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Unveiling the evolutionary significance: Atavism's transition from ancestral traits to a fundamental biological phenomenon

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Abstract. This essay delves into the nuanced concept of atavism, tracing its evolution from the abrupt manifestation of ancestral traits in wild populations to a pivotal element in contemporary biology. Explored through recent studies such as the Atavism Theory of Cancer, Single-Cell Atavism of Cnidocytes, and Atavism in the Developmental Polarity of Chicken Limb, this research reveals atavism's journey from speculative fiction to empirical reality. By scrutinizing cancer as a series of atavistic changes, experimental atavism at the single-cell level, and the atavism observed in avian limb development, the essay proposes that atavism offers fresh perspectives on evolution, adaptation, and the dynamic reuse of gene reservoirs. This study underscores atavism's transition into a tangible and crucial component of ecological and developmental biology, providing insights that traverse disciplinary boundaries and deepen our comprehension of the natural world.

Keywords: Atavism, Ancestoral traits, Atavistic theory

1. Introduction

In scholarly circles, the term "atavism" initially denoted the abrupt manifestation of ancestral traits in individuals within a wild population [1]. However, as research on atavism has expanded, its definition has evolved in multifaceted ways. Initially, studies focused on experimentally induced atavistic phenomena, such as the development of pelvic fins in stickleback fish [2] and the emergence of hindwings in flies [3], encompassing atavism as a descriptor for the reappearance of ancestral traits in wild-type individuals at large. Subsequently, the concept of 'taxic atavism' [4] confirmed that atavism could contribute to the evolutionary process, becoming stable phenotypes within wild populations rather than isolated occurrences. Finally, the emergence of the cancer atavism theory [5] has illuminated how cancer progression can be perceived as a systemic reversion to ancestral phenotypes in response to stress, thus positioning atavism as a phenomenon operating at the cellular and individual levels.

Today, atavism is employed to elucidate the occurrence or resurgence of ancestral forms at the phenotypic level, emerging as a concept central to developmental, hereditary, and medical biology. This paper aims to present recent advances in atavism sequentially and provide insights into its implications in related fields.

2. Atavism Theory of Cancer

Cancer, often viewed as a systemic somatic progression through multicellular cooperation, is increasingly conceptualized as a series of atavistic changes toward single-cell ancestors in recent studies.

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Rather than random mutations, the hallmarks of cancer are associated with the reactivation of ancestral genes [5]. While the foundational idea of this theory was initially proposed in 1914, recent developments have yielded a robust model that supports precise predictions. This model defines cancer traits (insensitivity to immunity, vascularization, cell mobility, proliferation, genome instability, and metabolic shifts) as indicators of a shift toward a unicellular, ancestor-like lifestyle [6].

Under the atavism theory, the interrelation among these hallmarks can be consolidated into characteristics of an ideal unicellular ancestor. The regulation of these "ancestral" genes can be quantitatively examined and predicted through phylostratigraphy methods. This novel framework has effectively accounted for the heterogeneity of cancer tissues, allowing us to arrange the hallmarks in an evolutionarily chronological order (Serial Atavism Model, SAM model), opening doors to potential therapeutic solutions.

2.1. The Hallmarks

In contrast to the previous somatic mutation theory, which described cancer progression as a breach of the ancient contract of cellular cooperation forming the basis of multicellular life [7], the atavism theory posits that the emergence of these traits represents a systemic atavistic phenomenon. A crucial requisite for supporting this theory is the determination that genetic and epigenetic changes in cancer adhere to an evolutionarily patterned framework. This entails that up-regulated gene fragments in cancer should have appeared prior to multicellularity and supported unicellular life while being suppressed in multicellular life, with the reverse true for down-regulated genes [5].

Multiple studies employing phylostratigraphy endorse the atavism theory. Phylostratigraphy traces gene lineage through homology and inferred orthology across species, thereby enabling the tracking of gene emergence times. Analyzing data from the Cancer Genome Atlas (COSMIC), a meticulously curated gene database associated with cancer, reveals an enrichment of collected genes related to cancer that shifted toward approximately 1 billion years ago, just before the advent of metazoan life [8].

Moreover, investigations into mutations in Homologous Synteny Blocks (HSBs) and Evolutionarily Reused Breakpoints (EBRs) within the human genome have underscored an observable pattern. EBRs represent evolutionary "hot-spot" regions, while HSBs denote highly conserved regions among species. Differences in the allocation of gene loci between these categories signify valuable information about gene ages. Genes predating 1 billion years ago tend to be enriched in HSBs and depleted in EBRs, whereas those emerging after this time exhibit the opposite trend [9]. In normal tissues, clustered mutations predominantly occur in EBRs, while cancer tissues exhibit mutations that disable functions in HSBs, further corroborating the atavism theory.

Additional evidence from studies on DNA damage repair, gene locus allocation, and stress response systems align with and further substantiate the atavism theory [10-12].

2.2. Serial Atavism Model

Following the advent of the atavistic model, various quantitative analyses and predictions, rooted in this model, suggest that cancer initiation and progression can be more accurately characterized as a series of reversionary transitions [13]. The Serial Atavism Model (SAM model) postulates that these reversionary transitions follow a consistent order across diverse cancer types and variations. This order typically mirrors the reverse sequence of the appearance of multicellular traits in evolutionary history.

