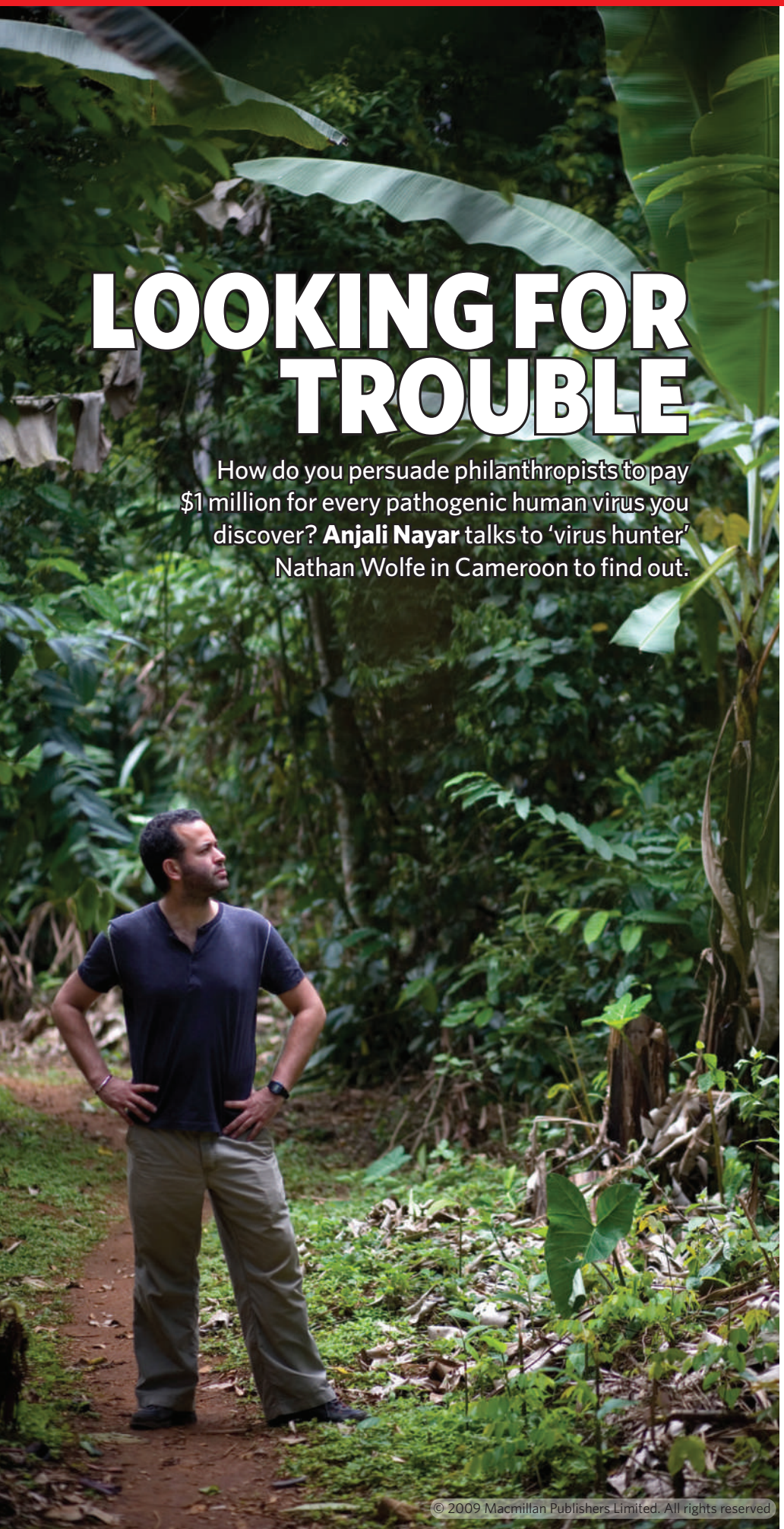

LOOKING FOR TROUBLE

How do you persuade philanthropists to pay $1 million for every pathogenic human virus you discover? **Anjali Nayar** talks to 'virus hunter' Nathan Wolfe in Cameroon to find out.

