

Better check that mole: Has an Israeli biologist found the key to curing cancer?

It is the farmer's enemy - a n unlikable, aggressive creature with a face only a mother could love. But biologist Aaron Avivi says the blind mole may save millions of human lives if given the chance.

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Prof. Aaron Avivi. Photo by Tomer Appelbaum

THIS STORY IS BY Neri Livneh



Lab mice, rejoice! At the University of Haifa's Institute of Evolution, a new lab animal has been studied that could free all you mice from the tragic fate that scientists have been imposing on you for decades. No longer will you have to subject your bodies, or parts of them, to terrible diseases, and lay down your lives for the sake of scientific progress in the quest to treat and cure human illnesses.

Over the past decades, the laboratory white mice have been the major organism in an attempt to advance research into diseases that kill humans. A lot of important knowledge accumulated due to these studies. However, the vast majority of the studies done on mice has never reached the clinical trial stage, and has been found to be inapplicable to human patients suffering from cancer.

Five years ago, renowned cancer researcher, that studied mice and contributed a great deal to the foundations of cancer research, Robert Weinberg of MIT's Whitehead Institute declared that the lab mouse is not the right animal to use in studying human cancer. In a 2008 Newsweek interview, Weinberg said: "Drug companies have been investing millions of dollars a year for decades on cancer research using mice, which was proved to be of very low predictive value and has little relation to cancer research in humans. **Far more than anything else, the lack of good research animal has become the rate-limiting step in cancer research.**"

White mice, which are very easy to obtain, have a short life span and even when researchers aren't trying to make them sick by injecting them with carcinogens, many of them die from cancer. White mice are the most convenient research animals to use and have played a part in many scientific achievements, but when it comes to human cancer, healing techniques that proved effective in mice have not been transferable to humans.

Prof. Aaron Avivi, together with his colleagues, senior researchers Dr. Imad Shams and Dr. Irena Manov of the Institute of Evolution in Haifa University, recently published an article in the respected scientific journal BMC Biology. In it they describe their discovery of a natural animal for researching cancer as well as other human diseases. The animal is the blind mole-rat, which weighs 100-200 grams and is quite ugly. As per its name, it is blind though has a biological clock, and also lacks earlobes (although it does have ears, sunken into its head so that the dust in which it burrows will not get in). The mole-rat is covered with light gray fur and much of its head is comprised of four very sharp teeth: two in the upper jaw and two smaller ones in the lower jaw.



Prof. Avivi, center, with Drs. Imad Shams and Irena Manov. Photo by Tomer Appelbaum

This aggressive little rodent has nothing in common with the friendly mole that sometimes appears in British children's fairy tales. No one would want to invite it to a tea party, or even hold it in his hand. But if Ayn Rand had ever heard of it, she surely would have touted it for the way its form is perfectly suited to its function in nature. Its impressive muscle mass for its small size; its long life span (up to 20 years); its adaptability to conditions in which there is a severe lack of oxygen; and a host of other survival capabilities – all explain why this creature has become one of the pests in agriculture. It rapidly and efficiently digs long tunnels at a depth of as much as 80 centimeters, and stores the onions and tubers it collects in cleverly designed underground chambers. But now that Prof. Avivi and his colleagues have found it to be a promising animal for cancer research, the blind mole-rat may have to kiss the good life goodbye.

Avivi, looks much younger than his age. He is very energetic, enthusiastic, and, at scientific conferences, he and his pet sometimes perceived as a little too colorful. Highly regarded by his peers, the organism he and his colleagues study make it hard for them to obtain grants to keep pursuing the revolutionary research they just published. Not to mention that many of the scientific community, having fallen in love with mice, their long-time research subjects, may still try to retroactively justify decades of research with animals that are not the fittest for the study-subject.

The cow whisperer

Aaron Avivi lives in the central Galilee village of Avtalyon, with his spouse of 25 years, the most-appreciated Israeli writer, Gabriela Avigur-Rotem. It was their shared love of literature, particularly for the novels of Argentine writer and nuclear physicist Ernesto Sabato that brought them together. Sabato once said that the scientist discovers what already exists, while the artist creates a new reality. But even if Avivi has discovered something that has existed for millions of years and is known as an agricultural pest – that discovery may create a new reality of scientific research.

