



Hyperindividualized Treatments

Sixth annual conference on Precision Medicine
June 10, 2020



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Introduction

The sixth annual conference on precision medicine was held virtually on June 10, 2020. It was hosted by Isaac Kohane, chair of the Department of Biomedical Informatics at Harvard Medical School.

The 2020 event focused on hyperindividualized treatments. The discussions were framed by the first example of a hyperindividualized treatment, which shows the immense challenges and potential opportunities of such treatments. Sessions looked at topics such as industrialization and scaling of hyperindividualized treatments, regulation, ethics, resource allocation, and the role for hyperindividualized treatments in common diseases.

Due to the timing of this event, COVID-19 was top of mind and was a thread throughout all discussions. Also, at noon, participants paused for eight minutes and forty-six seconds of silent reflection to focus on racial equity.

Key Themes

Short summaries of each keynote and panel discussion are provided below. Gleaned from all of the sessions throughout this conference are the following major themes about the state of hyperindividualized treatments and the intersection between hyperindividualized treatments and COVID-19.

Individualized care has long been a goal of medicine.

In his opening remarks, George Daley, dean of Harvard Medical School, said that individualized care has long been the crowning glory of medicine. He invoked William Osler, who cautioned his acolytes that the good physician treats the disease, while the great physician treats the patient with the disease. In today's era of precision medicine, it is becoming possible to truly fulfill the promise of individualized care by developing and providing hyperindividualized treatments.

Milasen shows the need for and the ability to develop hyperindividualized treatments.

Julia Vitarello, in the conference's keynote (see more detailed description below), explained the harrowing journey of her daughter Mila. After hitting all developmental milestones for her first few years, at age six—after seeing approximately 100 doctors and

therapists—Mila was diagnosed with Batten Disease, a rare degenerative neurological condition with no treatment. But only one of the pair of mutations known to cause Batten had been found in Mila's *CLN7* gene because she had an ultra-rare variant of an already rare disease.

After having Mila's whole genome sequenced, it was possible to identify the second mutation. Timothy Yu and his team at Harvard Medical School and Boston Children's Hospital then had the idea to develop a custom gene therapy for Mila (termed "milasen"). This was the first time in the world a drug was developed for just one person. This gene therapy has stabilized Mila's condition, though extensive neurological damage had already been done. Publication of Mila's story in the *New England Journal of Medicine* has sparked significant interest in the topic of truly personalized therapies for small groups, or an N of 1.

Mila's story, and the outpouring of interest from families in similar situations with other diseases and genetic mutations, shows the enormous need for and interest in hyperindividualized treatments. The development of milasen also shows that it is scientifically possible to develop individualized treatments.

But with the development of milasen arose other questions—which were discussed at this conference—about how to scale such treatments, how to determine who receives them, how to pay for them, how to regulate them, and more.

Multiple challenges and barriers hinder the development and use of hyperindividualized treatments.

While the need for hyperindividualized treatments is clear and the promise illustrated by milasen is exciting, the challenges and obstacles are many, including major systemic barriers. Among the obstacles are:

- **Not sharing data.** Multiple panelists shared stories of systemic deficiencies that frequently prevent important, relevant data from being shared—for individual patients and for populations.
- **Not working collaboratively.** While there are examples of successful collaboration, too often the players within healthcare, driven by differing incentives, have not worked together collaboratively.

- **Not taking a multi-dimensional view of patients.**

Panelists talked about how in the world of medical specialties, each specialist typically takes their own narrow perspective. Often there is not a multi-dimensional view of individual patients and not a broad view of patients and populations that takes into account social and environmental factors. Part of personalizing medicine is taking a multi-dimensional view, which is often neglected.

- **Not having an infrastructure that can scale hyperindividualized treatments.** Creating one hyperindividualized treatment—as occurred with milasen—is an amazing accomplishment. But to make a difference for the millions of patients who need hyperindividualized treatments, it is necessary to be able to replicate and scale the processes to provide these treatments. This is not yet possible.

- **Not having the ability to determine which patients to treat.** With high demand for hyperindividualized treatments and extremely limited supply, several panelists described the situation as a resource allocation problem and an ethical issue.

- **Not having incentives to motivate and reward innovation for hyperindividualized treatments.** Since hyperindividualized treatments are often for very small populations, including populations with an N of 1, there is not a financial or commercial incentive as the market is not large enough. With such small populations, treatments may not be available or affordable.