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Every day, more than 100 patients line up for treatment outside the bare cement walls of a rural health clinic in the Niete forest of southern Cameroon. Most of them suffer from what virologist Nathan Wolfe calls "the usual suspects": malaria and typhoid. But every once in a while there is something a little different: a case that is tough to diagnose, or that doesn't respond as expected to medication. For the patients and the medics here, this presents a problem. For Wolfe, it is also an opportunity. "I get all excited," he says. "These areas are choc-a-block full of interesting, unusual viruses."

In 2005, Wolfe and his colleagues identified two unusual viruses that had jumped from non-human primates into Cameroonian hunters[1], and that are closely related to pathogenic viruses that have spread through the world's population. Since then, Wolfe has made a name and a livelihood for himself in search of more. In 2007, he founded the Global Viral Forecasting Initiative (GVFI), an effort to monitor for new viruses and other microbes in communities around the world that are in intimate contact with animals. By identifying these agents as soon as they leap into humans, and before they start passing easily between them, Wolfe believes that researchers can predict and prevent human pandemics before they start, averting the next HIV, SARS, Ebola or pandemic influenza, diseases that have all been traced to animals.

Brand Wolfe

Other researchers share that belief and are involved in this type of infectious disease surveillance. But what sets Wolfe apart is his swashbuckling style — he chooses to do most of his work in the field — combined with a flair for communication and negotiation. "He's in the minority of scientists; he's good at science, politics, media and PR," says Jeremy Alberga, the chief operating officer at the GVFI. "We have a brand and it's Nathan Wolfe and the GVFI," he says, "not the GVFI and Nathan Wolfe."

That brand has sold well. In 2008, Google.org, the philanthropic arm of Google, and the Skoll Foundation, an organization in Palo Alto, California, that supports social entrepreneurs, announced they would invest up to US$11 million to help expand the GVFI's work in Africa and southeast Asia. In October 2009, the United States Agency for International Development (USAID) named the GVFI as a main partner in its $330-million Emerging Pandemic Threats programme, a project involving various experts in wildlife surveillance, and for which the GVFI will receive tens of millions of dollars over the next five years. Last month,

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Nathan Wolfe, above centre, is trying to find viruses that jump species as a result of bush meat hunting.

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Wolfe unveiled a new $600,000 update to his lab in Yaoundé, Cameroon's capital, marking ten years of research in the country.

Wolfe and his work have also found a wider audience, featuring in news outlets ranging from *Wired* to *Men's Journal*. Earlier this year, *Rolling Stone* magazine ranked Wolfe at number 53 of "people who are changing America", and an article in *Popular Science* magazine was simply titled: "Nathan Wolfe: did we mention this guy was brilliant?" "We joke about it sometimes," says Frank Rijsberman, a programme director at Google.org, about the unrelenting press Wolfe receives. "He's definitely audacious — he has big visions — but he has enough of a track record in the field to do it realistically."

Lasting mark

Other 'virus hunters' say that they are less interested by Wolfe's semi-celebrity status, and more interested in what he is going to find in the future. "Nathan's a bright, energetic young guy and I anticipate he will be successful," says Ian Lipkin, a specialist in pathogen surveillance and discovery at Columbia University in New York, who recently started collaborating with Wolfe. "For the sake of the field it's important that he is. A lot of resources are allocated to Nathan. He's going to have to deliver."

"The real breakthroughs are published in the literature, and not on CNN," adds Peter Daszak, a disease ecologist and president of the Wildlife Trust in New York, who is working with Wolfe on the USAID initiative (and says he has been on CNN, a US cable news network, himself). "If you look back on this field in 10 years, you will say who actually did the discovery, was there a paper that came out of this group and did they prevent the next disease."