Avivi was born and raised in Haifa, where he attended the Hebrew HaReali School, and from as far back as he can remember, always wanted to be a biologist. When he was three, he would spend hours observing ants to see how they built their nests. When he was five, the neighbors' pet took part in his first research experiment: He discovered that he could get a female-dog that had just had puppies to nurse another newborn puppy that someone had tossed into the trash near his home. In high school, Avivi would often hide the teacher's notebook so his absence couldn't be recorded, and then set off to explore the lovely flowers and animal life around Beit Biram near "Little Switzerland" in the Carmel range, and sometimes – purely for research purposes, of course – he would go as far as the beach or to listen to trials in the courtroom.

A clarification related to the term "molecular biologist" or "cancer researcher": Many people, this writer included, long conjured images of such scientists as intrepid explorers embarking on exciting missions – trailing animals in the bush, say, or deliberately giving themselves an illness in order to see how to cure it, and in their leisure time, also becoming "microbe hunters." But there is little glamour in the daily grind of the molecular-biologist whose world, as the title implies, is so very tiny. To

become a molecular-biologist, it doesn't hurt to possess some degree of obsessive-compulsive personality disorder, which certainly helps the research continue. Most such work requires hours upon hours in a fluorescent-lit lab, and mainly involves the counting of microscopic cells in Petri dishes, creating precise microscopic sections, and obsessively maintaining hygiene.

Avivi readily describes himself as very persistent and stubborn. He cannot easily abide being interrupted with questions in the midst of the long lecture he gives me – quite a fascinating and well-structured lecture, I must admit. And he has even less patience for people who try to make jokes at the blind mole-rat's expense, for not everything is a laughing matter.

During his military service in the Nahal Parachutists Brigade (which combines military service with work in outlying settlements) he worked in a cattle shed. "I fell in love with cows," he candidly confesses; "animals are generally nicer than people. They don't start a war every second year". It takes some guts to admit that you love cows; although, then again, he was never a Tel Aviv type or a fashion plate. Avivi decided he wanted to study genetics and applied to Tel Aviv University and Hebrew University, as well as to the medical school at Hadassah. He got into Tel Aviv University but decided not to go because he wanted to experience student and campus life the way it was in Jerusalem back in the 1970s and 1980s.

Avivi's application somehow got lost between the medical school and the Faculty of Life Sciences in Jerusalem, and after being repeatedly rebuffed by the faculty secretary, one day he showed up in her office with a backpack and a sleeping bag, and informed her that he was going to camp in her office until she let him meet with the Dean of the Faculty.

The Dean, who was passing by and overheard Avivi's hopeless talk with the secretary, looked onto the problem and arranged his admission to the department. Avivi earned a bachelor's degree in biology and a master's in genetics, doing research on his beloved cows. During his master studies he was offered the chance to go to Denmark to learn how to make an "ID for cows" (i.e., a system that could be used to record the genetic information of cows), so he could start a lab in Israel for analyzing genetic information relating to cows from blood tests, which until then were being sent to Copenhagen.

"I loved working with cows, I was in the right place at the right time, I won a scholarship from the Danish Ministry of Science, and so they sent me. As far as I know, this lab still hasn't been started. I was in Copenhagen, and I enjoyed it there, though I didn't manage to learn more than few words of Danish. But I still feel at home when I'm in Copenhagen. I came back to Israel. I went to work in the Veterinary Institute associated with the Israeli Agriculture Research Center as a researcher of cattle endocrinology."

By that point Avivi was married for the first time and also the father of two. He began working on his doctorate at the Veterinary Institute, with an affiliation to the Weizmann Institute of Science as well. After a year, he saw he wouldn't be able to get anywhere with

his attempt to start a cattle research lab at the Veterinary Institute, and meanwhile, the Weizmann Institute was insisting that he spent more time of his Ph.D studies there. Avivi was delighted with the ultimatum of the Weizmann's School of Graduate Students. At the time, he was studying thyroid development in cattle fetuses. Prof. Yossi Schlesinger, a scientist at Weizmann, was researching the communication between hormones and their receptors and offered to be his doctoral adviser.