- **Not having the ability to regulate hyperindividualized treatments.** Regulatory authorities don't have the resources, the ability, or the inclination to regulate each individual treatment that is developed.

Individually and collectively, these are significant, formidable barriers that must be overcome.

There are ideas to address these challenges and to accelerate the use of hyperindividualized treatments.

For each of the challenges and barriers discussed, panelists identified efforts underway and progress being made to address these issues.

- **Data sharing.** While silos of data, lack of interoperability, and proprietary attitudes have dominated healthcare, multiple efforts are underway to improve data sharing. One example is a COVID-19 data collection project led

by Isaac Kohane and colleagues that has amassed electronic records from thousands of patients from nearly 100 hospitals in five countries. This shows that sharing data across proprietary health records systems is possible and can be used to improve health outcomes.

- **Working collaboratively.** There is an increasing number of examples in healthcare of collaboration among labs, researchers, institutions, and disciplines, and cross-pollination across players including academia, industry, government, and patients. The efforts to develop milasen and multiple COVID-19 initiatives are illustrations that show collaboration is possible.

- **Taking a multi-dimensional view.** While too frequently taking a multi-dimensional view does not occur, it could. And this view could include social and environmental factors. The data and knowledge exist; they need to be considered and prioritized.

- **Having an infrastructure to scale hyperindividualized treatments.** Panelists discussed the concept of building platforms that allow for scaling, along with standards that make replication and scaling possible.

- **Deciding who to treat.** One approach is to develop criteria for who can receive treatments, with criteria possibly including the clinical situation of an individual, the biological plausibility, and a person's support network. In considering these criteria, it is important to address social inequities and to have an independent body making the decisions. An alternative put forth by George Church is to treat everyone by sequencing the whole genome for everyone who wants it. As genetic sequencing becomes more affordable and accessible, he sees this as a realistic option.

- **Thinking broadly about value creation and ways to incent innovation.** Economist Anupam Jena discussed different concepts for thinking about the value of hyperindividualized treatments, including insurance value, spillover value, and option value. (See more detailed summary below for more information.) These concepts and others need to be considered by payers in determining the total value of and payment for these types of treatments. In addition to traditional payers, other entities such as government, academia, and foundations have a role to play in early stages of innovation to prove concepts and pave the way for broader commercialization.

- **Having the ability to regulate hyperindividualized treatments.** Amy Abernethy from the FDA confirmed that the agency already has the authority it needs to support innovation and individualized therapies, like milasen. She explained how the FDA is upgrading its own technology infrastructure to have greater capacity and that while it will not be possible to regulate one individualized therapy at a time, the FDA is developing frameworks and guidance documents. These types of guidance along with practice and standards will allow for both adequate regulation and innovation.

Addressing each of these barriers entails significant work. But the thoughtful ideas and enthusiasm of the panelists indicated that progress and acceleration are possible.

The thinking and activity behind hyperindividualized treatments have the potential to influence the treatment of common diseases.

While much of the conference focused on individualized treatments for rare and orphan diseases, the consensus of the panelists on whether there is a role for hyperindividualized therapy in common diseases was a definitive “yes.”

Efforts are already underway to develop completely individualized treatments for cancer, with Gritstone Oncology developing a personalized vaccine that could be used to treat lung, gastric, and colorectal cancer. Also, more personalized treatment paths for cardiovascular disease are being developed that take genetic information into account.

Some insights related to hyperindividualized treatments are relevant to treating COVID-19.

The timing of this conference, amid the global COVID-19 pandemic, raised questions about whether there is overlap between hyperindividualized treatments and COVID-19. There is definitely overlap in areas such as the need to share data, be more collaborative, and look at patients with a multi-dimensional view that considers all medical disciplines as well as social and environmental factors.

There is also overlap in analyzing data to understand all possible treatment options and using this data to develop personalized treatment recommendations for different patients (or segments of patients) using existing drugs or a combination or cocktail of existing drugs.

However, an alternative view, expressed by Mark Namchuk, is that to broadly deploy an antiviral or antibiotic treatment at scale on a global basis, it is desirable to not depend on genetic predeterminants and instead to focus on the virus itself, not the patient. Still, there are many similarities in the approaches for dealing with COVID-19 and for providing hyperindividualized treatments for a multitude of diseases.