Wolfe's interest in virus emergence dates back to his master's degree in biological anthropology in the 1990s. Working under Marc Hauser and Richard Wrangham at Harvard University in Cambridge, Massachusetts, Wolfe was studying the behaviour of wild chimpanzees to see if they were consuming certain plants medicinally. He never answered the question — but while tracking chimpanzees in the forests of western Uganda, Wolfe witnessed several dramatic ambush hunts. "The chimps were up to their eyeballs in the blood and body fluids of all these animals," he says. "I just thought to myself what a perfect scenario for cross-species transmission of microbes." He postulated that the rural human populations of Central Africa, with a diet heavily dependent on bush meat, could be affected the same way. "I just thought it would be this wonderful grab-bag of new things jumping into humans and bouncing around," he says.

Wolfe started testing his ideas, looking at cross-species viral transmission first during doctoral work in Malaysian Borneo, and then back in Central Africa after being recruited by Donald Burke, an infectious-disease expert at Johns Hopkins University in Baltimore, Maryland. Wolfe started to follow subsistence hunters into the forest as they caught and butchered monkeys and other wild animals. As the hunters walked back with the catch over their shoulders, blood would run down their backs and into the cuts on their bare legs and feet. Wolfe thought that there was a high chance that viruses were passing between them, and he collected blood from the hunters and screened for retroviruses related to those found in non-human primates. There was precedent: researchers think that the retrovirus HIV was originally transmitted to humans from non-human primates in Central Africa, perhaps during hunting or butchering.

> "The chimps were up to their eyeballs in the blood and body fluids of all these animals."
> — NathanWolfe

In 2004, Wolfe showed that around 1% of those he tested had been exposed to a retrovirus called simian foamy virus, and sequence analysis showed that the virus had been passed into humans in the past from a mandrill, a gorilla and a type of monkey known as De Brazza's guenon[2]. The next year he reported the discovery of two new human retroviruses — called human T-lymphotropic viruses (HTLVs) — one of which is related to a group of simian viruses and both of which are likely to have crossed over from non-human primates[1]. Another member of this viral group, HTLV1, is also thought to have spread into humans and is associated with leukaemia and other conditions. Wolfe's studies suggested that certain viruses were passing from non-human primates quite freely and frequently into humans. "Retroviruses are jumping over all the time," says Wolfe, even though "only a few of them end up being significant".

Wolfe's work convinced him that the significant viruses could be identified and eliminated with proper surveillance of areas where cross-species transmission was a particularly high risk. Much of the challenge though, as other researchers have found, lies in getting funding to do the kind of large-scale field studies and genetic sequencing that this surveillance requires. Microbe discovery "doesn't rate real well" in funding applications that tend to focus on known threats, says Gregory Gray, who studies zoonotic infections at the University of Florida, Gainesville. It's hard to justify science "when you don't even know exactly what you are going to encounter", he says.

Wolfe was helped by his timing, his scientific findings and his eloquence. In 2005, he secured one of the National Institutes of Health five-year, $2.5-million Pioneer Awards, and the next year a tenured position at the University of California, Los Angeles (UCLA). Soon he was building up a public profile, with speaking arrangements around the world. Interest in wildlife surveillance had been rising on the back of scares over West Nile virus, SARS and the H5N1 avian influenza. "Nathan has been riding the wave of interest in the field," says William

Karesh, director of the Wildlife Conservation Society's Global Health Program. "It's like surfing, and the wave started getting really big," he says. "And, you know, if you are on a big wave, you look better if you know how to surf well."

Wolfe caught the eye of Google.org, which was looking to invest money and information-technology expertise in the field of emerging infectious diseases. The fact that Wolfe is "media-genic", was key, says Rijsberman. The parties discussed the collaboration for nearly a year before the $11-million funding deal was signed in October 2008. Wolfe had founded the GVFI the previous year, but the agreement "made it real" says Wolfe, and he left his position at UCLA to head the institute full time.

Viral marketing

Part of Wolfe's magnetism for money and media seems to lie in the niche he has carved out for himself as an adventuring field virologist — going into the field to collect samples himself, rather than sending students or postdocs to do it. This also helps the science. Lipkin says that tissue or blood samples can easily become contaminated — plus samples are best frozen quickly. "It has been difficult to collect high-quality materials and move them from remote sites in the developing world to laboratories," says Lipkin. "Nathan is doing us an enormous service with these collections."