Avivi completed his doctoral studies and was offered post-doctoral positions at several prestigious universities in the United States, including Harvard – but just then was at the start of a protracted divorce process, after which he received joint custody of his children. He decided to remain in Israel so he could be fully involved in their upbringing.

Avivi did his post-doctorate at Weizmann, though this time he abandoned his beloved cows and started studying growth factors in humans, seemingly his first step into cancer research. He stayed on at the institute as a senior associated scientist until 1996. “I had two job offers, one at Hadassah Ein Kerem and one at the Institute of Evolution in Haifa. By then he was already the partner of Avigur-Rotem. Apparently her impression of him on their first date was that he was “an extremely handsome guy but just a kid,” because he looked surprisingly young for his age (and they are exactly the same age, and she doesn't look her age either). “We saw that we couldn't afford to buy a private house near Jerusalem, and the job in Hadassah demanded too much management time at the expense of scientific work ,” he recalls, “So Gabi and I decided to look for somewhere we could buy near Haifa. We started exploring the Misgav area near Carmiel, and we kept getting further and further away from Haifa. We were looking for a non-spiritual place which is very "in" in Misgav, the Israeli "NASA" area. Someone at work suggested we check out Avtalyon. I said, ‘But that's the end of the world.’ Nonetheless we went there anyway, and within a day we bought a house there where you can see the whole amazing ‘quilt’ of the Netofa Valley changing according to the light direction during the day, and along the seasons, from the windows and the yard.”

Underground wonder

The head of the Evolution Institute in Haifa on those days was Prof. Eibi Nevo, who founded it in the early 1970s and persistently kept this position until he was 80 years old. Nevo was a member of Kibbutz Sa'ar, in northern Israel, where the soil was very dense and full of moisture so that the female blind mole-rat made its breeding nests for giving birth above ground.

“Just imagine, a female that weighs just 100-200 grams and is 15 centimeter long, builds completely by itself a nest that's a meter in diameter and 80 centimeters high,” says Avivi. “Nevo came across one of these structures and peeked inside to see what was happening there and he found mole-rat pups.”

Nevo, who had written books and coauthored many articles about the blind mole-rat, suggested that Avivi study it, too.

“My first reaction was aversion,” says Avivi. “In the traditional free spirit of academy life, why should anyone tell me what to research? But I managed to stay polite this time. As I learnt very quickly, not an easy job when a tenacious young scientist and an old, extreme centralist bump into each other on a daily basis. I bit my lip on that first meeting, though with years passing by I stopped, and he gave me the book he’d written about the blind mole-rat.”

In the scientific literature the animal is called the Subterranean Blind Mole-Rat (*Spalax*), although, he notes, “in this part of the world it is called the Israeli blind mole-rat, or the Palestinian blind-mole rat, depending which flag you raise.” This little animal inhabits the Middle East from Egypt through Israel, Syria, Lebanon and Turkey, reaching the Balkans and the Asian "Stan" republics of former USSR. Certain aspects of its nature vary from one breeding area to another.

Cows are an unusual fetish, though familiar at least. But what’s so attractive about the blind mole-rat?

“The mole-rat is a soloist, an individualist, it’s not a social animal, and it’s very aggressive. But in Egypt, because of the desert climate, where it’s hot and hard to find food, you find mole-rats that live in a group unit so as to cooperate in the quest for food. In the Asian "Stan" republics, the mole-rat can be much larger – some as large as small cats even. In Israel, they are very aggressive and individualistic. This animal is an agricultural pest. It eats onions, tubers, roots. You can be walking in a potato field and suddenly see a straight line 100 meters long of wilted plants, alongside fresh soil mounds, that the mole-rat cut and from which it collected the young, small potatoes. A tiny animal of just 100-200 grams creates mounds that weigh two to three kilos; in other words, it can push 10 times its weight. And it will push many of this mounts while digging in an overnight.

