

Regeneration in Lumbricidae: Cellular, Immune, and Molecular Mechanisms with Ecological Integration from Prince Edward Island Earthworm Assemblages

Type: Research Article

Received: May 20, 2026

Published: July 02, 2026

Citation:

John Warren., et al. "Regeneration in Lumbricidae: Cellular, Immune, and Molecular Mechanisms with Ecological Integration from Prince Edward Island Earthworm Assemblages". PriMera Scientific Surgical Research and Practice 8.1 (2026): 01-02.

Copyright:

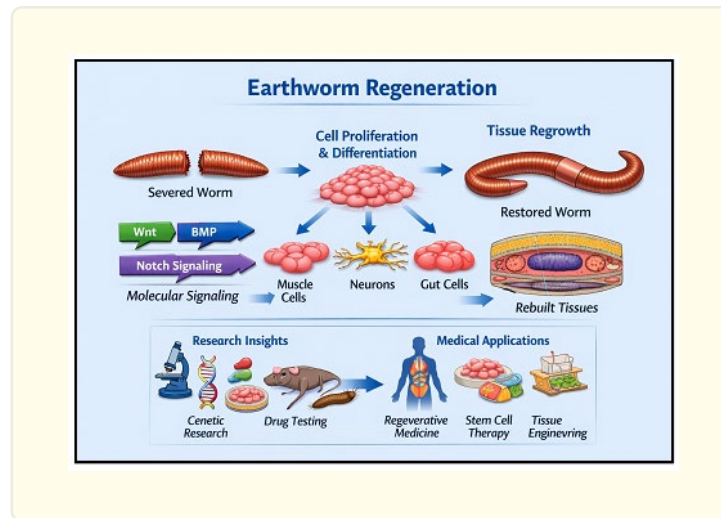
© 2026 John Warren., et al. This is an open-access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

John Warren^{2*} and Wilma M Reynolds¹

¹Oligochaetology Laboratory, 9-1250 Weber Street East, Kitchener, Ontario Canada N2A 4E1

²Research Associate, New Brunswick Museum, 277 Douglas Avenue, Saint John, New Brunswick, Canada E2K 1E5

***Corresponding Author:** John Warren Reynolds, Oligochaetology Laboratory, 9-1250 Weber Street East, Kitchener, Ontario Canada N2A 4E1; Research Associate, New Brunswick Museum, 277 Douglas Avenue, Saint John, New Brunswick, Canada E2K 1E5.



Abstract

Earthworms (Annelida: Oligochaeta) exhibit robust regenerative abilities that vary across species, body regions, and evolutionary lineages. This manuscript synthesizes classical and contemporary research on annelid regeneration—including wound closure, immune activation, blastema formation, segment reconstruction, and ventral nerve cord regrowth—and integrates these mechanisms with ecological observations from Prince Edward Island (PEI) earthworm communities. Drawing from cellular, molecular, and transcriptomic studies, we outline the processes that enable successful regeneration and contrast them with taxa that have lost regenerative capacity. We also contextualize regeneration within earthworm immunity, extracellular

matrix (ECM) remodelling, and segmental patterning. Figures illustrate the regeneration sequence, coelomocyte dynamics, molecular pathways, and comparative outcomes. This synthesis provides a mechanistic foundation for interpreting regeneration in PEI earthworm species and supports future ecological and applied research.

Keywords: earthworm regeneration; blastema; neuroregeneration; fibrosis; tissue engineering

Definitions

ECM = extracellular matrix, NK cells = natural killer cells, ROS = reactive oxygen species, MMP = matrix metalloproteinase, NGF = nerve growth factor, FGF = fibroblast growth factor, Wnt/ β catenin = Wntless related integration site / beta catenin, TGF β = transforming growth factor beta, HOX = Homeobox genes.

Introduction

Regeneration is a widespread, but unevenly distributed trait across the animal kingdom. Annelids, particularly oligochaetes, are among the most capable regenerators, though the extent of this ability varies across species and evolutionary lineages (Bely, 2010) [1]. Some taxa retain full anterior and posterior regeneration, while others exhibit partial or complete loss of regenerative capacity (Bely et al., 2010) [3]. Understanding the mechanisms underlying regeneration in earthworms is essential for interpreting ecological patterns, species resilience, and functional roles in soil ecosystems.

