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Editorial

Regeneration across life: From fundamental biology to future medicine

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Regeneration, the ability to restore lost or damaged tissues, organs or entire body structures, represents one of the most profound biological phenomena shared across life on Earth. From plants and animals that regrow entire organisms from small tissue fragments to organisms capable of rebuilding complex organs, regeneration challenges long-standing assumptions about biological limits. The launch of the Journal of Regeneration (JoR) reflects a growing recognition that regeneration is not a niche speciality but a transversal biological principle connecting developmental biology, evolution, ecology, agriculture and medicine.

JoR is founded on the premise that understanding regeneration requires exploration across kingdoms of life and across disciplines, ranging from molecular genetics to clinical translation. It aims at becoming a vehicle that publishes and disseminates scientific production in this wide-range field of inquiry. This editorial outlines the historical foundations of regeneration research, highlights insights gained from diverse model systems, explores how fundamental discoveries provide information for medicine and considers the future trajectory of this rapidly advancing field.

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History of regeneration research

(Dinsmore 1991; Maienschein and MacCord 2022)

The scientific study of regeneration dates back centuries, beginning with Aristotle who observed and documented the ability of organisms to repair or replace lost parts. The initial philosophical curiosity gradually evolved into a rigorous experimental discipline. Early observations in the 18th century, when experimental manipulation was introduced, systematically characterised how certain animals could regenerate entire body parts. Classic experiments revealed that fragmented freshwater organisms could reorganise into complete individuals, introducing the revolutionary concept that biological organisation is dynamic rather than fixed.

During the 19th and early 20th centuries, regeneration became central to experimental embryology. Researchers sought to understand whether regeneration recapitulates development or represents a distinct biological programme. Concepts such as morphogenetic fields, positional information and cellular plasticity emerged from these studies. Investigators recognised that regeneration

involves coordinated processes including wound healing, cell proliferation, apoptosis, pattern formation and differentiation.

The molecular era transformed regeneration research in the late 20th century. Advances in genetics, microscopy and molecular biology enabled the identification of signalling pathways governing tissue restoration. The discovery that conserved developmental pathways, including Wnt, FGF, BMP and Notch signalling, regulate regenerative processes revealed deep evolutionary continuity across species.

In parallel, plant biologists demonstrated remarkable regenerative plasticity in plant tissues. The ability to regenerate whole plants (including algae) from callus cultures or even single cells reshaped the understanding of cellular potency and totipotency. Plant regeneration research became foundational for biotechnology and modern agriculture, long before similar concepts entered animal stem cell biology.

Today, regeneration research stands at a convergence point: developmental biology, stem cell science, evolutionary biology and regenerative medicine now share a common conceptual framework rooted in decades of comparative research. In addition, the new technologies and tools available today (e.g. next-generation sequencing, ChIP-sequencing, single cell transcriptomics, CRISPR/Cas9 genome editing, epigenome profiling, mass spectrometry, transgenesis, metabolite and protein analysis, coupled with advanced bioinformatics and imaging tools) are paving the way towards a complete view of the molecular players involved in the regeneration process.

Diversity of animal and plant models and key discoveries

(Brockes and Kumar 2008; Sugimoto et al. 2011)

One of the defining strengths of regeneration biology is its reliance on diverse model organisms. Each system reveals unique strategies while exposing conserved principles (Fig. 1).

Animal models

Highly regenerative invertebrates have provided essential insights into whole-body regeneration. Cnidarians (mainly the freshwater *Hydra*) and flatworms demonstrated that adult organisms retain populations of pluripotent stem cells capable of rebuilding entire anatomical structures. Studies revealed mechanisms of polarity establishment, pattern scaling and continuous tissue renewal. Echinoderms and tunicates expanded the understanding of regeneration in deuterostomes, offering evolutionary bridges towards vertebrates. These organisms demonstrated that complex tissues, including nervous and circulatory components, can be regenerated through coordinated cellular reprogramming and stem cell activation.

