Sarah Alger: Welcome to Proto, the podcast that explores the frontiers of medicine. I'm Sarah Alger.

Dr. Harry Orf: And I'm Harry [Orf 00:00:12]. In less than a year, researchers have been able to create viable vaccines for the COVID-19 virus and establish effective treatments for people with severe infections. This is an historic achievement for the medical research community.

Sarah Alger: But the COVID-19 pandemic isn't the only risk to human health. For the past year, research teams have also tried to move their work forward on hundreds of other fronts, sometimes against daunting headwinds.

Dr. Harry Orf: How have the constraints of the pandemic affected medical research, and what lessons will we take from the past year as we look to the future?

Sarah Alger: The research year that was, coming up on this episode of the Proto podcast, brought to you by Massachusetts General Hospital.

From the news coverage, it can seem as if the COVID-19 pandemic and the heroic efforts to contain it have been the sole focus of the international research community, but work on other promising frontiers has also made incredible strides. Across the globe, teams have continued to expand our knowledge of the mechanisms behind cancer, test treatments for neurological conditions, and map out new vaccines for pathogens other than the Coronavirus. Some of the discoveries have been extraordinary. A team from the [Ragon 00:01:32] Institute of MGH, MIT and Harvard identified how some people infected with HIV are able to effectively quarantine the virus within their own genes, opening a new door to a functional cure. The universal flu vaccine took several important steps forward, an advance that could save tens of thousands of lives each year.

But research during the pandemic has been anything but business as usual. Here to discuss the challenges and successes of the past year is Dr. Harry Orf. Dr. Orf began his career as a researcher in bio organic chemistry. In 1983, he became the first director of molecular biology laboratories at MGH. And after a number of interesting career turns, including a stint as an Army Colonel in Operation Iraqi Freedom, returned to serve as the Senior Vice President for research at MGH, which hosts the largest hospital [east 00:02:27] research program in the country. Dr. Orf, welcome.

Dr. Harry Orf: Hi Sarah. Glad to be here.

Sarah Alger: I'd like to start us at the beginning of the pandemic. When cases began to rise and the first distancing measures were announced, what was the reaction from the MGH research community?

Dr. Harry Orf: Well, I think, Sarah, in a phrase, the reaction was how can we help? Our virologists, our geneticists, our infectious disease researchers, they all immediately began to look at what they could do with respect to the virus. For example, we formed a clinical trials committee that reviewed applications from our researchers to explore various parts of the COVID infection. In fact, there were over 330 clinical trials approved, 23 of these were therapeutic trials and a lot of progress was made.

And at the very beginning, the Ragon Institute had several of their investigators really lead the way toward the ability to develop vaccines. For example, Aaron [Schmidt 00:03:36] identified on sequences, spike protein on the virus, which then allowed Galit Alter also in the Ragon Institute to develop an antibody assay. And then that allowed another investigator, Dan Barouch to test the vaccine for antibody generation. So a lot happened in immediate period after COVID was realized as a [too 00:04:01] potential threat.

Sarah Alger: One of the ways that the National Institutes of Health decided to quickly fund projects was to offer what they called administrative supplements to existing projects they'd already approved. The idea was that some teams might be able to quickly pivot their existing work, to focus on COVID-19. What kind of teams would those be, and did you see any of that happen at MGH?

Dr. Harry Orf: We saw a tremendous amount of it at MGH and most of the people who pivoted immediately were obviously those associated with immunology and infectious disease. All in all, we had 127 COVID related grants come to Mass General in that short time period, once NIH announced the supplements. The total amount of money we received from the federal government was almost $58 million. And in all, in addition to that, a total of about $75 million when you count additional money from foundations and in the end so far at the end of 2020, we had published over a thousand articles on COVID.

Sarah Alger: I'd like to talk about what the pandemic has meant for research that couldn't easily pivot to COVID-19 such as clinical trials. To what degree were those interrupted and how has that changed over the past year?

Dr. Harry Orf: Well, that was a real issue. Clinical trials, that involved research subjects, much like patients were interrupted. And in fact, the only clinical trials that we were allowed to continue with those that were so-called therapeutic, that is when a research subject was actually getting treatment for their condition in the trial itself. So those continued, but what also we saw is that many of our trials that could be conducted virtually we're switched so that our clinical research coordinators conducted virtual visits with our research subjects over Zoom or some other medium.

Sarah Alger: What about nonclinical laboratory research? How was that affected early on and has that changed?

Dr. Harry Orf: Well, first of all, early on in mid March, we had to totally shut down our laboratories. And that was a major undertaking for us. We had over five months of both total and then partial shutdown. But one of the nice things that happened here, really a critical thing is that the NIH allowed people funded on research grants to continue to be paid, even though they were not allowed to work, only remotely. So what happened is our people for that period of time when we were totally shut down, they switched to remote work. They continued researching the literature, writing grant applications, writing papers. And in fact, in 2020, we saw continued production that surprisingly was a result of the ability to continue to work remotely during that shutdown period.

Sarah Alger: I wondered if you could talk about the folks who did have to come in and keep vital things going such as keeping cell lines alive.

Dr. Harry Orf: Yes. Actually, the first thing we did when we saw that we were going to be shut down except for critical research and for COVID research is that we identified over 200 people across our system that we designated as COVID safety officers. These people came in, they maintain the cell lines, they maintained the operations of the lab and they set the laboratories up to be ready for researchers to return, that is they placed hand sanitation stations. They placed up maximum occupation limits on the different rooms. And then simultaneously, to the work that the COVID safety officers did, we had our principal investigators submit work plans as to how they would have their researchers come back and maintain universal controls and work safely. Many of them submitted work plans that showed staggered shifts of people coming in early morning or late evening so that their work can continue with less personnel density in the labs themselves.

