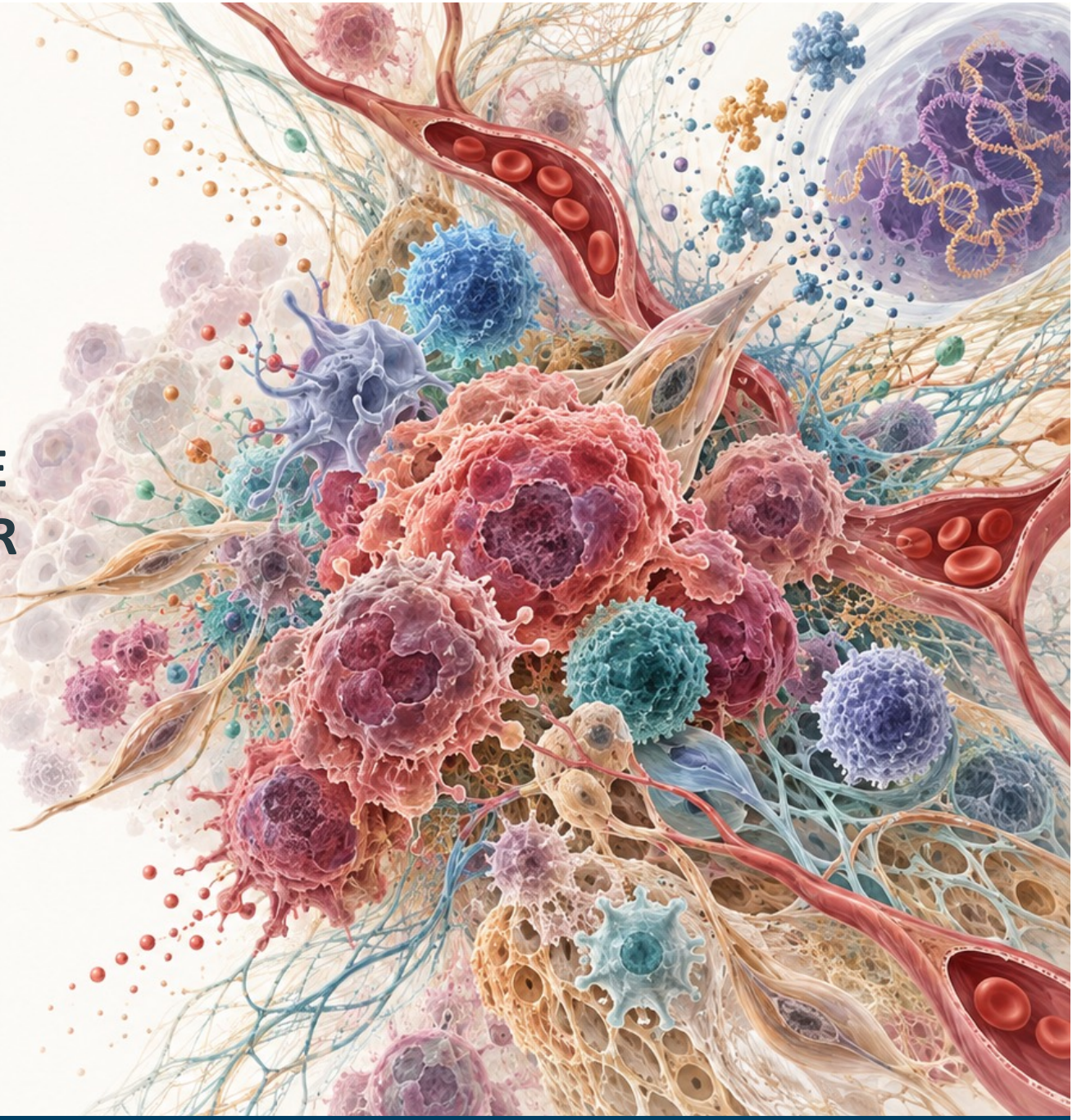
Cancer STEM Lab

Cancer Biology & Tumor differentiation therapies

THE EVOLUTION OF THE HALLMARKS OF CANCER