Amongst vertebrates, amphibians became iconic regeneration models. Limb regeneration studies in salamanders uncovered mechanisms of blastema formation, a transient population of proliferative progenitor cells capable of reconstructing patterned tissues. These findings reshaped our understanding of dedifferentiation and lineage plasticity. Then, teleost fish added genetic accessibility to regeneration research. Their capacity to regenerate fins, heart tissue, spinal cord and retina provided molecular entry points into vertebrate regener-

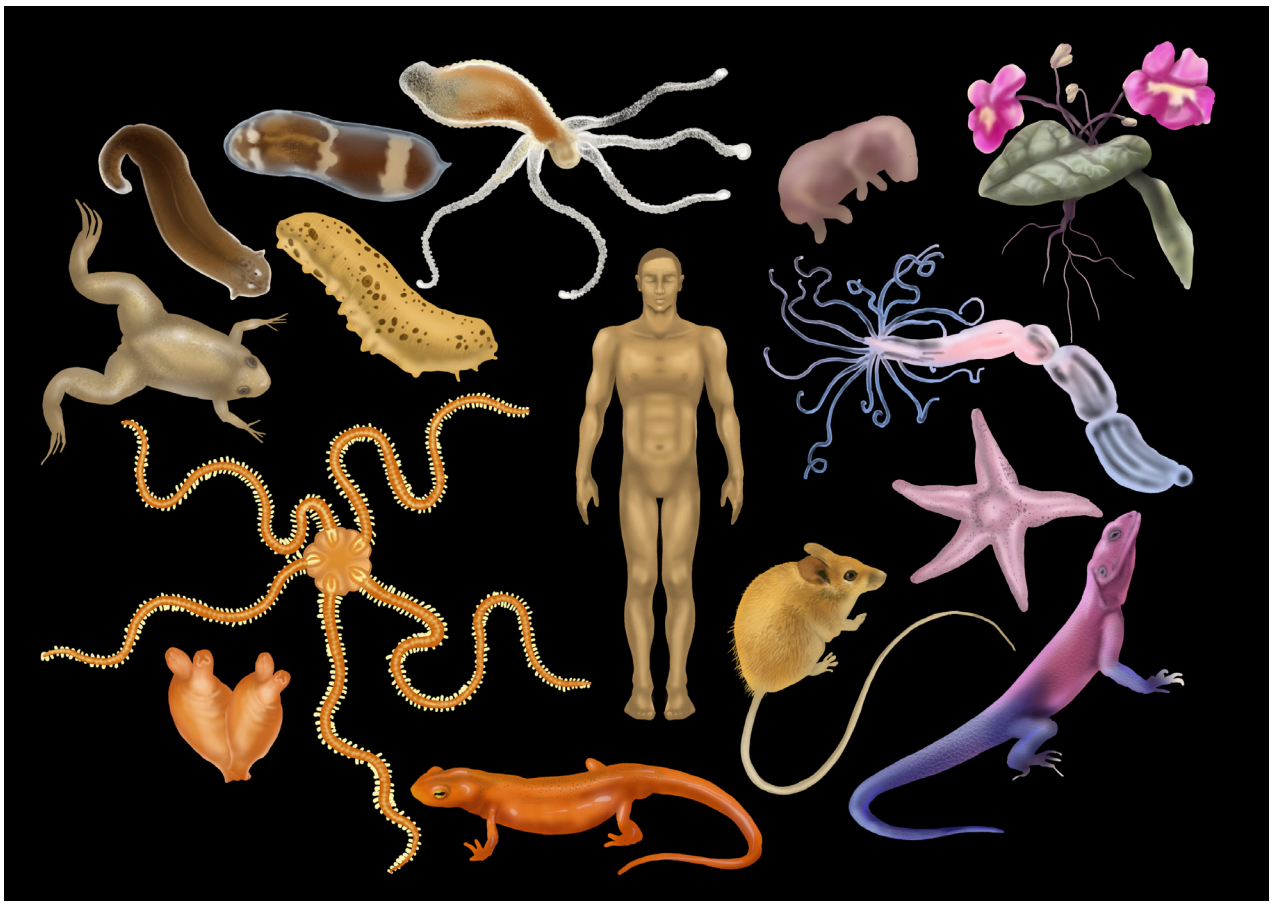

Figure 1. Schematic view of the organisms useful for regeneration studies.

ative mechanisms. Importantly, these models showed that regeneration can occur without fibrosis, highlighting contrasts with mammalian injury responses. Recently, scientific interest has been focusing on mammals, including mice and humans, once considered regeneration-deficient, that have revealed partial regenerative abilities. Liver regeneration, digit tip regrowth and neonatal heart repair demonstrate that regenerative potential exists, but is developmentally restricted or suppressed. These findings shifted the focus towards understanding both why regeneration fails rather than why it succeeds and mammalian regeneration through the lens of clinical applications. Non-standard mammalian models capable of more extensive regenerative abilities, such as spinal cord repair and skin regeneration in spiny mouse or antler regeneration in deer, have also showed that limiting research to only a few species is a missed opportunity to identify novel regenerative mechanisms.

