Go figure: Math model may help researchers with stem cell, cancer therapies

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The difficult task of sorting and counting prized stem cells and their cancer-causing cousins has long frustrated scientists looking for new ways to help people who have progressive diseases.

But in a development likely to delight math teachers, University of Florida researchers have devised a series of mathematical steps that accomplishes what the most powerful microscopes, high-throughput screening systems and protein assays have failed to do — assess how rapidly stem cells and their malignant, stemlike alter egos increase their numbers.

The method, published in the online journal *PLoS ONE* in January, may rev up efforts to develop stem cell therapies for Alzheimer's, Parkinson's and other diseases. It may also help get to the root of the cancer-stem cell theory, which puts forth the idea that a tiny percentage of loner cancer cells gives rise to tumors.

"Math is going to be the new microscope of the 21st century because it is going to allow us to see things in biology that we cannot see any other way," said Brent Reynolds, Ph.D., an associate professor of neurosurgery at UF's McKnight Brain Institute and a member of the UF Shands Cancer Center. "Stem cells and the cells that drive cancer may be as infrequent as one in 10,000 or one in 100,000 cells. The problem is how do you understand the biology of something whose frequency is so low?"

Inspired by a 2004 essay by Joel E. Cohen, Ph.D., of The Rockefeller

University and Columbia University that described the explosive synergy between mathematics and biology, Reynolds and postdoctoral associate Loic P. Deleyrolle set out to build an algorithm that could determine the rate stem cells and cancer stem cells divide.

High hopes to treat or prevent diseases have been pinned on these indistinguishable cells, which are often adrift in populations of millions of other cells. Scientists know stem cells exist mainly because their handiwork is everywhere — tissues heal and regenerate because of stem cells, and somehow cancer may reappear years after it was thought to be completely eliminated.

With Geoffrey Ericksson, Ph.D., a computational neuroscientist at the Queensland Brain Institute, and other scientists in Australia, the team proposed a mathematical interpretation of neurospheres — tiny collections of brain cells that include stem cells and their progeny at different stages of development.

They tested the mathematical approach by using brain tumor and breast tumor cells in cultures and in mice, correlating the estimates generated by the mathematical model with the aggressiveness of the cells they were studying.

"The unique thing about our study is we were able to do the biology," Deleyrolle said. "We took our simulation to the real world with real cells."

By offering a method to evaluate the effects of diseases and treatments on stem cell activity in the brain, as well as allowing the assessment of malignant stemlike cells, researchers believe they can better evaluate potential therapies for diseases.

"Estimating the numbers of stem cells one has in a particular tissue or culture has important implications in the development of therapeutics, including those for brain tumors," said Harley Kornblum, M.D., Ph.D., professor in residence at the Broad Center of Regenerative Medicine and Stem Cell Research at the University of California, Los Angeles, who was not involved with the study. "This method provides a mathematical model that will enable researchers to do just that. Certainly, it will help my own research in these areas a great deal."

Provided by University of Florida

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