The Scientists

The Ebola fighters in their own words

Dec. 10, 2014

Thomas Geisbert, 52

Virologist who conducted the first trials of the drug TKM-Ebola

Bryan Schutmaat for TIME

During the 1990s, a biowarfare expert named Ken Alibek defected from the Soviet Union and testified to Congress that the Soviet Union had been working on developing Ebola as a weapon. I was a virologist, and I was working at U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) in western Maryland, not far from where I grew up. At the time, the only biosafety level 4 (BSL4) labs in the U.S. were at the CDC and USAMRIID, and there was interest from the Department of Defense to study Ebola. We certainly were doing things to develop different countermeasures like vaccines, treatments, and we were trying to understand the virus.

That got us to a point—to the point of taking some of the better ideas and showing that they worked or didn't work. But that's where it stopped. There wasn't money or interest or time to take those products across the finish line.

But I've never been somebody who toes the line. I just looked at Ebola as a challenge. I'm not the kind of scientist who sits at a desk. I've got to be in the middle of it, in the space suit in the lab, in the thick of it. When I do this work, I take it personally. You go through all those times when it doesn't work, it doesn't work, it doesn't work, and it's so frustrating, so mentally draining, so demeaning, physically and mentally.

But after 9/11, everything changed. There was increased funding. It was fortunate for me, because Ebola was my main area of interest. When all the money became available, we started looking at developing a vaccine. The idea came from Heinz Feldmann, then at the Public Health Agency of Canada (now at the National Institute of Allergy and Infectious Diseases), and the first big success we had was in 2002 or 2003. We did two back-to-back studies, and this was the first vaccine that completely protected monkeys from Ebola.

Everything about the disease in monkeys is so much like in humans. So even though you can't say for 100% it's going to work in humans, you know the odds are 99% that if it works for monkeys, it will probably work for people.

I remember walking in that room where I was used to seeing dead monkeys, and five, six, seven, eight, twelve—all the monkeys are healthy, no signs of disease. In my field and what I do, that's the greatest feeling you can imagine.

When I started doing some of the first studies [on drug treatments] in the '90s, I would get excited because something I tried worked in guinea pigs or mice or something. Then you'd get excited: "Oh man, this is going to be great." But there's a quantum leap from rodents to nonhuman primates like monkeys. It turns out rodents aren't very good models for Ebola infection. All of a sudden you do it in monkeys, and all of the monkeys died. We had so many failures in the 1990s. It was a terrible feeling.

I've got shelves and shelves and shelves and shelves of stuff that slow or inhibit growth of Ebola in culture. Dozens of those protect mice or guinea pigs. Only two worked in nonhuman primates, out of all the studies done in the BSL4 lab—and those are ZMapp done by Gary Kobinger in Canada and TKM-Ebola, which I worked on with biotech company Tekmira.

When you do have success, like when we did the TKM-Ebola study, there is no greater feeling. There is no greater feeling than walking in when you know it's going to work, you've got healthy animals—that feeling is awesome. When we did our first study with TKM-Ebola on monkeys, I was like, It would be good if we get 50% protection, it's a home run. I didn't expect 100% protection.

In this Ebola outbreak, we know at least four to five people got the TKM drug, and all have survived. But we don't want to say the drug was the reason they survived. While we hope they helped in patients, we can't say for sure because the patients got so many other things. There are so many confounding variables, so how can you say any one thing made the difference?

But it's a great feeling knowing I was involved in the development of something that hopefully saved somebody. And if it saved one person, it matters. *—as told to Alice Park*

Dr. Peter Piot, 65

Co-discoverer of Ebola

In our lab at the Institute of Tropical Medicine in Antwerp we saw the Ebola virus for the first time on the 10th of October in 1976. We received one of those shiny blue

thermoses that you use to keep coffee or whatever. This [contained] blood from a Catholic nun who had died of hemorrhagic symptoms, which, retrospectively, should have triggered alarm bells.

Bryan Schutmaat for TIME

It was my colleague Guido Van Der Groen who opened it. We just wore latex gloves, opened it under laminar flow, which is negative pressure so the air is sucked up and doesn't blow into your face. What we saw was one intact vial swimming in half water, half ice. Another vial had broken. There was some blood, and therefore virus swimming in that thermos, but we didn't know then.

We had no clue this was so dangerous. What we did was good lab practice in terms of how to manipulate the samples. In theory that was enough for Ebola, but the problem is you don't want to use this regular infection control for Ebola because the slightest mistake can be fatal. That we didn't know.

Those days, isolating a virus was very artisanal, more like cooking than anything else. You bring the blood, which we diluted, in tubes and flasks with VERO cell lines, and you inoculate it into baby mice and a guinea pig. It took a few days before we saw the effect on the cells. Basically the virus kills cells—instead of a nice carpet of intact cells you see holes appearing because the cells with infected virus are dying off. Then some mice started dying.

That's when we got really excited. My colleague had prepared the fluid from the VERO cells for taking pictures on the electron microscope. We saw these pictures of a wormlike structure, which we really had never seen. This was pre-Google, so we had to go to the library to look at an atlas of viruses and confirm that there was only one known virus that had that kind of structure. Most viruses are kind of spheres or squares. This was like a worm type. The only one that it looked like was Marburg. That had been discovered a few years before.

That was the aha moment. We said "Wow, is this new, or this is Marburg"—which had never been shown to cause an epidemic before. In the meantime there was news of a very bad epidemic going on with lots of people dying in what was then Zaire. We got news to stop working on the virus from the WHO. It was too dangerous, a hemorrhagic fever.

