That's where the statistical physics expertise of Dr. Liu and Banigan came in.

"We looked at a much more complete way to quantify these tracks and found that the standard model didn't fit at all," Dr. Liu said. "After some work we managed to find a model that did fit the tracks beautifully."

"The model that finally led us down the right path," Banigan said, "had a strong signature of something really interesting," a model known as a Lévy walk.

This "walk," or a mathematically characterized path, tends to have many short "steps" and occasional long "runs." The model was not fully consistent with the data, however.

"Rather, I had to look at variations on the Lévy walk model," Banigan said, because the researchers also observed that the T cells paused between steps and runs. Like the movements of the cells, the pauses were usually short but occasionally long.

Dr. Hunter likened the model to a strategy a person might employ to find misplaced keys in the house.

"When you lose your keys, how do you go about looking for them? You look in one place for a while, then move to another place and look there," he said.

"What that leads to is a much more efficient way of finding things," Dr. Liu said.

And, indeed, when the team modeled the generalized Lévy strategy against other strategies, they confirmed that the Lévy walk was a more efficient technique to find rare targets. That makes sense for T cells, which have to locate sparsely distributed parasites in a sea of mostly normal tissue.

Interestingly, T cells are not alone in employing a Lévy-type strategy to find their targets. Several animal predators move in a similar way — with many short-distance movements interspersed with occasional longer-distance moves — to find their prey. The strategy seems particularly common among marine predators, including tuna, sharks, zooplankton, sea turtles and penguins, though terrestrial species like spider monkeys and honeybees may use the same approach to locate rare resources.

This parallel with animal predators also makes sense because parasites, like prey species, have evolved to evade detection.

"Many pathogens know how to hide, so T cells are not able to move directly to their target," Dr. Hunter said. "The T cell actually needs to go into an area and then see if there's anything there."

The model is also relevant to cancer and other immune-mediated diseases, Dr. Hunter noted.

"Instead of looking for a parasite, these T cells could be looking for a cancer cell," he said. By knowing what controls T cell movement, "you might be able to devise strategies to make the T cells more efficient at finding those cells."

On the physics side, while the Lévy-walk model is not new, the fact that T cells pause in between their steps or runs is something that hadn't been recognized before when mapping the paths in other contexts.

"From a physics point of view, to have runs and pauses is a new model," Dr. Liu said. "Biological phenomena can illustrate what we wouldn't have thought about otherwise."

The Penn collaborators are working to plot the tracks of other cell types and credit their unique partnership for their discovery.

"We've said all along that this study could only happen because [our physics colleagues] had such a great expertise and we had our own separate expertise," Dr. Harris said. "They took a chance working with us, and it turned out to be something really rewarding."

Additional Penn contributors to this study included Penn Vet's David Christian, Christoph Konradt, Elia Tait Wojno and Beena John.

The Penn team partnered on the work with Kazumi Norose of Chiba University in Japan; Emma Wilson of the University of California, Riverside; Wolfgang Weninger of the Sydney Medical School; and Andrew Luster of Massachusetts General Hospital.

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GRANTS

David Artis, PhD, associate professor of parasitology, has received a five-year grant to study cytokine regulation of anti-helminth immunity totaling $2 million.

Christopher A. Hunter, BSc, PhD, professor and chairman of the department of pathobiology, received a grant from the American Asthma Foundation totaling $750,000 over three years. The Foundation funds three percent of applicants.

Gustavo Aguirre, VMD, PhD, professor of medical genetics and ophthalmology, has received a three-year, $300,000 grant from the Macula Vision Research Foundation to study Gene Replacement Therapy in Bestrophin 1 Model: Implications for Recessive and Dominant Human BEST1-Disorders.

Mark Haskins, VMD, MS, PhD, professor of pathology, received a Penn pilot grant totaling $149,831 and spanning two years to study the pathophysiology and the effect of treatments on cardiovascular disease in Mucopolysaccharidosis I in dogs. The goal of the grant is to test simvastatin in combination with enzyme therapy in dogs with MPS I.

In addition, **Dr. Haskins** received a second Penn pilot grant totaling $164,686 and spanning two years to study the pre-clinical evaluation of TNF-antagonists for the treatment of MPS I in combination with enzyme replacement therapy. The goal of the grant is to test a cat-based anti-inflammatory drug in combination with enzyme therapy in cats with MPS I.

Regina Turner, VMD, PhD, associate professor of reproduction, received a two-year, $109,732 grant from the Grayson Jockey Club to study understanding testicular degeneration.

Ron Harty (PI), PhD, associate professor of microbiology, and Bruce Freedman (Co-PI), MS, VMD, PhD, associate professor received a $275,000 grant from the NIH to study host-oriented therapeutics targeting filovirus budding. The grant will span two years.

Tracy Bale, PhD, associate professor of neuroscience, received a $3.75 million NIH/NIMH grant to study prepubertal stress: windows of risk and sex bias for affective disturbance P50 SCOR. The grant will span five years.