Earthworm regeneration involves coordinated interactions among wound healing, immune activation, cellular undifferentiation, blastema formation, and segmental patterning (Müller & Bely, 2019) [10]. These processes are influenced by molecular pathways such as Wnt, FGF, and ECM remodelling (Rossan Mathews et al., 2024) [15]. The ventral nerve cord, a critical structure for locomotion and sensory integration, also regenerates following injury (Myohara 2004; Bely et al., 2010; Müller & Bely 2019) [11, 3, 10].

This manuscript synthesizes the current understanding of earthworm regeneration and integrates these mechanisms with ecological observations from Prince Edward Island (PEI), where diverse lumbricid species exhibit varying regenerative capacities (Reynolds, 2026) [13]. Figures illustrate the regeneration sequence and associated cellular and molecular processes.

Methods

This manuscript integrates

Primary literature on annelid regeneration, immunity, and molecular pathways.

Comparative analyses from classical and modern studies (e.g., Myohara, 2004; Bely, 2014) [12, 2].

Transcriptomic datasets from regenerating annelids (Rossan Mathews et al., 2024) [15].

Ecological observations from PEI earthworm assemblages (Reynolds, 2026) [13].

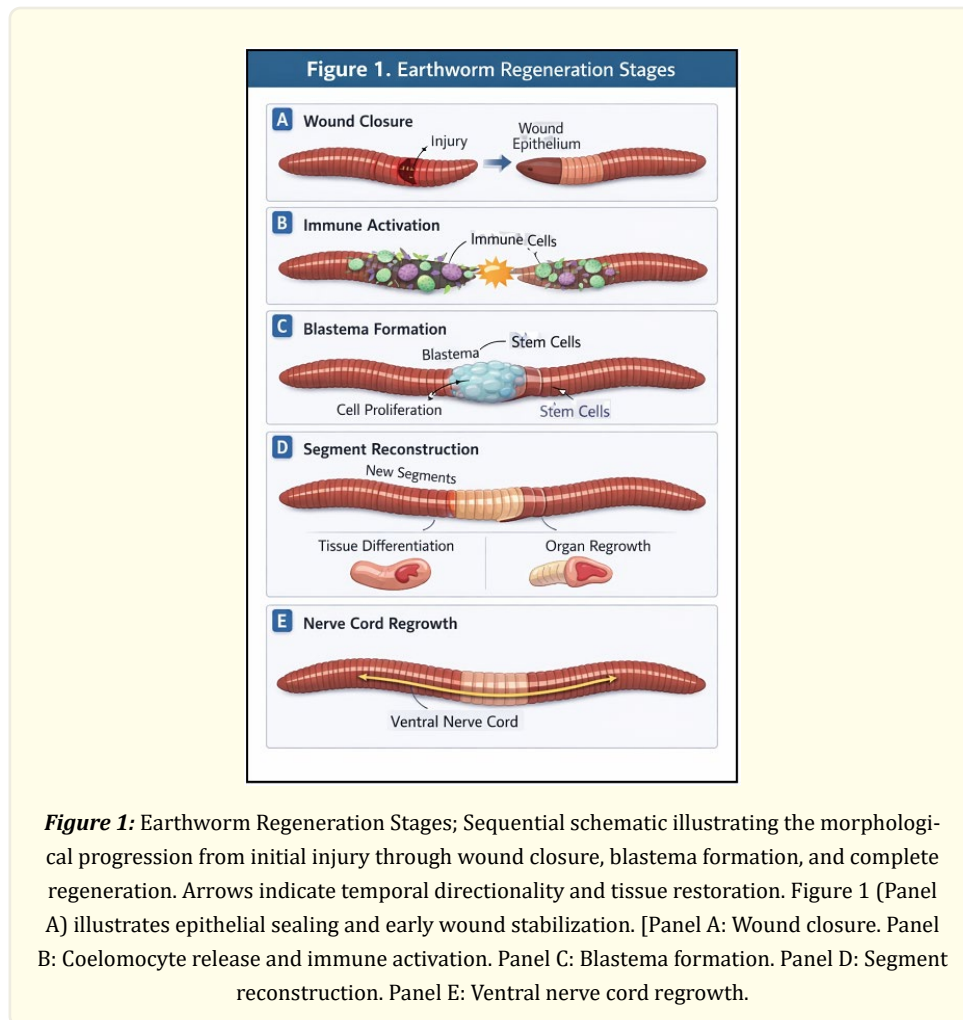
Comparative regeneration outcomes were synthesized from published annelid regeneration datasets and verified through direct observation of *Lumbricus terrestris* specimens collected in PEI. Illustrations were standardized to depict equivalent mid body amputations, with anterior and posterior regrowth assessed at 14-day intervals. Species selection represents terrestrial, marine, and parasitic lineages to highlight evolutionary divergence in regenerative capacity.