Session Summaries

Welcome & Introduction

Isaac Kohane, DBMI Chair, Harvard Medical School

At the first Precision Medicine Symposium, Professor Matt Might said data is the most powerful therapy of the 21st century. Those words are relevant for both hyperindividualized therapies and COVID-19. When we have the right data and the right instrumentation, we are able to accelerate the development of treatments. “The conference goal that we have every year is to accelerate change by bringing data together to treat patients appropriately,” said Kohane.

Opening Remarks

George Daley, Dean, Harvard Medical School

Dean of Harvard Medical School George Daley shared opening remarks at this unique moment. He described COVID-19 is a once-in-a-century global health crisis that has created new epidemiologic, scientific, and clinical challenges, and has raised existential questions about models of healthcare delivery and about health inequalities. However, Daley noted that while COVID-19 has dominated our attention, other scientific challenges are still with us—such as hyperindividualized medicine.

Daley cited commonalities between challenges posed by COVID-19 and hyperindividualized medicine. In both situations, patients present with a biological mystery. While the tools and techniques to solve the mystery may differ, what is common is the need to build bridges across labs, researchers, institutions, and disciplines along with cross-pollinations across academia, industry, government, and citizens.

In Daley’s experience, individualized care has always been the focus of medicine. With hyperindividualized treatments—with one medication for a single patient—questions arise about feasibility, replication, scaling, regulation, manufacturing, and costs.

How the health system has responded to COVID-19 provides, in Daley’s view, a cautionary tale for hyperindividualized treatments. With COVID-19, there are knowledge, tools, and expertise. But systemic problems cause us to know less than we should. For example, the global medical community has not taken full advantage of the data in electronic medical records.

“We have the knowledge, expertise, and capacity to define the biology of disease and design treatments. But it seems to me that we have serious pain points in the systems designed to translate, operationalize, and deliver the benefits of this knowledge.”

— GEORGE DALEY, HARVARD MEDICAL SCHOOL

Daley cited Harvard Medical School’s mission in dealing with the challenges that are faced, whether in the form of a novel pathogen or an unknown genetic disease. He stated that our collective charge is to generate new knowledge and harness it into therapies that transform human lives for the betterment of all.

Keynote Address

Julia Vitarello, Founder and CEO, Mila’s Miracle Foundation

Julia Vitarello told the story of her daughter Mila and the development of the world’s first truly individualized treatment. Mila Makovec was born on November 5, 2010. When she was born, she was strong and healthy. As a toddler, she walked, ran, talked, and met all developmental milestones. She was a healthy, normal kid.

At age three, things began to change. One of Mila’s feet turned inward, she walked strangely, and got stuck on words. At five, she began to have issues with her vision and speech, began to fall, and exhibited other symptoms. Visits to about 100 doctors and therapists yielded no results. No one could explain what was happening. Doctors said Mila was normal and would outgrow these problems. (Some mentioned the chance of something genetic, but said it was so rare, it was not considered.)

During this time, Vitarello kept a list of Mila’s symptoms, which grew progressively worse.

In a matter of weeks at age six, Mila got precipitously worse, which led Vitarello to take her to Children’s Hospital Colorado. After extensive tests, including a genetic panel, Mila was diagnosed with Batten Disease, a rare, horrible, neurodegenerative genetic condition.

Vitarello began reading everything about Batten Disease, speaking with other parents, and talking with scientists, and started a foundation. She realized it was necessary to find a lab to do whole genome sequencing to fully understand Mila’s variant of Batten Disease. A recessive disease requires that a mutation be inherited from both parents, but tests had so far only turned up one mutation for Mila. Through networking on Facebook, Vitarello was put in touch with Timothy Yu, a neurologist and geneticist at Boston Children’s Hospital, who agreed to sequence Mila’s genome and to try to help her.

After sequencing and analyzing Mila’s whole genome, Yu and his team found the second mutation. Yu had an idea. Inspired by the success of the gene therapy Spinraza for children with spinal muscular atrophy, Yu imagined making a Spinraza-like treatment just for Mila, targeted to her mutation.

Since Mila was rapidly declining, “The risk of not treating her was incredibly obvious,” said Vitarello. And, the drug developed for Mila seemed promising enough to give it a shot. As Vitarello shared, “This was an incredible opportunity for Mila that I never thought she would have.”

The drug that was developed—named milasen in honor of Mila—was given the green light by the FDA. After rigorous testing and animal studies, Mila received her first dose in January 2018.

