

How can cells with the same DNA do different jobs?

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A muscle cell and a nerve cell can differ dramatically without each having acquired an entirely different genome. Much of their difference concerns which parts of a shared genetic repertoire they use, when they use them, and how their products interact with the cell's existing organization. The DNA sequence matters, but sequence alone is not a complete description of a cell's current state.

The phrase “the same DNA” is an approximation. Somatic mutations, specialized DNA rearrangements and differences in chromosome content can create genuine exceptions. Some differentiated cells even lose their nuclei. Those exceptions should not obscure the main question: how can cells that retain broadly the same genome sustain distinct patterns of activity?

1. Possession is different from expression

A gene can be present without being transcribed at the same rate in every cell. An RNA can be made, processed, degraded or translated at different rates, and a protein can be modified, moved or removed after synthesis. OpenStax's account of eukaryotic regulation distinguishes these control points. [1] A cell's function depends on the resulting molecules and interactions, not simply on an inventory of possible sequences.

This is more than switching a few named genes on and off. Two cells can express many of the same genes at different levels, while differing strongly in a smaller set of regulatory or functional components. A categorical label such as “muscle” compresses a pattern, and the boundaries between states may depend on the question being measured.

The useful analogy is a shared repertoire used in different ways. It becomes misleading if it suggests an independent reader standing outside the cell and choosing instructions. The molecules that regulate expression are themselves physical parts of the cell, affected by its history and surroundings.

2. How the difference is observed

Single-cell RNA measurements provide one way to compare cellular states. The 2022 Tabula Sapiens study assembled a reference atlas of nearly 500,000 cells from 24 human tissues and organs and characterized more than 400 cell types. It examined tissue distributions and variation in gene expression rather than assuming that one generic cell represented an entire organ. [2]

An RNA profile is not a complete measure of function. It samples molecules at a time and through a measurement process. A low or missing signal can reflect biological absence, low abundance or imperfect detection. Protein activity, location, mechanical properties and interactions with neighboring cells may require other measurements.

The inference is consequently layered. Reproducibly different profiles establish organized differences in molecular state. They do not by themselves establish which difference caused the cell to adopt that state, or which is required to maintain it. A map of states and an explanation of transitions are complementary products.

3. A minimal model of cellular memory

Suppose, as an explicitly hypothetical model, that a regulatory protein promotes production of itself. Let its concentration be x , and write the rate of change as basal production plus feedback-dependent production minus removal: $dx/dt = b + a x^2/(K^2 + x^2) - d x$. Here b , a , K and d are positive parameters describing the proposed rates and response scale.

The equation can, for some parameter choices, admit more than one stable steady state. A transient input can then move the system into a state that persists after the input disappears. For other choices, only one stable state exists. The equation does not demonstrate that any named cell type uses this exact circuit; it shows what a testable persistence mechanism would require.

The distinction matters because a brief initiating signal and a continuing maintenance process are not the same cause. If removing a signal after differentiation leaves the state intact, the signal was not necessarily irrelevant. It may have triggered a system that now maintains itself through different interactions.

4. Chromatin is part of regulation, not a universal explanation

DNA is packaged with proteins, and its accessibility can influence expression. Regulatory changes involving chromatin belong among the mechanisms of eukaryotic gene control. [1] But calling a difference “epigenetic” does not specify which modification occurred, how it was established, whether it is inherited through division, or whether it causes the observed function.

Those questions need separate tests. If a chromatin mark appears after a cell changes state, it could help stabilize the state, reflect an earlier change, or do both. Merely measuring the mark and naming it does not determine the direction of causation. Removing or altering it may clarify its role, provided the intervention's other effects are considered.

Cellular memory also need not mean perfect immutability. A maintained state can respond to strong perturbations, change gradually or fail under altered conditions. Stability describes resistance to specified disturbances over a specified time, not a guarantee that a cell can never change.

5. A stronger causal comparison

Imagine two otherwise comparable cell populations with the same starting state. In one, a proposed regulator is perturbed; in the other, a matched control is applied. Measuring only a single marker would leave open whether the regulator altered a label while leaving the wider function unchanged. Measuring several molecular features and the relevant activity would make the test more informative.

Timing provides another distinction. A regulator required to establish a state might not be required to maintain it. Conversely, a component with little effect on initial differentiation could be necessary for long-term stability. The experiment needs to intervene at the stage corresponding to the claim.

A rescue experiment can strengthen the inference when restoring the component restores the affected behavior. Even then, the outcome remains bounded by the system and conditions. It does not establish that the same regulator controls every cell type or that a particular network is sufficient to construct an entire tissue.

6. What the answer leaves open

Cells with broadly the same DNA can do different jobs because regulatory activity, molecular abundance and cellular context differ. Expression atlases make these differences observable, while interventions are needed to distinguish their causes from their consequences. [1,2]

The remaining problems concern how particular states are established, stabilized and changed, and how accurately measurements capture them. Neither a genome sequence nor one epigenetic label closes those questions. The conceptual error is to mistake a shared set of possibilities for a shared current state.

Related reading

Article 029, “Why are siblings different?”, concerns inherited differences between individuals. Article 031, “How does a developing organism find its shape?”, concerns the geometry produced when cells act together. Both associations are optional and reciprocal.

References

[1] OpenStax. Biology 2e, section 16.1: Regulation of Gene Expression.

<https://openstax.org/books/biology-2e/pages/16-1-regulation-of-gene-expression>

[2] The Tabula Sapiens Consortium. The Tabula Sapiens: A multiple-organ, single-cell transcriptomic atlas of humans. Science 376, eabl4896 (2022). <https://doi.org/10.1126/science.abl4896>