effective metagenomic sequencing. The probe sets, which comprehensively and compactly reflect extensive genomic variation, improve detection and genome characterization of viruses and other microbes from samples with unknown contents. CATCH employs alignment-free algorithmic techniques to cope with vast sequence diversity. We have used CATCH to design panels that successfully enrich whole genomes of all human-associated viral species and all their known subspecies variation. It has also been applied by groups to generate targeted human viral surveillance panels, as well as agricultural viral, bacterial, and human leukocyte antigen (HLA) typing panels.
`https://github.com/broadinstitute/catch`

TALKS AND POSTER PRESENTATIONS

Designing sensitive viral diagnostics with machine learning

- *Gordon Research Conference on Tropical Infectious Diseases*, Galveston, TX. Talk, Mar. 2023.
- *STAT Open Doors*, Broad Institute. Flash talk, Nov. 2022.
- *HHMI Science Meeting*, HHMI Janelia Research Campus, Ashburn, VA. Poster, Nov. 2022.
- *National Biodefense Analysis and Countermeasures Center*, Fort Detrick, MD. Talk, July 2022.
- *Models, Inference, & Algorithms Initiative*, Broad Institute. Talk, Feb. 2021.

Designing genomics-based tools that surveil and combat pathogens at scale

- *Mt. Sinai Dept. of AI & Human Health Seminar*, Mt. Sinai School of Medicine. Talk, Mar. 2022.
- *BU Dept. of Biomedical Engineering Seminar*, Boston University. Talk, Jan. 2022.
- *BWH-HMS Center for Data Sciences Seminar*, Brigham & Women's Hospital. Talk, Apr. 2021.
- *JHU Dept. of Computer Science Seminar*, Johns Hopkins University. Talk, Feb. 2021.

Metagenomic sequencing techniques for detecting and characterizing pathogens

- *Pediatric Grand Rounds*, Newark Beth Israel Medical Center. Talk, Mar. 2021.

Capturing sequence diversity in metagenomes with comprehensive and scalable probe design

- *MIT-Harvard Microbiome Symposium*, MIT. Poster, Mar. 2019.
- *Virus Genomics and Evolution Conference*, Wellcome Genome Campus, Cambridge, UK. Poster, June 2018.

Genomics-guided pathogen surveillance and outbreak response

- *Bio-IT World Conference & Expo*, Boston, MA. Talk, May 2018.

Sequencing Zika virus and tracing its evolution and spread in the Americas

- *Bauer Forum*, Harvard University. Talk, June 2017.
- *Infectious Disease & Microbiome Program*, Broad Institute. Talk, June 2017.
- *BroadWay*, Broad Institute. Talk, Nov. 2016.

Capture methods for identification and whole-genome sequencing of viral pathogens

- *NHGRI Research Training and Career Development Meeting*, Bethesda, MD. Poster, Apr. 2016.

PATENTS AND PATENT APPLICATIONS

Sample analysis, presence determination of a target sequence
US patent 11,332,783.

Designing sensitive, specific, and optimally active binding molecules for diagnostics and therapeutics
US application US17/065,504.

Crispr system based droplet diagnostic systems and methods
International application PCT/US2019/061577. US application US17/294,179.

Multiplexing highly evolving viral variants with sherlock detection method
International application PCT/US2019/061574. US application US17/294,232.

SELECTED HONORS

Dimitris N. Chorafas Prize 2020
Awarded by Dimitris N. Chorafas Foundation to "the best doctoral student(s) in the hard sciences in each partner university."

Frederick C. Hennie III Award for Outstanding Teaching 2014
Awarded by MIT EECS Department to recognize excellence in teaching.

Anna Pogosyants Award 2013
Awarded by MIT EECS Department to an undergraduate for an "outstanding undergraduate research project" in computer science.

Finalist in Intel Science Talent Search 2009

SKILLS

Scientific project planning and coordination; junior scientist mentorship and management; scientific writing and oral presentation; high-throughput screening and experimental design; genomic sequencing and analysis; machine learning; Python; TensorFlow and PyTorch; git/GitHub.