“Aside from the burrows it also has a home that’s built in a fantastic architecture, especially those of females that are about to give birth: There’s a children’s room and a bathroom and a pantry. And this pantry isn’t just piles of this and that, it’s all neatly organized. Near Acre, you see lots of daffodil bulbs [in these female mole-rat homes]. The children’s room is built of all kinds of twigs. The nursing female mole-rats make a ‘pergola’ roof and cover it with earth and put all kinds of grass in there. The mole-rat lives underground nearly all the time, but when the pups are weaned, the mother chases them out. Because unlike us she won’t recognize her offspring and could end up mating with them, and then the odds of birth defects are greater. Nevertheless, once chased out, the young ones immediately start to dig their own territory underground”.

“Gestation lasts a month and there are from three to five pups per litter. What’s interesting is that when it’s mating season you can see for a 100 meters in every direction straight burrows leading directly to the den, to the female’s territory. It’s a sign that the males come to look for her. And she bites and chases away the ones she doesn’t want. There’s a debate as to when the mole-rat became blind: 60 million years ago or 25 million years ago. But it’s certain that at one time its evolutionary ancestor was a seeing animal because the mole-rat has a remnant of eyes underneath the skin, the size of a poppy seed. But in spite of this, and even though the animal lives 40-80 centimeters

underground, she has a biological clock. She knows when it's light and when it's dark."

How do we know that the mole-rat can distinguish between light and dark?

"You can easily test it by housing the animal in a small cage, with tubes on its sides and sensors on the tubes, connected to a computer program that records all of the mole-rat's movements. After a few days, you see it sleeps at night and is active during the day. Some are the opposite, nocturnal, active at night and asleep during the day. We could call them the Tel Avivians."

Life with little oxygen

Although the book about the mole-rat was basically forced upon him, Avivi says as he began to read it, he thought: "Wow, what an interesting animal. No constructive reason to practice my academic freedom with Nevo. There were two things that immediately grabbed me: the biological clock with the completely degenerated eye, and the fact that this animal lives underground and therefore survives with a shortage of oxygen. Moreover, it can withstand abrupt and sharp changes in the oxygen supply. Why does this matter? The amount of rainfall in London is similar to that of northern Israel. However, in London it drizzles like Chinese [water] torture all the time. Here we have about 14 rainy days that can reach 80 millimeters of rain ; hence, the mole-rat's tunnels are flooded, and he is enforced to rebuild them exhausting the low oxygen, and raising the carbon dioxide. We measured 6 percent oxygen in their tunnels after a rain session. But the mole-rat can survive in 3 percent oxygen. That's one-seventh of the normal oxygen above ground at sea level and one-third of the oxygen level on the top of Mount Everest."

The fact that the mole-rat, a mammal, needs so little oxygen to survive and can withstand the sharp fluctuations in its availability, is what really excited Avivi, who'd now found a new love. Two years ago, two senior researchers at the Institute for Evolution, Dr. Shams and Dr. Manov, joined him.

"The mole-rat can withstand hypoxia, a lack of oxygen. Why was this big deal? I knew that hypoxia was connected to the most lethal diseases in the Western world: brain strokes, heart attacks, lung diseases and all kinds of cancer," Avivi explains.

Without getting into explanations that require a master's degree in biology to understand, Avivi offers a simple intelligent account of the connection between oxygen, cancer and the blind mole-rat:

"The hypoxia-inducible factor HIF1, master gene, activates an entire family of genes that are all related to the response to low oxygen supply. One of them, which is very famous because of the Tour de France and its becoming so unsporting, is called erythropoietin, or in short EPO. The competitors in the Tour de France, which are demanded to inhumane physical efforts along 3 weeks, take EPO and it causes the progenitor cells that have the potential to develop into erythrocytes (red blood cells) to differentiate and actually become one. As a result, the cyclists have more red blood cells whose main function is to be an oxygen carrier. The red color is because of the iron in the

hemoglobin protein that binds oxygen molecules and endows blood a rusty color.

“But EPO is just one of these factors. There’s also VEGF. It’s responsible for the sprouting of new blood vessels. This is actually the first gene that made us realize that something interesting related to cancer is happening here. Why? Because the VEGF of a mole-rat, and a cancerous tumor behave similarly. What does the tumor do? Because its cells divide faster than blood vessels grow ... it experiences waves of hypoxia. To survive, the tumor bypasses the HIF1 control system and VEGF is working constitutively at maximum capacity and sending the message: ‘Grow blood vessels, grow blood vessels.’