Results

Wound Closure and Early Healing

Earthworms exhibit rapid wound closure and blastema formation with minimal collagen deposition and no fibrotic scarring, consis-

tent with prior ultrastructural and comparative analyses (Myohara 2004; Bely 2014; Müller & Bely 2019) [11, 2, 3] (Figure 1).



Immune Activation and Coelomocyte Response

Coelomocytes—multifunctional immune cells—are rapidly mobilized to the wound site, where they phagocytose debris, release antimicrobial peptides, and modulate inflammation (Cooper & Roch, 2003; Chang & Chen, 2005) [5, 4]. Their activity creates a permissive environment for regeneration and prevents fibrotic outcomes typical of vertebrate wound healing. The diversity of coelomocyte types and their functional roles is summarized in Figure 2 plus Figure 1 (Panel B) depicts coelomocyte release and immune activation.

Blastema Formation and Cellular Dedifferentiation

Blastema formation marks the transition from wound healing to true regeneration. Dedifferentiated cells proliferate to form a mass of pluripotent progenitors capable of generating multiple tissue types (Müller & Bely, 2019) [10]. Transcriptomic analyses reveal up-regulation of Wnt, FGF, and ECM remodelling pathways during this stage (Rossan Mathews et al., 2024) [15]. Key molecular pathways active during blastema formation are illustrated in Figure 3 plus Figure 1 (Panel C) shows blastema formation and proliferative zones.

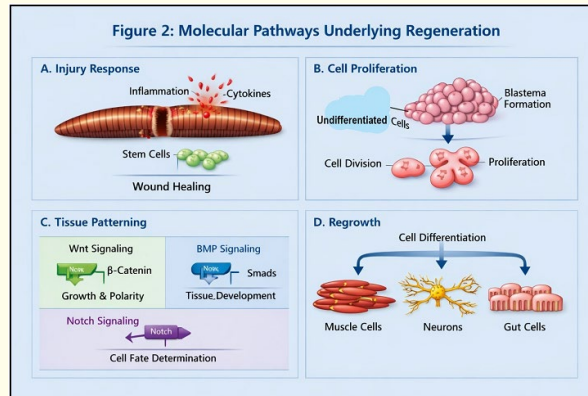


Figure 2: Coelomocyte types and immune functions during regeneration.

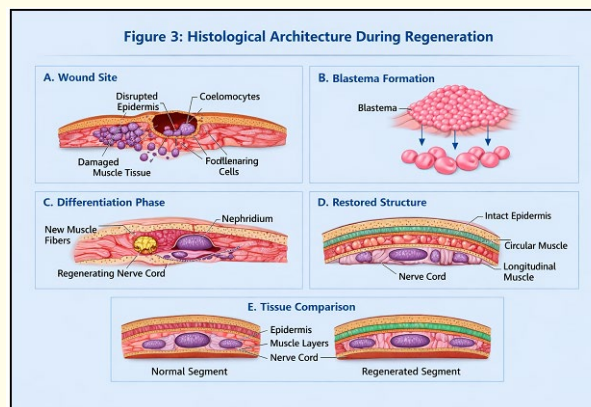


Figure 3: Molecular pathways (Wnt, FGF, ECM remodeling) upregulated during blastema formation. BioRender style diagram summarizing the cellular and molecular mechanisms driving regeneration. Panels depict injury response, cell proliferation, tissue patterning via Wnt, BMP, and Notch signalling, and final regrowth with differentiated cell types.