Wolfe thrives on the difficulties involved in securing the right samples from people or animals. "There is a lot of logistics in what I do, there's a political angle to what I do, and there's a tremendous amount of negotiation," he says. "I love when people say: you simply can't collect specimens like that in China, or it is impossible to have a long-term program in the Democratic Republic of the Congo. I sort of enjoy that challenge."

The GVFI now runs human and animal collection sites in the Democratic Republic of the Congo, Malaysia and China — some of these from the types of markets where humans and animals are cheek by jowl, sites that helped SARS and H5N1 emerge and spread. Wolfe narrows down his hunt by focusing on these 'hot spots' for emerging disease, along with pathogens (such as retroviruses) that have a history of making the jump. "It's not like you are picking randomly from space what's going to be your next pandemic," says Wolfe, who maintains academic affiliations with Stanford University in Palo Alto, California, and with Johns Hopkins University.

The Cameroon team is more than 30 strong, and has collected blood and tissue samples from more than 27,000 humans and 26,000 animals. With the re-vamped laboratory there, equipped with PCR machines to amplify DNA, and separate facilities for animal and human work to avoid contamination, Wolfe plans to boost the group's capacity to do molecular analyses on-site. But for the most part, he collaborates with world-class laboratories in Europe and the United States for his gene-sequencing work. Identification of a new virus is only the first step though: to spawn a pandemic, a virus has to adapt to humans and spread easily between them, something that can be examined by surveillance and modelling. Wolfe is monitoring the novel viruses he identified in bush-meat hunters to see if they are spreading.

> "If you are on a big wave, you look better if you know how to surf well."
> — William Karesh

How to stop a potential pandemic, if Wolfe finds one, will depend on the case in hand, but might involve some combination of diagnostics, behaviour change and vaccines or treatments, if they could be found. Karesh points to the Republic of the Congo, where scientists found out that Ebola outbreaks were spread into humans through handling dead gorillas and chimpanzees. Communities were trained to avoid handling sick animals and there has barely been another outbreak since. Wolfe's group is already working on prevention programmes that might reduce transmission — such as encouraging hunters to wrap slaughtered animals in leaves when they are being transported.

Wolfe has not yet identified a nascent pandemic, but he is finding out something about existing ones. Earlier this year, his team used samples from chimpanzees in Cameroon and the Côte d'Ivoire to shed some light on the origin of the human malarial parasite *Plasmodium falciparum*. Genetic analyses showed that all existing populations of *P. falciparum* originated from the chimp version, *Plasmodium reichenowi*, and that the chimp parasite probably transferred across species between 10,000 years and 2–3 million years ago[3].

There is pressure on Wolfe to deliver much more. Only $5 million of the $11 million from Google.org and the Skoll Foundation came up front and the group is eligible for another $1 million every six months — if they earn it. They earned the first $1 million by collecting nearly 10,000 new samples and enrolling around 900 people in their studies in Asia. Rijsberman, who now sits on the GVFI board, helped the team to establish goals they call "scientific home runs": the origin of a major infectious disease or the identification of a new pathogenic virus circulating in human populations. With each home run, the group earns another $1 million. The group has submitted the malaria work to the Google.org board and hopes to hear in the next few weeks if it qualifies as their first home run.

Wolfe, aware of the scientific competition, is careful not to say much about what his next million will be for. But he surely has a strategy to earn it.

During a retreat to the coastal Cameroonian resort town of Kribi last month, Wolfe and his team were plotting their next scientific articles, making notes on papers and laptops. After a day of hard work, they sit down for drinks and take in the setting sun. Wolfe takes on his laboratory director in a game of backgammon, starting the game with an aggressive move. "Nathan always has to do things differently," says Alberga, looking on.

After a few more dice rolls, it's neck and neck. But, despite his nonchalance, Wolfe is constantly calculating probabilities — and in the end, he comes out on top. ■

J. CARRIER/GETTY

The GVFI collects thousands of blood samples from non-human primates (NHPs).

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