“This was the first time in the world where a drug had been customized to one person and had never been given to another human.”

— JULIA VITARELLO, MILA’S MIRACLE FOUNDATION

Mila, now nine years old, is two and a half years into receiving milasen. In the first year of treatment, her disease stabilized. For example, the frequency and severity of her seizures dramatically declined. However, progress has since stalled. This is not surprising since the disease was already quite progressed.

Mila's story was published in the *New England Journal of Medicine*. This has inspired thousands of families touched by a rare disease, who are looking for a similar treatment path. Currently, gene therapy is promising but is the only tool in the toolbox—and requires a great deal of time and money. Hyperpersonalized treatments have the potential to cut across rare diseases for which there is no treatment.

Together, Vitarello and Yu have started a foundation to make hyperpersonalized treatments like Mila's accessible across many rare diseases. This requires collaborating, sharing data, focusing on funding models, and educating physicians.

PANEL 1 — How do we scale up? What is the path to industrialization?

David Shaywitz (moderator), DBMI, Harvard Medical School
Amy Abernethy, FDA
Arnaub Chatterjee, AcornAI, Medidata
Amy DuRoss, Vineti
Anupam Jena, Harvard Medical School

David Shaywitz led a diverse panel of experts who examined the challenges with scaling up hyperpersonalized treatments. Amy DuRoss discussed operational challenges; Arnaub Chatterjee looked at data management issues; Amy Abernethy discussed regulatory hurdles; and Anupam Jena looked at economic considerations.

Vineti, explained DuRoss, is an enterprise software orchestration platform for personalized medicine. Vineti is focused on creating an infrastructure and a platform to scale out mass customization. The company provides the “connective tissue” that ensures an automated chain of identity, chain of custody, and chain of condition. This ensures that the right patient receives the right therapy at the right time. A big part of Vineti's value proposition is to create and promulgate standards, ranging from data standards to process standards to standards in areas such as labeling. A platform and broadly adopted standards are important elements to scaling and commercializing.

“The infrastructure is struggling to keep up with the pace of discovery. . . . There's a fundamental belief behind Vineti that if you can put smart plumbing in place, then you can really hasten true access to patients.”

— AMY DUROSS, VINETI

Amy Abernethy of the FDA agreed with the importance of standards to support industrialization, including data standards, interoperability standards, and more. An additional type of standard is a systemic regulatory framework, including a checklist, which ensures that all key topics are addressed, such as safety and manufacturing scrutiny. As Abernethy said, “A framework is an additional kind of standard. Frameworks allow us to scale from a regulatory perspective.”

AcornAI is a company aiming to be an enabler of data science to bring hyperindividualized treatments to patients and the market. AcornAI is part of Medidata, which manages data on behalf of pharmaceutical sponsors and academic institutions for about 22,000 clinical trials involving 6.3 million patients. This is part of the progress underway among pharma companies to build out data sets, data science capabilities, and data-enabled drug discovery. Data-focused activities also include using data science in carefully selecting patients for clinical trials. The key to scaling up these data activities is making data auditable and traceable, and building trust.

“How we scale this? We have to make data auditable and traceable and qualified and still build that trust.”

— ARNAUB CHATTERJEE, ACORN AI, MEDIDATA

Scaling also requires wrestling with the idea of value. Anupam Jena said that estimating value in healthcare is always difficult. One tool that has been developed and is often used is a QALY, a measure of a quality adjusted life year. But with highly specialized therapies, thinking about value is even more difficult. Three ideas to consider are:

- **Insurance value of medical innovation.** If a person has insurance for their house, the insurance pays for the house to be replaced due to a fire. Obviously, the person with the insurance benefits, but individuals also receive value even if their house doesn't burn down, just by knowing they have insurance. The same logic applies to therapies that affect few people. People receive value from the possibility that a therapy would be available if necessary for them or a loved one. The insurance value of medical innovation is probably around 10% of the value.

“There's value that comes to us that is meaningful from therapies that we hopefully will never have to use.”

— ANUPAM JENA, HARVARD MEDICAL SCHOOL

- **Spillover value of medical innovation.** This is value that extends beyond the person receiving a treatment to family members, caregivers, employers, or others who benefit in some way. This is value that should be measured and considered for any therapy.
- **Option value.** This is considering the value created by extending a person's life so that they have the possibility of receiving another, additional, better treatment.