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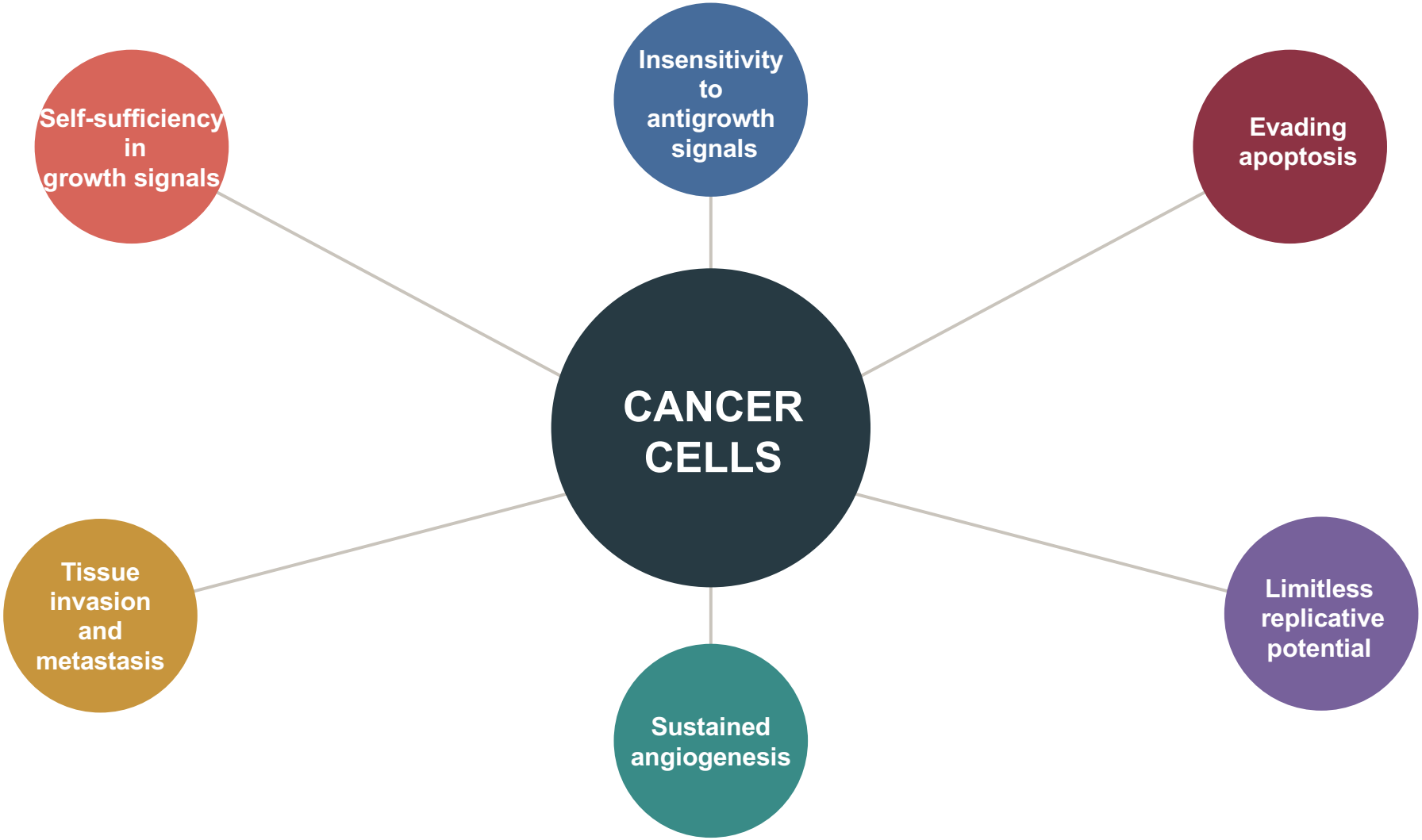
Before the hallmarks: cancer already had several explanatory traditions