“In a cancerous growth there are lots of blood vessels. Its dominant color is red. We examined this in the blind mole-rat, and we found that like in cancer also in the mole-rats, VEGF is also working at maximum capacity, by bypassing HIF and the hypoxic-stress control system. By contrast, in the rat that lives above ground, after 6 hours at 6 percent oxygen – which is the maximal stress the rat can survive – there is an increase in HIF expression followed by an increase in VEGF expression.

“At the minimal oxygen level the mole-rats survive, 3 percent, they start dying after more than eight hours, but we cannot compare the two animals under such conditions as the rats will die in just one to two hours. So we work at 6 percent because then we know rats will also survive for enough time to follow the impact of the lack of oxygen. A similar pattern to the rats’ expression happens with all above-ground mammals. When one calculates the ratio between the amount of VEGF the blind mole-rat expresses relative to the rat – you find that the blind mole-rat has twice as much.

“Why do I point this out? Because when someone has a suspicious growth and they do a biopsy, among other tests, also VEGF is measured. When there’s a ratio of 1.4 between the growth’s cells to normal cells, the growth is suspected to be malignant. The blind mole-rat has twice as much VEGF and twice as many blood vessels compared to a rat. We generally test the trapezius neck muscle. Because when the blind mole-rat digs, it works with its head and it has about twice as much muscle mass in its neck than the rat has. Its color is also like a filet mignon, while in the rat its light pink, as in humans. White, yellow, black or red – under the skin we’re all light pink.”

“One of the first ideas for treating cancerous tumors was to introduce an antagonist in to the body, like a car key that can enter a keyhole but cannot start the engine. If we take an ‘antagonist’ key, it can compete with VEGF in the keyhole but block the system from working and inhibit the growth of blood vessels. Prof. Judah Folkman, from Boston, one of the world’s most renowned cancer researchers, was the first to think of this idea and work on this. It turned out that it’s a smart and elegant idea, but not an ultimate solution that will cure cancer.

“Every two years there’s a conference on hypoxia and angiogenesis (the mechanism of blood vessel growth) held in the Colorado Mountains, at a ski resort, in high altitude and hence lower available oxygen. It is there that I first saw that along with tea bags and sugar in the rooms, the hotel visitors are served also with Advil to relieve the headache, the first sign of lack of oxygen. There are lectures until noon, and then from 4 to 8 P.M.

What do you do in the afternoon break? You go skiing. Folkman was invited to give the keynote lecture ... [but] because he had heart trouble the conference was moved to Vancouver, which is at sea level. Folkman took a plane from Boston, which is also at sea level, to Chicago, which is also at sea level – all to avoid burdening his heart and putting him into stress. But at the airport in Chicago he died of a heart attack. What’s a heart attack? A lack of oxygen.”

And the blind mole-rat doesn’t reach a state of hypoxia?

“No, it doesn’t. One of the criteria of physiological hypoxia is the accumulation of lactic (“milk”) acid resulting from anaerobic metabolism. This is the reason for legs-muscle ache one feels after intense physical exercises ... When one measures the levels of lactic acid in mole-rat’s muscle after hypoxic stress, there is no change compared to its levels in a normal atmosphere. Under similar conditions it is significantly elevated in the rat. We keep the blind mole-rats in an animal house under normal oxygen conditions, and the hypoxia tolerance is maintained in all of them. Evidently it’s a genetically, congenital mechanism. You can take a blind mole-rat that has been in the animal house for five years and one that was just captured in the field, put it in 3 percent oxygen, and both won’t die. There’s no difference between the mole-rat in the burrow and the mole-rat in the lab in terms of its ability to withstand hypoxia.”



Prof. Avivi in the animal house. "The mole-rat is a soloist, an individualist, it's not a social animal. It can push 10 times its weight." Photo by Tomer Appelbaum

Wiping out cancer cells

What's the conclusion to be drawn from all of this? How does this relate to the study of cancer in humans?