Sarah Alger: I'd love to talk about some of the successes to come out of 2020. What's some of the most interesting non COVID research you've seen come out of the hospital during the pandemic?

Dr. Harry Orf: Well, there's a long list. Just to mention a couple of the highlights. I think the work with CRISPR and gene editing to treat disease continued unabated, a ton of new discoveries in imaging to help us quote unquote, see disease in real time occurred during this period, a lot of progress on the microbiome's role in disease was made. I'm sure you remember the ice bucket challenge and the funding that was gained there allowed combination drug treatment much like was developed for HIV to be developed for ALS. And we think that's going to be a breakthrough in hopefully the treatment and slowing of the decline of people with that disease. And I think also CAR-T therapy that is gene and cell therapy, is really beginning to now come into its own as a potential treatment for cancer and other diseases. So just a lot going on.

Sarah Alger: The pandemic also saw some broader collaborative innovations happen in the past year. Paywalls fell for journals. Data in some cases was more widely shared. And we saw collaborations between rival institutions. Do you think any of these will outlive the pandemic?

Dr. Harry Orf: Oh, I'm sure they will. I can just cite a couple of examples across the Mass General Brigham system. Mass General and Brigham Women's Hospital came together to form the Mass General Brigham Center for COVID Innovation. That was an amazing, amazing development where over 120 researchers came together under the leadership of Gary [Tierney 00:10:36] from Mass General and Dave [Walt 00:10:38] from Brigham to basically develop new tools for the clinicians to use in COVID. They formed over 20 working groups and they had over 2000 investigators helping in all aspects of this work and they developed new devices. And they also, for example, validated the process that brought the Battelle N-95 sterilization unit to Massachusetts. So a tremendous amount of collaboration developed around the need to do so.

The other one, I think to cite, was a statewide one called the Mass Consortium for Pathogen Readiness that was stood up. And this was stood up, led by people from Harvard and the Ragon Institute with participation from other hospitals in the area. And they have again done a tremendous amount of work on testing vaccines and the testing itself.

Sarah Alger: Is there any other kind of change that you hope will outlast the pandemic?

Dr. Harry Orf: One thing that we really observed that was very favorable, was the dramatic reduction in the turnaround time of getting approvals done. Agreements were done more quickly. Protocols were reviewed and approved much more quickly simply because they had to be. There was an urgency to it. And now that we've devised these means to do things more efficiently, I hope that we'll be able to keep those short timelines as we go forward and not revert back to the longer times it has taken us historically to get administrative approvals done.

Sarah Alger: Another upheaval in 2020 was a national accounting of racial bias, which has also shaken the hospital. We've seen a number of pieces from MGH researchers about how we can spot and adjust for racial bias in healthcare. How has that conversation affected the work of the Research Institute?

Dr. Harry Orf: Well, MGH has done a lot as has the Research Institute itself. The hospital recently published a plan, a structural equity 10 point plan, and this is now being realized under the office of Joe Betancourt, who was recently named the new senior vice president for equity, diversity, and community health. The hospital has given his office now, new resources and new employees to devote across a research enterprise, for equity and inclusion purposes.

Within the Mass General Research Institute itself, we formed actually over a year ago, a task force on equity and respect in the research workplace and our animal care group which has a staff of over 130 people, many of them consisting of underrepresented minorities initiated a specific program called Be Better to sensitize that workforce toward the concerns of racial bias and the opportunities to improve equity and diversity.

Sarah Alger: I wonder if you can talk about how your military experience has guided your leadership of this vast research enterprise during this crisis.

Dr. Harry Orf: That's a great question, Sarah. Actually being in the army reserve as I had been for 34 years, military leadership education is required at every level as one progresses through the system. So my entire concept of leadership was really formed by what is taught in the military. And there, I think their programs really allow you to understand the importance of communication, the importance of actually leading by example, and specifically the see one, do one, teach one. You really need to know the elements of what you are instructing and having other people do before you can confidently lead them in doing it. And it's that element of the military education in leadership that I carried with me and I try to be as communicative and open with my people as possible. And also to some extent, be a cheerleader for them. Being a motivator is a big component of military leadership, and you motivate by being as much a cheerleader as you are a mentor.

Sarah Alger: As you and your fellow researchers talk about the pandemic in the years ahead, what will you remember most about this time?

Dr. Harry Orf: I would say we'll remember that we answered the call. I think the work that was done on COVID innovation, the cooperation across our entire research community and with other researchers across our system and across the hospital, I think will be one of the most memorable aspects of this really difficult time. I'd also mention that over 300 members of our research family volunteered to help out during the surges and working in clinical areas. So it was a true team effort and research played its part to help the hospital get through these difficult times.

Sarah Alger: Thank you, Doctor Orf.

Dr. Harry Orf: Thank you, Sarah.

Sarah Alger: And listeners, thank you for tuning in to the Proto podcast.

Dr. Harry Orf: Today's podcast was produced by Emily Silver, Bradley Klein, and Jason [Heckey 00:16:23].

Sarah Alger: Thanks also to our technical directors, Adam Keller and Chelsea Andes. Subscribe to the Proto podcast on iTunes and Stitcher and follow us on Facebook, Twitter, and Instagram. Stay safe and see you next time.