2000: six acquired capabilities become one organizing framework

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2000: six acquired capabilities organize the complexity



2011: the framework opens toward metabolism, immunity and context

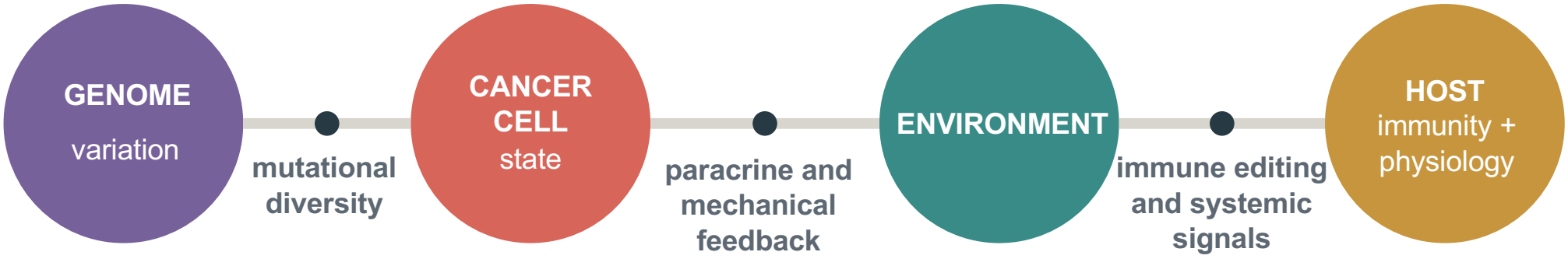
- Sustaining proliferative signaling
- Resisting cell death
- Inducing angiogenesis
- Reprogramming energy metabolism
- Evading growth suppressors
- Replicative immortality
- Invasion and metastasis
- Avoiding immune destruction

ENABLING CHARACTERISTICS

- Genome instability and mutation
- Tumor-promoting inflammation

Tumors recruit normal cells into a tumor microenvironment

The **conceptual shift** in 2011: causation crosses biological levels



The same phenotype can arise through different mechanisms at different levels

2022: **four new dimensions** surround the established core



By 2022, the framework contains different kinds of entities

Capabilities, enabling processes and contextual regulators should not be read as equivalent boxes

WHAT THE TUMOR CAN DO

Hallmark capabilities

proliferate, survive, invade, reshape metabolism

WHAT MAKES ACQUISITION EASIER

Enabling characteristics

mutation, genome instability, inflammation

WHAT CHANGES ACCESSIBLE STATES

New dimensions

plasticity, epigenetics, senescence, microbiomes

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2026: Hanahan reorganizes the framework into four dimensions

The new synthesis separates functions, enabling conditions, cellular contributors and systemic interactions



