Josh Schiffman, MD: Genetic clues as to why elephants rarely get cancer
Providence native hopes research will help target pediatric cancers

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When Dr. Joshua Schiffman, (Brown ’96, Alpert Medical School ’00), took his three kids to the Hogle Zoo in Utah several years ago, he paused in front of the massive African elephants and pondered the conundrum: “Why do elephants rarely get cancer?”

Despite their massive size, which can reach a whooping 14,000 pounds, just 4.8 percent of known elephant deaths are cancer-related, as compared to between 11% and 25%, for people.

“Nature has already figured out how to prevent cancer. It’s up to us to take a lesson from Nature’s playbook and adapt those strategies to prevent cancer in people,” Dr. Schiffman said.

He hopes his study, of which he is senior co-author, recently published in JAMA online on the elephant genome, will translate into arresting cancer in children.

Titled “Potential Mechanisms for Cancer Resistance in Elephants and Comparative Cellular Response to DNA Damage in Humans,” it reported that elephants have 38 additional modified copies (alleles) of a gene that encodes TP53, a well-defined tumor suppressor, as compared to humans, who have only two.

In addition, elephants may have a mechanism for killing damaged cells at twice the human cell rate, suggesting the extra TP53 could explain elephants’ enhanced resistance to cancer.

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Q. What in your background in RI, for example, as the son of a prominent oncologist, and a PLME student at Brown medical school – influenced and informed your decision to become a pediatric oncologist?

A. When I was fifteen years old, I was diagnosed with Hodgkin’s Lymphoma, first by my own father and then later confirmed by Dr. Edwin Forman. As a PLME student at Brown medical school, I had the very meaningful experience of shadowing Dr. Forman at Hasbro Children’s Hospital. When it came time to choose a career, I wanted to deliver the same type of compassionate care that I had always witnessed growing up which my father delivered to his own patients, and then personally experienced as one of Dr. Forman’s own patient, and then later witnessed Dr. Forman delivering to his other patients while a medical student. Truly, when I grew up, I wanted to be just like Dr. Forman (and my dad!). There is no substitution for the truly wonderful, talented, dedicated, and caring mentors at Brown!

Q. What was the genesis of this study? Did you see an elephant and wonder why they were not prone to cancer?

A. After medical school, I trained in Pediatrics and Pediatric Hematology/Oncology at Stanford University. Although I initially wanted to just take care of patients [like my father and Dr. Forman], I was very much attracted to the potential of translating laboratory science to our patients in the clinic. I moved to Primary Children’s Hospital and the University of Utah in Salt Lake City, Utah, to start a translational genomics laboratory to better understand the origins of pediatric cancer. Along the way, our lab became very interested in understanding increased cancer risk in other animals [I had minored in animal behavior while an undergraduate at Brown]. We were very focused on cancer predisposition in humans and dogs.

While attending an evolution and medicine conference in Bar Harbor, Maine [sponsored by Dr. Randy Nesse, one of the founders of the field of Evolutionary Medicine], I learned that elephants rarely develop cancer and it might be due to extra copies of TP53. This intrigued me because we care for children and families with Li-Fraumeni Syndrome who are missing functional TP53 and have nearly 100% lifetime risk of cancer [as opposed to elephants with extra TP53 who almost rarely develop cancer]. This was “a-ha moment” for me when I realized we can focus on cancer resistance instead of cancer risk, and see what we could learn to apply to our patients.

We immediately began a collaboration with the speaker from this evolution and medicine conference [Dr. Carlo Maley, Arizona State University], and then reached out to Utah Hogle’s Zoo to get fresh elephant blood to do our functional DNA repair experiments. Eventually, the Ringling Bros. and Barnum & Bailey Circus reached out to us, and we have developed an extremely productive partnership including tremendous research support and collaboration with their Center for Elephant Conservation. Link: https://www.ringlingelephantcenter.com/cancer-research/

Q. Is evolutionary medicine an emerging field and can you explain the conceptual approach?

A. This is the idea that if you look at why disease occurs (or doesn’t occur) from an evolutionary perspective, that you may gain clinical insight into how to apply these evolutionary mechanisms to patients.

Q. What is the next step in this research?

A. We are now trying to raise enough support and awareness to continue to...
fund this research. We want to search for natural or synthetic compounds that will mimic the effects of extra copies of TP53 (i.e., shift all of the cells to apoptosis instead of just DNA repair). We also are working with collaborators from Israel to try to use novel genomic technology to deliver elephant TP53 to human cells as potential therapeutic for either cancer prevention or treatment. We don’t want to overpromise; we have not found the cure to cancer, although we do believe we may have discovered one of the potential mechanisms for how elephants are protected from cancer [multiple copies of TP53, the “guardian of the genome”]. Now we want to work as hard as we can – and as fast as we can – to see if we can apply this discovery to humans. This will require significant philanthropic funding. However, one child with cancer is one child too many, and we now want to take advantage of 55 million years of elephant evolution to try to figure out how to prevent cancer in people.

Q. When you meet with your little patients, do you share elephant stories with them?
A. Yes, absolutely! This has been one of the unexpected joys of this research. I can now take a situation that is desperate and full of fear and anxiety, and just by sharing the research that we’re doing, we are now able to turn the situation into a happy discussion that leaves everyone smiling and wanting to visit elephants at the zoo or circus.

Q. Do your children think you are really cool now that you are a researcher in the Animal Kingdom?
A. They think that I am a mixture of coolness and weirdness that I am so interested in elephants and other animals! They do like seeing me discuss the research, and are particularly amused by the cartoon explanation made by Ringling Bros [see link above]. Personally, I am just pleased that my children are able to learn a little bit more about what I do for a living. Maybe, one day, they will want to continue to help patients and their families just like I grew up wanting to help continue what my father does through his dedication to his own patients that he demonstrates on a daily basis [like father, like son, except for the elephant part!].

WATCH THE VIDEO: https://www.youtube.com/watch?v=ThRRIVSH7wk