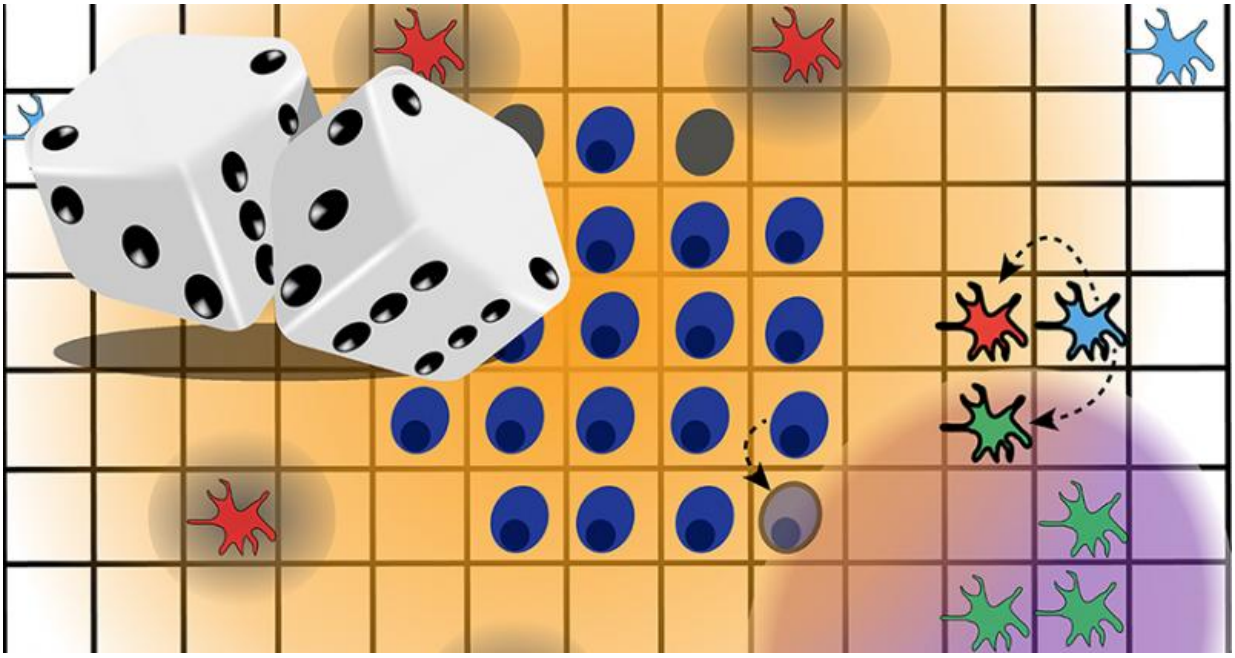
Chance and circumstance tip immune control of cancer

April 23 2015, by Amanda Morris



How does one's immune system 'decide' whether or not to attack a tumor (represented above by the dark blue cells), especially when each individual immune cell may adopt a state that either suppresses (red cells) or promotes (green cells) tumor growth? Joshua Leonard's team is working to understand the roles of chance and collective decision making in this aspect of cancer, toward the goal of therapeutically biasing immune 'decisions' to improve cancer treatment. Credit: Danny Wells

You think that your immune system is there to protect you. But what

happens when it starts working against you?

In the earliest stages of cancer formation, the immune system is forced to make a momentous decision. It either activates and suppresses tumor growth to help the body fight disease, or it becomes dysfunctional, helping the tumor grow and making treatment more difficult. Because this tipping point occurs before a person even realizes something is wrong, doctors are unable to directly observe this critical stage.

"We believe that when immune cells enter a tumor site, they essentially flip a coin, and thus any one immune cell can go one way or the other," said Joshua Leonard, assistant professor of chemical and biological engineering in Northwestern University's McCormick School of Engineering. "What we didn't know is how this element of chance impacts whether the tumor survives or is instead controlled by the immune system."

Led by Leonard and his graduate student Danny Wells, an interdisciplinary team of researchers has created a computational model that enables one to examine how emerging metastatic tumors interact with the immune system. A better understanding of this sensitive early stage could potentially inform new strategies to overcome immune dysfunction, leading to better outcomes.

So far, the model has helped explain something that doctors have observed in the clinic: spatial disorganization within a tumor is a bad sign. Leonard and his collaborators found that greater disorganization within tumors can promote immunosuppression and tumor growth.

"We know there was correlation between disorganization and poor prognosis, but the reason behind this connection wasn't clear," Leonard said. "This study helps explain how heterogeneity might give rise to an environment that tips the immune system toward a tumor-promoting

state."

The research is described online in the April 23 issue of *PLOS Computational Biology*. Other authors on the paper include William L. Kath, professor of engineering sciences and applied mathematics, former McCormick professor Dirk Brockmann, former graduate student Yishan Chuang, and former undergraduate researcher Louis Knapp. Wells is first author of the paper. The interdisciplinary team came together through interaction supported by Northwestern's Physical Sciences-Oncology Center, a flagship program of the Chemistry of Life Processes Institute.

The team also used the model as a virtual test bed to evaluate potential strategies for engineering cell-based therapies to overcome tumor-associated immune dysfunction. Leonard said that researchers could introduce biological therapies to shift the system away from becoming immunosuppressive, and their investigation suggestions some relatively straightforward strategies that could be effective.

"Our ability to engineer customized biological therapies using technologies like synthetic biology is rapidly expanding," Leonard said. "Computational tools like this one will play a key role in helping us design and build therapies that are both safe and effective."

More information: *PLOS Computational Biology*, journals.plos.org/ploscompbiol … journal.pcbi.1004181

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