The hallmarks become one layer in a multiscale model of cancer

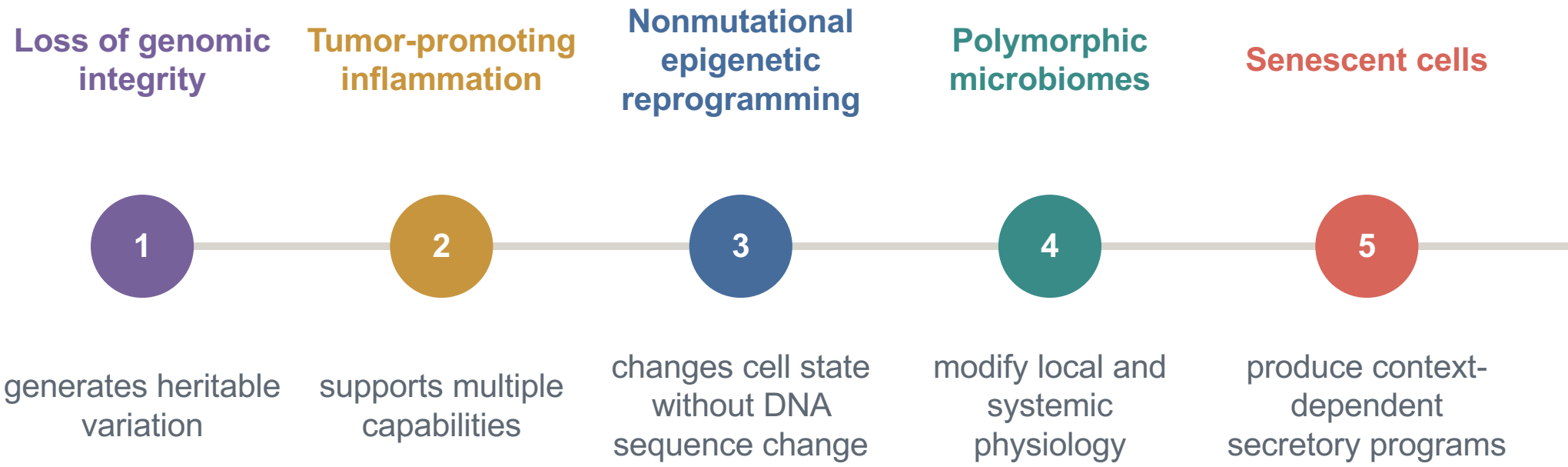
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Nine **acquired functional capabilities** in 2026

1. **Sustaining proliferative signaling**
2. **Inactivating growth suppressors**
3. **Resisting programmed cell death**
4. **Establishing replicative immortality**
5. **Inducing or accessing vasculature**
6. **Activating invasion and metastasis**
7. **Deregulating cellular metabolism**
8. **Evading immune destruction**
9. **Unlocking phenotypic plasticity**

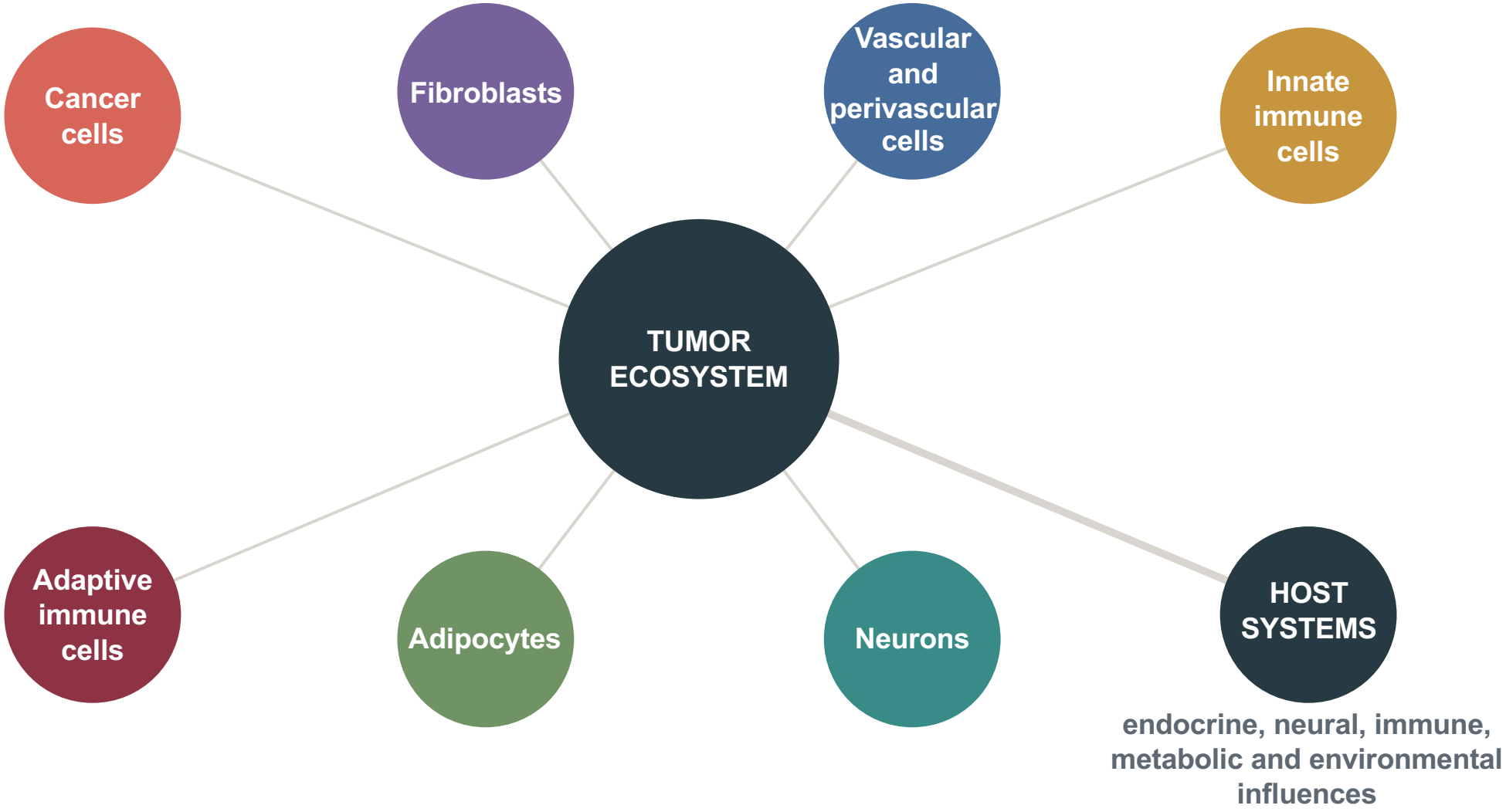
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Five **phenotypic characteristics** facilitate hallmark acquisition