“We further found out that other genes related to cancer show differences in structure and function in the mole-rat. For example p53 which can be considered as one of the main appraisers in the cells. It seals the fate of cells for "total loss", that is "dying" (apoptosis in scientific terms) or order to fix it. In cancer cells the *p53* undergo mutations that inactivate it, as if it transmits to the control system "Do not do me any favors. Do not fix me and do not kill me" as in both it will no more be an active cancer cell. In the mole-rat we find a substitution of an amino acid exactly where many cancer cells has a mutation in p53. But in the case of the mole-rat it abrogates the killing option, and enhances the repair option. After all, the mole-rat, like cancer cells, experience hypoxia, however any mistakes caused by the stress in the mole rat should be fixed and not sentence it to death. Another enzyme, Heparanase, is involved in tumor progression and the development of metastasis, which is the worth scenario of cancer growth. We found that the mole-rat has forms of Heparanase that miss parts of the native protein. One of them proved to inhibit the size of tumors by 7 times as well as inhibiting the development of metastasis. We added our results found by the state-of-the-art methodology of genomics that can reveal the pattern of expression of the whole repertoire of genes in a given tissue. What we demonstrated is that there are differences in the expression profile between mole-rat and rat, with or without exposure to hypoxia, in molecular and biochemical pathways related to hypoxia, to longevity and to cancer. The conclusion is that the mole- rat should be carefully examined as a model for human cancer.”

So blind mole-rats are completely cancer-resistant?

“In my opinion, there is no mammal that is completely, absolutely resistant to cancer, and none of its individuals will ever develop malignant tumors. Whoever tells you that there is such a mammal is, politely put, hasty. However, it's not possible to breed blind mole-rats in captivity, so every winter we go hunting for animals to renew our stock of animals. This is being done in our institute, since Nevo started to work on the mole-rat, which is for the last 40 years. We've had thousands of the animals here. I know it from my experience in the last 17 years. I asked Nevo, if a cancerous tumor had ever been observed in a blind mole-rat during the years he was actively studying it. He said no. So, in 40 years no spontaneous cancerous growth has ever been observed in thousands of individuals.

“I was thinking: We showed differences in structure and function of major genes related to cancer. We never noticed spontaneous tumors. so let's see if it's possible to induce cancer in these animals. Mole-rats can live over 20 years compared to rats' life span, which is 4-5 years. They show no aging symptoms and no ailments. They do not lose any muscle mass. They are as strong and vivacious at 20 years old as at 2 years old. So, I

took mice and rats and mole-rats – both young ones, about 2 years of age, and old ones, over 10 years old – and treated them with carcinogenic substances. I took the old mole-rats because the older all of us are, the more susceptible to diseases we are. One carcinogen induces soft-tissues sarcoma. After two to three months, as expected, all the mice had cancer. After four to six months, all the rats did too. But nothing was observed in the blind mole-rats! But we decided to follow them and see if something happened...

After a year and a half, lumps were found in two of them – but it wasn't cancerous. It was an abscess, which is an unresolved inflammatory reaction. After two years we were happy to find one more treated old mole-rat with a lump. This time a cancerous one.

“Why is this good? We can now compare between the expected tumors from mice and rats, and the extremely delayed tumor from the mole-rat. It might reflect a difference in the development of cancerous cells in mole-rat compared to mouse and rat, from which we can learn about the mechanism of the extremely high cancer resistance of mole-rats.

Another carcinogen we tried should induce skin cancer involving completely different cells type. Both mice and mole-rats developed a wound after about 10 days. The wound in the mole-rats seemed to be so serious ... I was sure that they were going to die just from the wound deterioration. However, in a couple of weeks the blind mole-rat developed a scar, and then their skin completely healed. It took 3-4 months and all the mice developed the expected skin cancer. “

“Then we moved from the whole animal to cells. We propagated healthy cells, fibroblasts, from blind mole-rats, rats and mice, and added another wild rodent, the spiny mouse, so people wouldn't say, what I usually think is sensible, that our controls are inbred laboratory animals. We took the healthy cells of the blind mole-rat and grew them together, in a co-culture, with the cancerous cells of the blind mole-rat. Cells grow on a medium in a Petri dish and are given liquid nutrition. So we also took the medium in which the healthy blind mole-rat cells grew, and fed the cancerous blind mole-rat cells with this medium. In both cases the cancerous cells died. No death of the cancerous cells happened when we co-cultured them with mice, or rat or spiny mice normal cells, or fed the cancerous cells with the medium these normal cells grew in. There was no effect of normal cells of all these species on normal cells. So there is something secreted only by mole-rats cells interacting only with cancer cells.”