It is important to think about value in healthcare holistically because value is a key factor in making decisions about allocating scarce resources and in deciding where to invest public and private funds. Thinking broadly about value is necessary in contemplating scaling.

In thinking about scaling as a regulator, Abernethy said the FDA has to be efficient and scaled to manage the increasing demands it faces. There are already over 900 Investigational New Drug applications (INDs) for cell and gene therapies and the FDA expects to be approving 10 to 20 cell and gene therapies each year for the next several years. This requires working fast. To deal with these demands, the FDA is putting in place a modern cloud infrastructure, is working to increase efficiency and reduce grunt work, and is making sure the agency has adequate scientific expertise.

“We’re going to need to work fast and keep the evidence development and diligent regulatory activity going for a long time. And so, at the FDA, we need to be ready along with you. That’s one other aspect of scaling that is quite important for our future.”

— AMY ABERNETHY, FDA

Fireside Chat

Amy Abernethy, Principal Deputy Commissioner and Acting Chief Information Officer, FDA

Amy Abernethy responded to questions from Isaac Kohane about the regulation of hyperindividualized therapies and the FDA's response to COVID-19. Among topics Abernethy discussed were:

- The FDA already has the authority it needs to support innovation and individualized therapies. The FDA can work within the laws in place.

- The FDA defines its thinking through frameworks and guidance documents. There has been a great deal of guidance related to cell and gene therapies.
- It will not be possible to regulate therapies, one therapy at a time, that may be appropriate for only one or several people. A more practical approach is to look at platforms where a customized therapy sits on top of a platform. Platforms are a more scalable approach, which allows regulatory streamlining.
- Practice leads to standards. With standards, there is more effective, efficient communication.
- Real-world data is extremely important. With rare diseases it will be necessary to rely on high-quality natural history to provide benchmarks and to bring in data from multiple sources. Also, longitudinality is important. It is also possible for data to be small (with cohorts of only 30 or 60) but mighty; data can be mighty if it is deep and longitudinal. Ideally real-world data will include case notes to fill in understanding. This combines the quantitative and qualitative.
- How to right-size sequencing? A way to think about this is: 1) what information is clinically actionable for a patient right now? (this is probably not broad sequencing for an individual patient, as it is not immediately actionable); 2) What information points a clinician and a patient to the future? and 3) What information has service beyond this particular patient?
- The FDA is responding to COVID-19 by prioritizing its work and quickly reviewing the influx of incoming INDs for repurposing drugs. The FDA uses regulatory flexibility where appropriate.
- The majority of articles submitted in medical journals right now about COVID-19 are not well done, randomized clinical trials. They are analyses of EHR data or small cohorts where people are trying to make assessments that have clinical impact but are not based on credible evidence.
- The FDA thinks about regulating medical products, not the practice of medicine.

PANEL 2 — How do we decide who to treat?

Isaac Kohane (moderator), Chair, DBMI, Harvard Medical School
 Mildred Cho, Stanford
 George Church, Harvard Medical School
 Timothy Yu, Boston Children's Hospital
 Julia Vitarello, Mila's Miracle Foundation (Q&A portion)

Timothy Yu commented on developing a hyperindividualized drug for Mila and offered thoughts on deciding who to treat. The other panelists shared their perspectives on this question.

The drug developed for Mila uses the same chemistry as other FDA-approved drugs, but a different sequence. This approach of developing and using platforms for drugs represents a new approach to provide customized treatments, quickly and efficiently. However, the experience of developing milasen for Mila—truly an N of 1—is still a “clinically unproven good.” More examples and practice are needed to develop standards.

When the article about milasen was published in the *New England Journal of Medicine*, inquiries from more than 200 groups poured in. This caused Yu and his team to think about what created the unique opportunity to intervene with Mila. There were three unique features:

- Clinical motivation: Mila had a progressive, devastating disease with a high medical toll. The risk of not trying was greater than the risk of trying.
- Biological plausibility: It was a biologically simple condition—a single gene mutation—with a scientifically feasible fix.
- The treatment was for a small population, an N of 1.

These features lead to criteria for considering similar opportunities, which include:

- Single-gene disorders that are very severe for which there are no existing treatments. This requires having the right type of mutation and sufficient natural history data.
- Small populations.
- Having a family that understands the risks and is able to provide monitoring.