This concept bears a striking resemblance to Haeckel's aphorism, "ontogeny recapitulates phylogeny," which posits that the development of higher animal forms recapitulates various stages of lower animal forms. The SAM model proposes that the atavistic processes in cancer tissue can be subdivided into distinct stages, each characterized by the recovery of specific traits from a unicellular ancestor or the abandonment of multicellular traits in the reverse order of their acquisition or suppression [13].

Extensive evidence from phylostratigraphy, morphology, and related fields bolsters the validity of the SAM model at both the individual stages and as a whole. Moreover, the SAM model has generated novel predictions, further enriching our understanding of cancer and its ecological and evolutionary

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implications. It promises to refine our comprehension of the underlying mechanisms and biological significance of cancer in the future.

3. Single-Cell Atavism of Cnidocytes

Cnidocytes, specialized stinging cells employed for predation and defense, are unique to cnidarians and are believed to have existed in the common ancestor of this phylum. Recent research conducted by L.S. Babonis and colleagues employed CRISPR/Cas9-mediated genome editing in the sea anemone Nematostella vectensis. By knocking out the transcription factor NvSox2, they successfully reactivated a cnidocyte type (ensnaring cells) that was present in other branches of sea anemones but silenced in this specific type [14].

3.1. Cnidocytes

Cnidocytes represent one of the most morphologically diverse cell types in the natural world, broadly classified into three categories based on cell structure and appearance: nematocytes (piercing cells), ptychocytes (adherent cells), and spirocysts (ensnaring cells) [15].

Upon the knockout of Nox2 [16], the original small piercing cells in Nematostella transformed into robust ensnaring cells with partial functionality—a cell type that had disappeared in the evolutionary history of Nematostella, giving rise to this genus [17].

3.2. Conclusion

This groundbreaking experiment has bridged the gap by demonstrating experimentally induced atavism at the single-cell level. The findings suggest that such atavism may indeed contribute to the natural evolutionary processes of cnidocytes [14]. The ability to temporarily silence ancestral traits while retaining their underlying genetic architecture provides species with flexibility in adapting to new environments. By allowing a single gene, Nox2, to control this trait binarily, a single mutation can facilitate the full recovery of an entire set of traits, thus contributing to increased cell type diversity [18].

4. Atavism in Developmental Polarity of Chicken Limb

In the realm of developmental biology, self-mutant samples, particularly those exhibiting atavistic traits, have proven to be invaluable tools for studying morphogenesis. C.H. Lineweaver and colleagues have recently identified several atavistic traits in the chicken mutant talpid, known for its limb and craniofacial defects. This research has shed light on the origins of asymmetry and the development of avian limbs [9].

4.1. Avian Limb and Its Mutant

In most tetrapods, the tibia and fibula are of equal length, joining distally into the ankle. A defining feature of extant birds is the reduction of the fibula into a short proximal spur closely aligned with the tibia [9, 19].

The talpid2 (ta2) mutation, an embryonic lethal Mendelian recessive allele in chicks, results in developmental defects in various organ systems, including the neural tube, face, and limb. It arises from a 19-bp deletion in the C2D3 gene, a distal centriolar protein facilitating ciliogenesis. Together with the hedgehog pathway, the C2D2 mutant protein causes the limb to lose its asymmetry, reverting to a tetrapod-like limb configuration [20].

4.2. Contribution

The ta2 mutant serves as an experimental atavism, offering a molecular model for the emergence of atavistic characteristics in the avian hindlimb. This aligns with embryological, molecular, and genetic studies of limb patterning [9]. Importantly, the phenotypic outcomes observed in this research are linked to common changes in signaling during limb development, potentially revealing correlations with variations in limb traits during evolution. In sum, the study of atavistic models continues to unveil new insights into evolution and its mechanisms.

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5. Summary

From its origins in science fiction to its establishment as an empirical phenomenon, atavism has completed its transition from an obscure concept to a significant component of ecology and developmental biology. Research on atavism has progressed from animal models to the single-cell level, demonstrating that atavism not only contributes to evolutionary processes but also serves as a systemic response to stress and environmental adaptation—whether at micro or macro levels, whether initiated intentionally or not. In addition to its role in understanding natural phenomena, experimentally induced atavism plays a pivotal role in developmental biology, driving discoveries in mutation theories, signal pathways, and morphogenesis.

6. Conclusion

As a concept that permeates various branches of biology, atavism has been woven into different theories and models. Over time, as research transcends disciplinary boundaries, the notion of reactivating ancestral genes, in conjunction with atavism, forms a cohesive system that can potentially account for many natural processes—representing the stable reutilization of gene reservoirs. This process, after multiple mutations and shifts in signaling systems, facilitates the emergence of entirely new traits. Numerous examples of this phenomenon can be found in the natural world, from genes that aided plants in colonizing land to the reuse of enzymes in oxidative phosphorylation, each contributing to pivotal steps in the history of evolution. Presently, ongoing research seeks to integrate various aspects of atavism into a holistic perspective, promising fresh insights and perspectives.

It is foreseeable that atavism will continue to find applications in various models across different fields, carrying diverse connotations and contributing to a multitude of theories. As the natural world perpetually evolves, so too will the study of atavism persist, pushing the boundaries of our knowledge.

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