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Math could help cure leukemia

When kids complain that math homework won't help them in real life, a new answer might be that math could help cure cancer.

In a recent study that combined math and medicine, researchers have shown that patients with chronic myelogenous leukemia (CML) may be cured of the disease with an optimally timed cancer vaccine, where the timing is determined based on their own immune response.

In the June 20 edition of the journal *PLoS Computational Biology,* University of Maryland associate professor of mathematics Doron Levy, Stanford Medical School physician and associate professor of medicine (hematology) Peter P. Lee, and Dr. Peter S. Kim, Ecole Supérieure d'Electricité (Gif-sur-Yvette, France) describe their success in creating a mathematical model which predicts that anti-leukemia immune response in CML patients using the drug imatinib can be stimulated in a way that might provide a cure for the disease.

"By combining novel biological data and mathematical modeling, we found rules for designing adaptive treatments for each specific patient," said Levy, of the University of Maryland Center for Scientific Computation and Mathematical Modeling. "Give me a thousand patients and, with this mathematical model, I can give you a thousand different customized treatment plans."

Math and Leukemia

While the marriage of math and biology is only beginning to catch on in science, there have been other attempts to use equations to understand how leukemia develops and evolves over time. Levy, Lee, and Kim's study differed in that it took into account the patient's natural immune response in conjunction with the effects of imatinib, a drug that has been successful in putting CML patients into remission.

They wanted to see if they could develop a mathematical model, or set of rules, that would increase chances for long-term remission in individual patients. Over four years, Lee's laboratory collected data from CML patients, measuring the strength of each patient's immune response, in the form of the numbers and the activity of the anti-leukemia T cells, at different times during imatinib therapy.

"Our results suggest that it is not only the drug that sends the leukemia into remission, it's also the natural immune response," Levy said. "After starting imatinib, the anti-leukemia immune response gradually increases. However, it begins to weaken after it reaches a peak. This typically happens well into the treatment.

"Leukemia cells are still present, but in relatively low numbers that causes the immune response to wind down. Unfortunately, this is an ideal time for the cancer cells to develop drug resistance and render the therapy ineffective."

Best Time for Immune Response

Incorporating Lee's clinical data on immune response, Levy's model suggests that the immune response of the patients should be boosted at the time when their immune response starts weakening.

The authors suggest that such a stimulation can be provided in the form of "cancer vaccines," in which pre-therapy blood taken from patients is irradiated to kill active cancer cells, then

introduced back to the patient. A strong stimulation of the immune system was shown to be active in vitro in Lee's lab experiments.

"The mathematical approach showed that it is imperative to connect the timing of the cancer vaccine with the individual profile of the immune response of each patient," Levy said. "The mathematical simulations suggest that a vaccine administered within the initial months of the treatment will have no effect on the progression of the disease. On the other hand, a well-timed vaccine can potentially cure the disease."

Individual Therapy Plan

But the dynamics of each patient's immune response differ. That's where the math comes in, says Levy. "We can find rules for application to a specific patient. We can measure each patient's parameters to find when the dosage will be most effective. Mathematics provides the tools that are necessary to tailor the treatment to the patient."

"While some parameters can be measured in the lab," said Levy. "The mathematical model helps us understand the mechanisms that control the disease and show how to use this knowledge to our advantage."

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Levy and Lee are currently conducting further extensive study to expand on the results of this research, to prepare for possible experiments on animal models and conduct clinical trials.

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Media accessible paper: http://www.plos.org/press/plcb-04-06-20-levy.pdf

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