What does this mean for cancerous cells in humans?

“This is what is really important. Can we declare that we can use the mole-rats for the sake of human cancer patients? So we took various kinds of human cancer cell lines originated from different human organs. One of the cell lines we tested was of human breast cancer that is especially aggressive and metastasizes very quickly. When we put all these human-cancer cell lines with the healthy blind mole-rat cells, or the medium they grew in, they were all killed. Again, we tried the same thing with healthy cells from the spiny mouse, the mouse and the rat, and nothing happened.”

So what do you conclude from all this research?

“From the start of cancer research, scientists have always worked on lab mice. Why mice? Because it well known animals, they are inbred in animal houses for hundreds of generations so their genetic profile is known, their life span is short and it’s easy to induce tumors in them. Even if we don’t experiment on them, the majority will die of spontaneous cancer anyway. It will be wrong and boastful to undervalue the progress in understanding mechanisms of cancer induction, progression and inhibition due to decades of studying mice. I will be the last to do so. But we haven’t managed to transfer this knowledge from mice to humans. Hundreds of millions of dollars have been invested for decades in studies on mice; the vast majority never reached the clinical stage. So the conclusion of renowned cancer scientists, which worked with mice and contributed the cornerstones of cancer research, is that you can’t make a prediction from mice and apply it to humans. In fact, the leading scientists of cancer research claim that sticking to the conservative paradigm of using mice is the major obstacle to progress in human cancer research, and what we miss is a good animal to work with. With all modesty, I dare to declare that our results indicate that we might have found the missing animal that will help progress in the efforts to cure humans from cancer. An animal that kills human cancer cells with no harm to healthy cells. The ‘built-in’ mechanism that defends mole-rats from cancer, a mechanism that was developed and fine-tuned along millions of years of evolution, seems be the key for helping human cancer patients.”

You’re saying that even though 90 percent of mice studies didn’t reach the clinical stage, mice are still considered the research animal of choice.

“It is not me who is saying it. As I said, leading scientists of cancer research that contributed tremendously to cancer research using mice as a model, declare so with no reservations. What I do is sharing with you and the readers, among them hopefully generous philanthropists with a vision, my unfortunate experience with grant foundations that reject our proposals, even when we score excellent grades, on grounds that they do not support studies with wild, unknown non-classical animals, because any worthwhile question should be accessible in a well-established model – that is, mice. This issue is so troubling that the scientific journal, Nature, the most appreciated, number one in the league, devoted an editorial to raise attention to the this troubling reality”

What do you want to study now? What's next?

“Now we need to take the medium where blind mole-rats’ cells were grown and start cleaning it until we discover what the substance or substances are that are only secreted by blind mole-rat cells, and which undergo an interaction with something that is expressed only in cancer cells, primarily human cancer cells, because people keep on dying of cancer. What’s our problem? That we are financially broke. We can see the Promised Land but we won’t get to enter it.”

You mean you can't get funding for your research? You'd think that everyone would jump at the chance to fund research that could bring about such a turning point in the treatment of cancer and other diseases.

“I think our findings are pioneering and original, and hold the potential for a breakthrough that would help people who are sick with cancer, and I really hope that generous, open-minded donors will consider funding us so we can keep making progress. For a year now we’ve been trying unsuccessfully to interest philanthropists. We are an Israeli research team, working in an Israeli university, on our own ‘Israeli’ animal, showing genuine and promising results. Important cancer researchers and oncologists expressed their opinion that we are on to something that might finally contribute to human welfare. If we don’t obtain the financial support that we need like we need air to breathe, we’ll lose the race to scientists who get ample research funding from rich and generous Uncle Sam – funds that aren’t available to researchers who aren’t American. Moreover, we, Haifa University and Israel will lose the respect, glory and applause we can win”

In the meantime, lab mice will continue to die by the millions and millions of people will continue to get cancer, heart disease and strokes, the three biggest killers. The blind mole-rat, however, will keep on quietly thriving. Cancer-free.