Can maths be used to cure leukemia?

Although the alliance of maths and biology is still in its early stages, a team of researchers may have found a new way to treat chronic myelogenous leukemia (CML) by combining biological data and mathematical modeling. The researchers explained that by using a mathematical system to monitor the immune response of patients during imatinib treatment, they can calculate the optimal time to administer a cancer vaccine. This form of therapy can potentially be used to cure the disease.

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

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Recent data had shown that treatment with imatinib produced an antileukemia immune response as patients entered remission. Over a period of 4 years, the researchers analyzed the strength of the immune response of each patient undergoing imatinib treatment, as well as the activity of the antileukemia T cells. The data were collected and used to develop a mathematical model.

"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."

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It appears from the model that a patient's immune response should be boosted when it first starts to weaken. This boost can be administered in the form of a 'cancer vaccine', in which pretherapy blood is taken from a patient and irradiated to kill any cancerous cells; the blood is then injected back into the patient. It was found that this method caused a significant stimulation of the

> immune system in an *in vitro* model, according to Peter P Lee, a physician and associate

professor of medicine at Stanford Medical School (CA, USA).

"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."

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Levy goes on to explain the advantage of using mathematical modeling to specifically adapt treatment to each patient: "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 ... The mathematical model helps us understand the mechanisms that control the disease and show how to use this knowledge to our advantage."

Although further work is needed, this new and exciting approach may offer hope for sufferers of CML.

Sources: www.sciencedaily.com/releases/2008/06/ 080619203247.htm; Kim PS, Lee PP, Levy D: Dynamics and potential impact of the immune response to chronic myelogenous leukemia. *PLoS Comput. Biol.* 4(6), E1000095 (2008).