Boston Children's Hospital is setting up processes to evaluate opportunities that include an oversight committee. Also, Yu and Julia Vitarello have created a foundation to provide assistance to stakeholders who are pursuing such opportunities.

Mildred Cho sees the question of deciding who to treat with hyperindividualized treatments as an ethical question, for which there is not an existing framework. She sees this question as a resource allocation issue and a justice issue. An important consideration is whether the context is research or clinical care. Cho stressed the need for fair distribution of potential benefits and potential harms. She also emphasized the need to learn from others' experiences, to collect and analyze pooled data, and to collaborate in a more systematized way.

“We need to really consider new ways of evaluating anticipated risks and benefits to open up the treatment path. . . . It must be a broadly, publicly supported endeavor to fulfill societal obligations to create fair benefits.”

— MILDRED CHO, STANFORD

George Church doesn't see the question of who to treat as a resource allocation problem. His answer of who to treat is “everyone.” And he wants to get there as quickly as possible. Church's solution is to start with whole genome sequencing. With the cost of sequencing coming down, it will soon be conceivable and affordable to sequence everyone's genome who wants it, along with genetic counseling at various stages. This eliminates resource allocation issues, could prevent trillions of dollars in spending, and would be humane and equitable. This could lead to the ultimate form of prevention. Insurers and payers would have incentives for this idea as it will help reduce costs.

In the absence of widescale whole genome testing, resource allocation is a major issue since there are not commercial incentives to make drugs for orphan diseases, as there are too few patients. This is an area where academia, nonprofits, foundations, and government may need to step up.

PANEL 3 — Is there a role for hyperindividualized therapy in common diseases?

Isaac Kohane (moderator), Chair, DBMI, Harvard Medical School
Pradeep Natarajan, Mass General Hospital
Linnea Olson, cancer survivor, patient advocate and activist
Stanley Shaw, Harvard Medical School
Roman Yelensky, Gritstone Oncology

The panelists discussed how thinking about hyperindividualized therapies can play a role in treating common diseases such as cardiovascular disease and cancer.

Cardiovascular disease is the leading cause of death in the United States and the leading cause of premature death worldwide. Researchers such as Pradeep Natarajan are looking at risk factors for a first heart attack, trying to understand the role of genetics, and then trying to understand whether those risk factors can predict specific therapies. One surprising finding from observational work is that individuals who were genetically predisposed to coronary artery disease to a high degree had a greater absolute and relative benefit from statins. Many of these individuals with a high genetic risk are not recognized by current clinical paradigms as benefitting from statins. This isn't necessarily a hyperindividualized therapy but is an example of using genetic information to guide a therapeutic decision.

“Surprisingly, we observed that individuals who were specifically genetically predisposed to coronary artery disease to a high degree had a greater absolute and relative benefit from statins.”

— PRADEEP NATARAJAN, MGH

More of a hyperindividualized therapy is what Gritstone Oncology is developing for cancer. Gritstone's therapeutic hypothesis is to immunize with neoantigens to provide T-cell responses that go on to eliminate tumors. The product Gritstone has in development is a truly personalized therapy for each patient. Gritstone is currently looking at this treatment for lung cancer, gastric cancer, and colorectal cancer.

“The product we have in development in phase 1 clinical trials is called Granite. It is a personalized neoantigen cancer vaccine. It is really a completely individualized treatment for a common cancer.”

— ROMAN YELENSKY, GRITSTONE ONCOLOGY

Linnea Olson is a cancer patient and advocate with a rare form of the disease, who was told in 2008 she had 3-5 months to live. She has received targeted therapies that have been successful for her mutation and is now in her fourth phase 1 trial. As she has continued to survive, she has become part of a smaller and smaller group of patients. There are not a lot of financial incentives to explore treatments for this group.

For anyone diagnosed with lung cancer, Olson recommends extensive genomic profiling. She also observed that the terms “personalized medicine” and “targeted therapies” are misnomers and are a blunt hammer. She said, “I'm hoping that as we have access to more information, it truly can become personalized even in the trial stage.” Isaac Kohane termed this a recommendation for even more hyperindividualization.

Increasing the use of gene therapies and hyperindividualized treatments is going to require significant education for all types of stakeholders.

“My thesis is that we're going to need education of different kinds for stakeholders across the ecosystem.”