Segment Reconstruction and Patterning

New segments form sequentially, guided by molecular gradients and positional cues. Hox and Wnt pathways regulate segment identity and anterior-posterior patterning (Myohara 2004; Bely 2014; Müller & Bely 2019) [11, 2, 3]. Species differ in the number of segments they can regenerate, reflecting evolutionary and ecological constraints (Myohara, 2004) [11]. Comparative outcomes across annelid species are presented in Figure 4 plus Figure 1 (Panel D) illustrates segmental patterning and organogenesis.

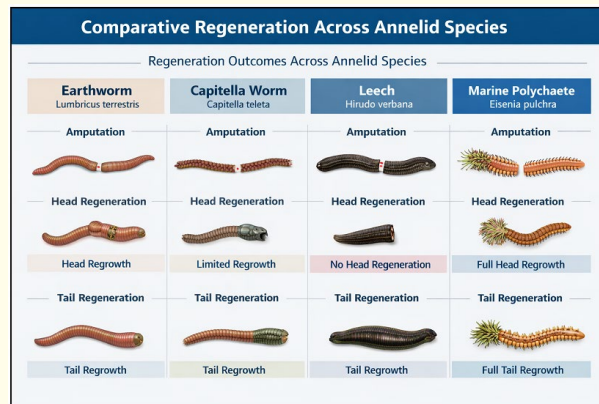


Figure 4: Comparative regeneration outcomes across annelid species. A four species comparative schematic illustrating variation in anterior and posterior regenerative capacity across representative annelids. Panel A (*Lumbricus terrestris*) shows robust head and tail regeneration following mid body amputation. Panel B (*Capitella teleta*) demonstrates limited anterior regeneration but consistent posterior regrowth. Panel C (*Hirudo verbana*) exhibits no anterior regeneration and restricted posterior regrowth. Panel D (representative marine polychaete) displays full anterior and posterior regeneration, reflecting high regenerative plasticity. Together, these comparisons highlight lineage specific constraints and evolutionary divergence in annelid regenerative programs.

Ventral Nerve Cord Regrowth

Earthworms regenerate the ventral nerve cord through coordinated axonal sprouting, reconnection, and blastema mediated tissue replacement (Myohara 2004; Bely et al., 2010; Müller & Bely 2019) [11, 3, 10]. Although slower than epithelial or muscular regeneration, neural regrowth is essential for restoring locomotion and sensory function Figure 1 (Panel E) depicts nerve cord regrowth and synaptic reformation.

Comparative Regeneration Across Earthworm Species

Across annelid taxa, regeneration outcomes reveal a clear phylogenetic gradient. Terrestrial oligochaetes such as *Lumbricus terrestris* exhibit complete anterior and posterior regeneration, whereas marine polychaetes retain full regenerative plasticity. In contrast, parasitic leeches (*Hirudo verbana*) show pronounced reduction in anterior regrowth, suggesting functional trade-offs linked to host specialization. The intermediate pattern in *Capitella teleta* underscores the evolutionary transition between full and partial regenerative modes. These findings support the hypothesis that annelid regeneration reflects lineage specific modulation of conserved developmental pathways, including HOX mediated positional re specification (Figure 4).

Additional species capable of regeneration

Eisenia fetida (Savigny, 1826) [16] - Highly regenerative, capable of both anterior and posterior regeneration, with rapid blastema formation and strong immune-regenerative coupling, ideal laboratory model (Myohara, 2004) [11].

Lumbricus terrestris Linnaeus, 1758 [9] - Limited anterior regeneration and variable posterior regeneration, with slower blastema growth, larger body size complicates lab use (Bely, 2010) [1].

