

Expert discusses the deeper complexities of cancer

June 21 2019



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Geeta Mehta studies cancer not simply as masses of cells but as structured organs with multiple cell types that communicate with each other and interact with the body—much like your lungs or liver.



"Tumors are not merely cancerous cells that undergo mindless proliferation. Rather, they are highly organized and interconnected <u>organ</u> <u>systems</u>," she writes in a recent *PLOS One* review paper.

"As <u>cancer</u> bioengineers, it is our responsibility to create physiologic models that enable accurate understanding of the multidimensional structure, organization and complex relationships in diverse tumor microenvironments."

Her paper, "Integrated cancer tissue engineering models for precision medicine," discusses the current impactful cancer bioengineering models and recommends ways to improve them.

Mehta is the Dow Corning Assistant Professor of Materials Science and Engineering, an assistant professor of both materials science and engineering and biomedical engineering, and head of the Michigan Engineering Engineered Cellular Microenvironments Lab at the University of Michigan.

Does this perspective hold more benefit for some types of cancer than others?

Mehta: No. All <u>types of cancer</u> should be viewed and studied as "cancer organs" including solid tumors, leukemia and lymphoma. But, just like actual organs, each type of cancer organ works differently.





Geeta Mehta. Credit: University of Michigan

How similar are cancer organs to actual organs? Where do those similarities end?

Mehta: Cancer organs and normal organs both have complex internal environments and a series of complex interactions that govern their behavior. Both are composed of many <u>cell types</u> that communicate dynamically with each other, and both have a specific three-dimensional structure that influences how they interact with the rest of the body.

One big difference is that actual organs are tightly regulated to maintain their integrity and stability. Cancer is not regulated this way—the environment inside a tumor promotes uncontrolled growth rather than stability.

How does looking at cancer as an organ change the way you approach cancer research?



Mehta: Because the organ-like traits of cancer influence its response to treatment. Traditional <u>cancer research</u> mainly involves 2-D slides and petri dishes that fail to recognize and incorporate these traits. These 2-D cultures don't respond to treatments the same way as cancer inside the body, and that makes them less useful.

By viewing cancer as an organ, we can develop more realistic bioengineered models that replicate the conditions inside the body, including three-dimensionality, heterogeneous cell populations and mechanical stimuli—reactions from physical forces the cells experience by virtue of being in the body. By taking these features into account, we can obtain more clinically relevant results, steer development of new therapeutics and accelerate clinical progress.

What kinds of new treatments might we see in the future as a result of this approach?

Mehta: By designing cancer organ models, we hope to better understand how cancers progress and to understand the specific interactions that turn healthy cells into cancer. Then, we hope to develop targeted therapies that interrupt those interactions. This approach can also improve development of therapies that are tailored to individual patients.

What's another big challenge in cancer research that you're working to address?

Mehta: We're finding that not only does cancer work like an organ, but that the same type of cancer organ works differently in different patients. So we're developing three dimensional heterogeneous models that can recreate tumors from individual patient samples.

This enables us to look at differences between individual microtumors from a single patient, and at the differences in cell composition, gene



expression and chemoresistance that occur from patient to patient.

More information: Michael E. Bregenzer et al. Integrated cancer tissue engineering models for precision medicine, *PLOS ONE* (2019). DOI: 10.1371/journal.pone.0216564

Provided by University of Michigan

Citation: Expert discusses the deeper complexities of cancer (2019, June 21) retrieved 26 March 2023 from <u>https://medicalxpress.com/news/2019-06-expert-discusses-deeper-complexities-cancer.html</u>

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