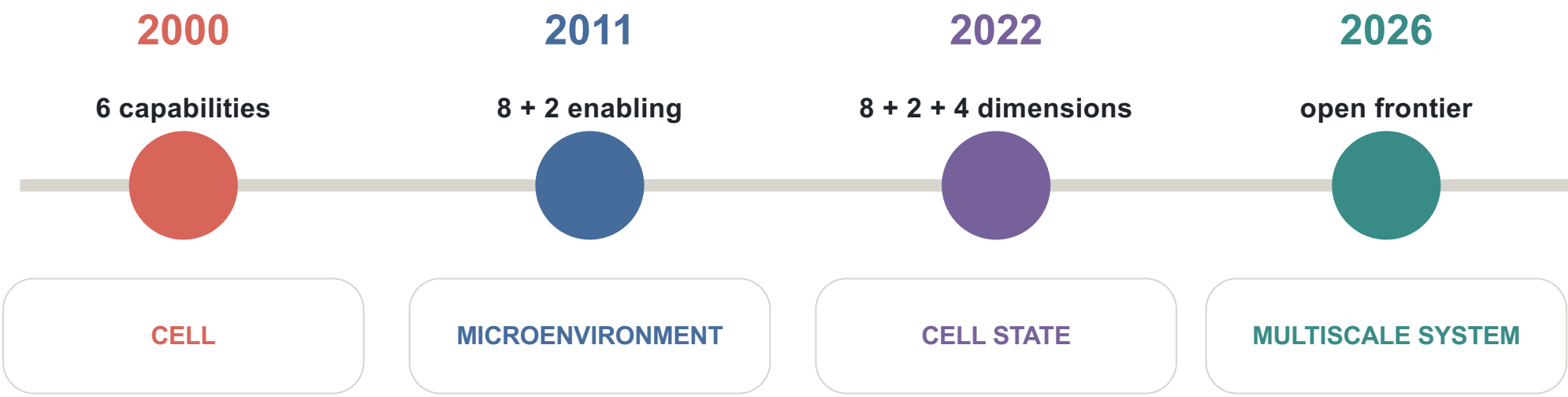


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The tumor microenvironment as an **explanatory dimension**



One visual history: explanation **keeps expanding**



Cancer biology shifts from a list of parts toward the dynamics of organized living systems

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