Perionyx excavatus Perrier, 1872 [12] - Exceptional anterior regeneration, fastest regeneration among common species, and strong transcriptomic resources, high translational potential (Rossan Mathews et al., 2024) [15].

Amyntas gracilis (Kinberg, 1867) [8] [aka *A. hawayanus* (Rosa, 1891) [14]] - Moderate regeneration, strong immune responses, and useful for comparative immunology (Chang & Chen, 2005) [4].

Discussion

Earthworm regeneration is a multi-stage process involving coordinated cellular, immune, and molecular mechanisms. The integration of immune responses with regenerative pathways distinguishes annelids from vertebrates, where inflammation often leads to fibrosis rather than regeneration (Gurtner et al., 2008) [7]. Figure 5 integrates these mechanisms into a unified model.

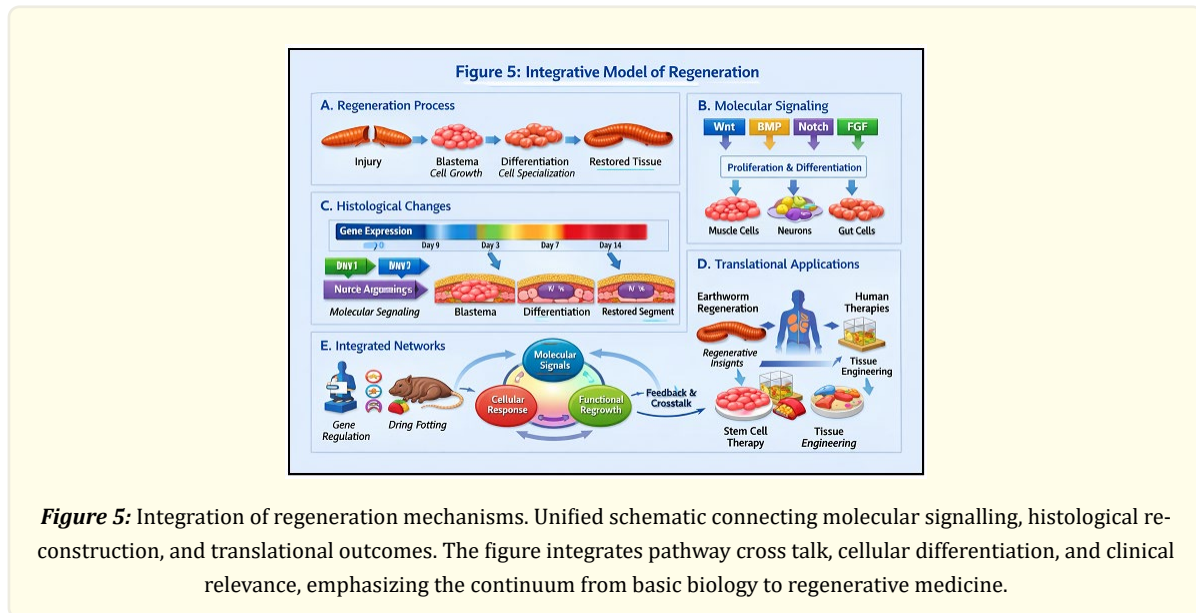


Figure 5: Integration of regeneration mechanisms. Unified schematic connecting molecular signalling, histological reconstruction, and translational outcomes. The figure integrates pathway cross talk, cellular differentiation, and clinical relevance, emphasizing the continuum from basic biology to regenerative medicine.

Translational Potential for Human Medicine

Anti fibrotic Therapies

Earthworms regenerate complex tissues without forming scar tissue, indicating the presence of endogenous anti fibrotic regulators that suppress collagen hyper accumulation and redirect wound healing toward functional tissue reconstruction. These mechanisms offer a promising comparative model for human fibrosis research. Insights from earthworm extracellular matrix (ECM) remodeling, immune modulation, and blastema formation may inform therapeutic strategies for keloids and hypertrophic scarring, organ level fibrosis (including liver, lung, and cardiac tissues), and the prevention of postsurgical adhesions. Identifying the molecular factors that enable scar free healing in annelids could guide the development of next generation anti fibrotic drugs and biomaterials (Myohara, 2004; Bely, 2014) [11, 2].