— STANLEY SHAW, HARVARD MEDICAL SCHOOL

Stanley Shaw cited research showing that more than half of practitioners responding to a survey had one to five patients with a new rare disease diagnosis in the last year. Still, there is low awareness among physicians about gene therapies, cell therapies, and DNA- or RNA-based therapies.

PANEL 4 — COVID-19 Therapeutics

Galit Alter (moderator), Harvard Medical School
 Russ Altman, Stanford
 Albert-László Barabási, Northeastern University
 Paul Farmer, Harvard Medical School
 Mark Namchuk, Harvard Medical School

The final panel looked at what can be learned from the assessment and treatment of COVID-19 that is relevant to hyperindividualized treatment. There are some areas where the panelists see significant overlap and other areas where there are major differences. A major theme is using data to find existing drugs or combinations that can improve results for individual patients, while awaiting new vaccines and treatments.

A key area of overlap, emphasized by Paul Farmer, is the need for a multi-dimensional view that includes social conditions. This is extremely important, as social conditions and social inequities are often not adequately considered when analyzing either infectious diseases or precision medicine.

“To have truly precision medicine, we are not going to be able to look at the pathogen to describe its radically varied course in different populations . . . we really do need to look at conditions that are not readily and not often studied in medicine.”

— PAUL FARMER, HARVARD MEDICAL SCHOOL

Albert-László Barabási terms himself a “network scientist.” He uses network-based tools to predict the impact of existing drugs and to design new drugs. His fundamental thesis is that nothing that happens in a cell happens in isolation; everything is interconnected. He said, “You must account for that interconnectivity to really think about how a disease emerges and how do we intervene to cure it.”

The tools of network medicine allow defining a disease module and identifying drugs and drug combinations that have the potential to perturb a disease. This eventually leads to personalized network medicine (or what others term “precision medicine”).

When COVID-19 hit, Barabási began using network medicine tools to rapidly identify existing drugs that could be repurposed for COVID-19. Starting with the targets of the SARS-CoV virus and about 320 human proteins, his team identified 7,500 approved drugs. Using three different methodologies, his team prioritized about 80 that are potentially clinically relevant. Hopefully clinical trials will begin on some of these. The lesson here is that a rapid methodology can test any drug for its potential relevance to COVID-19. This can be a model not just for COVID, but also for other diseases.

“We have a very rapid methodology now to test any drug for its potential relevance for COVID . . . and I think this will be a model not only for COVID but also for future diseases.”

— ALBERT-LÁSZLÓ BARABÁSI, NORTHEASTERN UNIVERSITY

Russ Altman is a biomedical informatician, a data scientist, and an AI person. He and his team focus on looking at the data—and first categorizing data in groupings such as variations in the virus, environmental factors, and genetics. Data can provide correlations and can be used to generate hypotheses.

“The task is to look at correlations and mechanisms to try to understand what we might be able to focus on in an individual in order to give them the best chance at success in going through with this disease.”

— RUSS ALTMAN, STANFORD

Altman’s team is working with UnitedHealth Group, which has claims and lab records on about 90 million people. His team is able to look at what drugs patients were on to look for evidence about drugs that might be protective or risky. This could potentially lead to more hyperindividualized treatment for COVID.

His team is also working in collaboration with the University of Western Australia on trials for early intervention, which can involve a cocktail of drugs. This is not a cocktail for the entire population, but drug cocktails tailored to individual patients.

A different view was expressed by Mark Namchuk. He said that in dealing with an infectious disease on a global scale, “The precision can’t be in understanding the patient response; the precision has to be in the molecule.” Historically, the most successful way to treat a virus has been to design molecules specifically to go after viral targets expressed by the virus. With this in mind, the probability of success goes up if efforts are constrained and focused on the virus. In the future, the best approach is to design drugs with a broad spectrum of action.

“One of the challenges with an antiviral or antibiotic is that to deploy worldwide, you hope to deploy something that does not depend on the genetic predeterminants. . . . As a goal, to make something broadly deployable, you need to go to the highest common denominator of the biology, which my argument would be, is the virus itself.”

— MARK NAMCHUK, HARVARD MEDICAL SCHOOL

The panelists were in general agreement about working aggressively to repurpose existing drugs in the short term while focusing on the virus and molecules in the longer term. While working to repurpose treatments, there may be an opportunity to tailor treatments for patients from an arsenal of existing drugs. Also, panelists stressed the importance of adding precision medicine to the front end of drug development, not just to the back end.