Predicting the Fate of Developing Cells Before Cancer Appears

The new—and free—computational tool, CoSpar, integrates two sources of data about a cell.

March 29, 2022 By Damon Runyon Cancer Research Foundation

Many blood cancers, including leukemia and multiple myeloma, arise when early blood-forming cells do not develop properly. Mistakes in cell differentiation—the process of maturing from a stem cell into a specialized cell type—can cause these abnormal blood cells to grow and divide uncontrollably. But exactly what goes wrong (and why) in the course of cell development is often difficult to determine after the tumor has already grown.

When Shou-Wen Wang, PhD, of Harvard Medical School, began his Damon Runyon Quantitative Biology Fellowship in 2020, he aimed to develop a computational tool that could predict the order of events in cellular differentiation based on genetic data from individual cells. This month, he published his method in Nature Biotechnology and made the tool freely available.

Dr. Wang's novel method, known as CoSpar, makes predictions about cell fate based on two sources of information: the cell's RNA sequence, or transcriptome, and lineage tracing datasets. The cell's transcriptome offers a detailed picture of its current state, but does not indicate what early genetic events determined its fate. Lineage tracing, which identifies all cells descended from a common stem cell, provides this history by situating the cell within its cell line. Single-cell transcriptomics and lineage tracing have both been used in attempts to map cell development before, but CoSpar is one of the first tools to integrate the two sources of data. The method also makes reasonable assumptions to improve the prediction: neighboring cells tend to share similar fates, and cells have limited differentiation potential (i.e., a blood stem cell will not naturally develop into a bone cell). These two assumptions are, respectively, the principles of coherence and sparsity, and together they give the tool its name.

By studying CoSpar's predictions and outcomes, scientists can gain a better understanding of the genes and signaling molecules that govern cell fate. In fact, Dr. Wang's team has already identified a number of transcription factors (proteins that convert DNA to RNA) that play the role of "fate determinants." With further study, it may be possible to identify biomarkers, such as mutant versions of these transcription factors, that indicate a higher likelihood of cancer development, and target those molecules to change this outcome. CoSpar may be able to predict the future, but unlike most fortune tellers, it welcomes the chance to be proven wrong.

CoSpar is available here.

This post was originally published March 16, 2022, by Damon Runyon Cancer Research Foundation. It is republished with permission.

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