Cell Biology Insights: Extracellular Matrix is More Than Just a Cellular Scaffold

Current ECM research is impacting progress in numerous other fields

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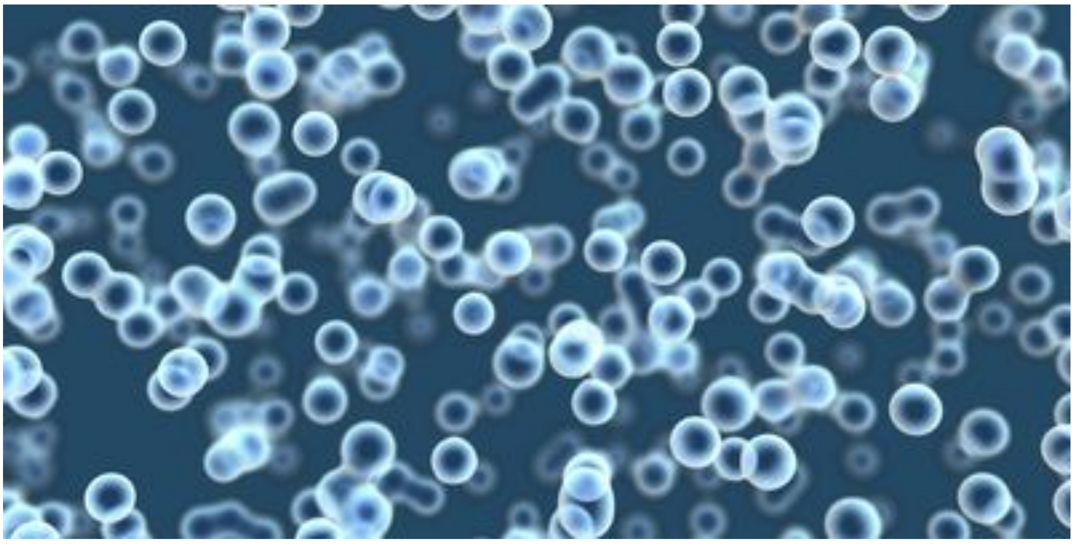

Cells don't act alone. They interact with their neighbours in a dynamic and complex fashion. However, cells also interact with their environment, and their closest environment is the extracellular matrix (ECM). Recent trends are allowing scientists to study cells in the context of their microenvironment. As a result, researchers are learning how the ECM is actively involved in tissue function.

Why study the extracellular matrix?

An ECM structure called the basement membrane acts as a defensive wall between cancer cells and the underlying tissues. If cancer cells break through that membrane, they can become invasive. Some cancer genes are known to be activated by mechanical stresses, which makes those cancers more aggressive. These cancer cells use both enzymes and physical force to rupture the basement membrane, and all of that is regulated by the genes being turned on and off in the cancer. The process of genes being regulated by the physical environment is known as mechanotransduction. By studying both the chemical make-up of the ECM, but also the physical properties of the ECM, scientists are learning about tumor aggressiveness. Studying the ECM is also helping to uncover other biological processes that interact with the ECM, such autoimmunity or how scar tissue develops.

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Spatial biology

The past five years have seen the advent of the spatial biology discipline. Originally focusing on protein and RNA information in the context of a tissue contexts, spatial biology offers the potential for substantial breakthroughs to understand expression patterns in whole tissues. This is especially important to understand how the cells in a tissue not only interact with each other, but also how they interact with their environment, including the ECM.

Mechanobiology and the ECM

Technologies developed to study the ECM and its relationship to cells, and the cellular environment spawned the field of mechanobiology. Micropipettes were originally used to simply pull on cells stuck to surface to measure how strong that connection was. Today, tools such as optical tweezers use light to hold cells, or molecular force sensors to see mechanical forces based the heat they generate when forces are applied.

These tools, combined with continuously improving imaging technologies, are teasing out mechanotransduction mechanisms. Many early experiments used synthetic substrates that are linearly elastic, but the ECM is far more complex. More recent studies define how the complex elasticity of the ECM directly impacts cellular processes. These results are inspiring the development of biomaterials reflecting the properties of real tissues, which can be used in research to better mimic biological tissues in a lab, or in synthetic biology to create tissues that are more like real tissues.

ECM Omics, online atlases, and databases

Research into the ECM is also being aided by the explosion of omics being developed. The original omics, transcriptomics and proteomics, studied the expression of RNA and proteins in tissue-specific contexts. Those fields now include spatial transcriptomics and proteomics, which characterize expression down to individual cells or even subcellular locations. However, a vast proliferation of other omics is defining the characteristics of biological patterns in a tissue-specific and spatial context. For the ECM, some of the new omics include the matrisome (molecules of the ECM and their changes throughout development) and the adhesome (molecules involved in cell to ECM adhesion).

Tightly associated with omics are online databases and other resources. For the ECM, new websites exist, such as adhesome.org or an atlas of basement membrane composition (bmbase.manchester.ac.uk). These new sites add to and complement existing resources such as:

MatrixDB, which offers information on ECM biomolecules and their interactions
Tabula Sapiens, a single-cell transcriptomic atlas
Open Cell a database for protein localization and interactions in human HEK293T cells

iSpatial tool, for single-cell, spatial transcriptomic information

These sites can be used together to provide researchers with the ability to quickly search for their targets. Such invaluable information can guide experimental design and provide information to extend research to target networks and interactions.

Biofabrication and synthetic biology

Another exciting application for cell biology is biofabrication. Global climate change is raising concerns over crop-destroying climate shocks. Combine those risks with the greenhouse gas impact of ranching, there is great interest in the concept of cultured meat as an ethical, sustainable meat alternative. Scientists are actively working on understanding the best composition not only for nutrition, but also desirability, such as juiciness, taste, and texture. Mesenchymal stem cells are the source for these tissues, but one of the aspects under consideration to improve the quality of the product is the matrix these tissues will ultimately be seeded upon. Therefore, understanding both the ECM and stem cells for muscle will be increasingly important to the production of cultured meat.

Other exciting synthetic biology applications, such as bioartificial muscle implants, biorobotics, or use of synthetic biology for disease modeling are also impacted by these studies. Very similar to the research into cultured meat, use of 3D printing and growth on external media could make these tissues available for therapeutic uses. Whether it is growing a biohybrid implant, creating a genomically minimal cell, or 3D printing a cancer cell, these technologies offer to revolutionize cell biology research and the benefits we see from it.