Plant models

Plants exhibit perhaps the most dramatic regenerative capacities amongst multicellular organisms. Somatic cells can revert to pluripotent states and regenerate entire organisms under appropriate hormonal conditions. Studies of auxin and cytokinin signalling uncovered molecular frameworks governing cell fate reprogramming. Further, meristem biology revealed persistent stem cell niches enabling lifelong growth and regeneration. Unlike most animals, plants

continuously generate organs throughout life, integrating environmental cues directly into developmental decisions.

Key discoveries from plant systems include epigenetic reprogramming, cellular dedifferentiation and positional signalling mechanisms that parallel processes later identified in animal regeneration.

Cross-kingdom insights

Across animals and plants, five recurring shared principles suggest that regeneration is an ancient and conserved biological capability, shaped by evolution rather than an isolated phenomenon: (a) Cellular plasticity rather than fixed identity; (b) Injury-triggered signalling cascades; (c) Epigenetic remodelling; (d) Integration of metabolism, immunity and regeneration; and (e) Environmental modulation of repair processes.

Linking basic regeneration research to medicine

(Stocum 2012; Sampogna et al. 2015)

The translation of regeneration biology into medicine represents one of the most exciting developments of modern biomedical science. Fundamental discoveries from model organisms have directly provided information for clinical strategies. As an example, stem cell biology, central to regenerative medicine, draws heavily from insights gained in regenerative species. The recognition that differentiated cells can revert to progenitor-like states contributed to breakthroughs in cellular reprogramming and induced pluripotent stem cell technologies. Furthermore, understanding scar-free healing in regenerative animals has transformed research in fibrosis, a major barrier to human tissue repair. Comparative studies revealed that immune responses play instructive roles in regeneration, shifting medical perspectives from inflammation suppression towards immune modulation.

Cardiac regeneration research illustrates this translational pathway. Observations that certain vertebrates regenerate heart tissue inspired investigations into cardiomyocyte proliferation and regeneration in humans, providing information for emerging therapeutic strategies for heart disease. Similarly, neural regeneration studies have guided approaches to treat spinal cord injury and neurodegenerative diseases by identifying molecular inhibitors and growth-promoting pathways. Plant regeneration research also contributes indirectly to medicine through biotechnology, synthetic biology and bioengineering. Techniques derived from plant tissue culture provided information for large-scale cell culture systems and genetic engineering methodologies now applied in pharmaceutical production and therapeutic development. Thus, regenerative medicine does not arise independently; it is the cumulative outcome of a long history of comparative biological research across species.

The future of the field

The future of regeneration research lies in integration, across scales, species and scientific disciplines. JoR will support main transformative directions such as:

Systems-level understanding

Regeneration is increasingly viewed as a systems property rather than a single pathway. Advances in single-cell sequencing, spatial transcriptomics and live imaging allow reconstruction of regenerative processes at cellular resolution across time.

Evolutionary regeneration biology

Comparative approaches are revealing why regenerative capacity varies dramatically amongst species. Understanding evolutionary trade-offs between regeneration, immunity, aging and cancer suppression may explain limitations in humans and guide therapeutic innovation.

Bioengineering and synthetic regeneration

Tissue engineering, biomaterials and organoid technologies are merging with developmental biology. Future therapies may combine biological signalling with engineered scaffolds to recreate regenerative environments.

Aging and regeneration

Declining regenerative capacity with age represents a central biomedical challenge. Integrating aging biology with regeneration research may uncover strategies to restore youthful repair mechanisms.

Cross-kingdom collaboration

Bringing plant and animal regeneration researchers into shared scientific dialogue remains an underexplored opportunity. Similarities in cellular reprogramming, signalling logic and environmental responsiveness suggest that cross-kingdom comparisons will yield unexpected insights.

Closing remarks

Regeneration research stands at a historic moment. What began as curiosity-driven observation has matured into a multidisciplinary field with profound implications for biology and medicine. The diversity of regenerative strategies across animals and plants reveals that restoration is not an exception in nature, but a fundamental biological capability expressed to varying degrees. Within this arena, JoR aims to serve as a platform where discoveries from all regenerative systems converge, from molecular mechanisms to clinical applications, from evolutionary perspectives to technological innovation. By fostering dialogue across traditionally separated disciplines, JoR seeks to accelerate the transition from understanding regeneration to harnessing it.

The future of regeneration science will depend not on a single model organism or discipline, but on collective insight across life itself. In embracing this integrative vision, JoR aspires to advance a field whose ultimate goal is both ancient and forward-looking: the restoration of form, function and biological potential.

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Additional information

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Data availability

All of the data that support the findings of this study are available in the main text.