

'Humanized' mice will lead to better testing of cancer immunotherapies

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Human tumors grown in mouse models have long been used to test promising anti-cancer therapies. However, when a human tumor is transplanted into a mouse, the mouse immune system must be knocked down so that it doesn't attack the foreign tumor tissue, thus allowing the tumor to grow.

A University of Colorado Cancer Center study published in the journal *Oncogene* describes a new model, XactMice, in which human [blood stem cells](#) are used to grow a "humanized" mouse [immune system](#) prior to [tumor](#) transplantation. Now, with a human-like immune system interacting with a human-like tumor in this model, researchers can test anti-cancer therapies in an environment much more akin to that found in real patients. The [new model](#) may be especially important in testing immunology-based therapies, which attempt to recruit the immune system to target tumor tissues.

"One of the reasons that anti-cancer [immune therapies](#) have been difficult to develop is that perhaps we haven't had adequate models. Now we have a model that will enable some of those studies," says Antonio Jimeno, MD, PhD, the paper's senior author and director of the University of Colorado School of Medicine's Head and Neck Cancer Clinical Research Program. Work was performed in collaboration with the Gates Center for Regenerative Medicine of which Dr. Jimeno is a faculty member.

"We essentially did a bone marrow transplant on those [mice](#)," said Dr

Yosef Refaeli, co-corresponding author on this work and faculty member in the Dermatology Department and Gates Center. Mice were treated with radiation to knock down the existing blood system and then human [stem cells](#) from human cord blood were introduced to regrow the blood system with elements of the human immune system. "After a few months, the mice became chimeras - with human blood cells and hence a human immune system," Refaeli says.

A protocol aiming at improving humanized models from human patients is currently recruiting patients at the CU Cancer Center. First, small tumor samples will be taken from melanoma and also head and neck cancer patients. Blood stem cells from these patients will be used to "humanize" mice, and then patients' tumors will be grown on mice matched with their immune systems. The mice will then be treated with anti-cancer therapies, and the results will be compared with results in the human patients.

"This might be a better model for several areas of cancer (and non-cancer) research, and since each mouse provides a lot of information, we will be able to do more with less mice" Jimeno says. "We know that even the response to traditional chemotherapies depends on host factors and not just on what goes on inside the cancer cell. In addition to a humanized immune system, our model allows patient-derived tumors to develop in a much more [human](#)-like environment, overall. For example, this will be a valuable platform to understand the basis of response to immune therapies and find better ways to give the right drug to the right patient at the right time."

More information: *Oncogene* , [www.nature.com/onc/journal/vao ... full/onc201594a.html](http://www.nature.com/onc/journal/vao...full/onc201594a.html)

Provided by University of Colorado Denver

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