To be honest, we continued for 24 hours to work with the virus. But we packed it all, sent it to Proton Down in the U.K., which is a military lab equipped for working with highly dangerous pathogens. I wanted to go to Africa to see what was going on there, how [the virus] was transmitted, how many people were dying. That was a very unique opportunity to figure out how the pathogen is spread in a community.

The rest is history. It changed my life. It was a kind of dream come true because I always wanted to work in Africa dealing with epidemics. Our protective gear was a surgical mask, motorbike goggles, gloves and a paper surgical gown—that's all. We didn't have more than that.

Before leaving for the epidemic zone in Yambuku, I met a woman in a hospital in Kinshasa who was not yet terminal but was in a very poor state. I felt a mixture of curiosity and then sadness to see this was a young woman around my age. She was a

nurse so she was also getting ready to go to the U.S. She had gotten a fellowship to further train in the U.S. She had this look in her eyes, which I later saw a lot when I went to the epidemic zone. These people know they are going to die. I also found this later in the Congo and Kinshasa, when I started working with AIDS—this empty look of starting into infinitum.

I drew her blood and I examined it under a microscope. What I remember was that this woman had basically no platelets. There was clearly a major problem with her blood coagulation. But it all came too late. We didn't know what to do.

I returned from our first visit to Yambuku while the epidemic was still going on. One night in Kinshasa we had a late-night meeting, and we said this virus needs a name. [CDC researcher and team leader] Karl Johnson said, 'If you name it after the place where the epidemic first occurred, you really stigmatize the place. Imagine you introduce yourself, say, "Hi, I'm from Lassa." That's not a safe introduction.'

So he said, "Let's take a river." We had a fairly small map of Zaire—Zaire is about the size of all of Europe. We were looking at rivers close to Yambuku, and that was Ebola. In the end it was not the nearest river, but still, it's a beautiful name. You remember it. *—as told to Alice Park*

Dr. Pardis Sabeti, 38

Geneticist who sequenced the Ebola genome from the outbreak

Bryan Schutmaat for TIME

I think I first encountered Ebola from the movie *Outbreak*. Then there was the book *The Hot Zone*. It's the type of thing you either read and say, "Oh wow, that's terrifying," or you read it and say, "Oh wow, I want to do that." I read it and said, "Oh wow, I want do that."

With my colleagues in Africa and at the Broad Institute [of MIT and Harvard], we had for a long time considered the possibility that there could be Ebola circulating in West Africa. One of the many reasons we thought that could be the case was that often we see Ebola cases centered where there are a lot of chimp populations. One of the only places where there were chimps that didn't have Ebola at that point was West Africa. We considered the possibility that the virus could have been circulating undetected in populations for many years, misdiagnosed as other diseases that look

similar, like malaria or typhoid fever.

We, like everybody else in the field, follow Ebola news closely. We all have alerts on various systems for anything that comes up on these viruses, and we saw the alert on cases in Guinea, declaring the outbreak in Guinea in March. Everybody agreed we needed to move.

We had [set up research collaborations with] the Kenema Government Hospital in Sierra Leone. The outbreak was on the border of Sierra Leone, Guinea and Liberia. When it was recognized there were cases in Guinea, we knew it was possible the hospital would see cases. Our colleagues there and at the Ministry of Health in Sierra Leone said, “We need to do surveillance and diagnosis,” and we said,”Absolutely. We’ll help.”

The genome sequencing that we do is so critical to the development of diagnostics, treatments and vaccines. The diagnostic that is needed to even confirm Ebola is only possible because we know the genome sequence of the virus. The process of diagnosis comes first for patients, but in the arc of knowledge, you need the sequencing to develop the diagnostic, and you need to do this continuously, because viruses change over time. Essentially what we are doing is reading out the virus’ genome to find out what is the organism at play, what we are dealing with at any point in time.

Therapies—like the monoclonal antibodies used like ZMapp—are based on attacking the protein sequences of the virus. If the genome changes, the proteins change and the antibodies may no longer work. It’s the same for the vaccine—if the proteins change, the vaccine may not work. So the genome sequence is the fundamental first piece—what defines the agent that is circulating, how we detect it, how we treat it and how we prevent it from spreading.

Sequencing data is amazing. It can tell you so much. Obviously, epidemiology is incredibly important too. One thing that was to our advantage is that the outreach team at Kenema Government Hospital were able to overlay details of the epidemic outreach as well, to form a complete picture of how things were moving.

We fully sequenced a total of 99 samples from 78 different patients in the first three weeks of the outbreak in Sierra Leone and made the data available publicly.

We found a number of things, including that there is a lot of genetic similarity between the viruses we sequenced and those from Guinea early on in the outbreak, suggesting that the epidemic started with a single transmission into the human population from a natural reservoir such as an animal, and there weren’t multiple transmissions but a continuous set of human-to-human events that started this outbreak.

That’s important in how we thought about the response, in the sense that what people really need to be doing is reducing contact between themselves—because it wasn’t being spread widely by animals or contact with animals. It is critical to continue to sequence this virus as it evolves. We have finally been able to get another shipment of inactivated samples from hundreds of Ebola patients in Sierra Leone. We are committed to sequencing the virus in these samples and making the data available publicly immediately. We need as many minds working on this important problem as we can have. We will only beat this virus together. *—as told to Alice Park*

TIME’s 2014 Person of the Year: The Ebola Fighters
Why We Chose the Ebola Fighters as Person of the Year
Read the Ebola Doctors’ Stories
Read the Ebola Nurses’ Stories
Read the Ebola Caregivers’ Stories
Read the Ebola Directors’ Stories