Neuroregeneration

The complete regeneration of the ventral nerve cord in earthworms provides a tractable model for understanding conserved mechanisms of neural repair. Axonal sprouting, guidance, and reconnection occur rapidly and with high fidelity, suggesting the involvement of potent neurotrophic cues and permissive ECM environments. These processes have direct translational relevance for spinal cord injury repair, peripheral nerve regeneration, and the design of neurotrophic biomaterials capable of supporting axonal extension and synaptic re-establishment in mammalian systems (Ebrahimi Fana et al., 2023; Shi et al., 2023) [6, 17].

Biomaterials and Tissue Engineering

Earthworm ECM and bioactive peptides represent an underexplored reservoir of biologically active components with potential applications in regenerative medicine. Their structural proteins, antimicrobial peptides, and wound modulating enzymes could be incorporated into hydrogels, nanofiber scaffolds, and antimicrobial wound dressings to enhance tissue integration, reduce infection risk, and promote constructive remodeling. Such biomaterials may serve as platforms for controlled release of regenerative factors or as scaffolds that mimic the pro regenerative microenvironment observed in annelid blastemas (Ebrahimi Fana et al., 2023; Wu et al., 2023) [6, 18].

Regeneration Inspired Drug Discovery

High resolution transcriptomic and proteomic profiling of earthworm regeneration offers a powerful discovery pipeline for novel therapeutic molecules. Differentially expressed genes and proteins during blastema formation may reveal previously uncharacterized growth factors, anti-inflammatory peptides, ECM modulating enzymes, and neurotrophic molecules with direct biomedical relevance. These candidates could seed new classes of biologics or small molecule therapeutics aimed at enhancing wound healing, reducing fibrosis, or promoting neural repair in humans.

Evolutionary analyses show that regenerative capacity has been lost multiple times across annelids (Bely, 2010) [1], yet latent abilities may persist even in species with reduced regeneration (Bely et al., 2010) [3]. This suggests that regeneration is a modular trait influenced by ecological pressures, reproductive strategies, and developmental constraints (Bely, 2014; Müller & Bely 2020; Shi et al., 2025) [2, 10, 17].

In PEI earthworm communities, species such as *Lumbricus terrestris*, *Aporrectodea tuberculata*, and *Dendrobaena octaedra* exhibit varying regenerative capacities. Understanding these differences is essential for interpreting population dynamics, soil disturbance responses, and ecosystem functioning.

Conclusion

Earthworm regeneration is a robust, evolutionarily dynamic process governed by immune activation, blastema formation, molecular patterning, and neural regrowth. Integrating classical studies with modern transcriptomics provides a comprehensive understanding of these mechanisms. This synthesis supports ongoing ecological research in PEI and offers a framework for future comparative and applied studies.

References

1. Bely AE. "Evolutionary loss of animal regeneration: Pattern and process". *Integrative and Comparative Biology* 50.4 (2010): 515-527.
2. Bely AE. "Early events in annelid regeneration: A comparative perspective". *Journal of Experimental Zoology (B)*, 322.7 (2014): 633-645.
3. Bely AE, JM Sikes and D Futuyama. "Latent regeneration abilities persist following recent evolutionary loss in asexual annelids". *Proceedings of the National Academy of Sciences* 107.4 (2010): 1464-1469.
4. Chih-Han Chang and Jiun-Hong Chen. "Axonomic status and intraspecific phylogeography of two sibling species of *Metaphire* (*Oligochaeta*: *Megascolecidae*) in Taiwan". *Pedobiologia* 49.6 (2005): 591-600.
5. Cooper EL and P Roch. "Earthworm immunity: A model of immune competence". *Pedobiologia* 47.5-6 (2003): 676-688.
6. Ebrahimi Fana S., et al. "Earthworm as a peripheral nerve regeneration biomaterial: a comprehensive review". *Traditional and Integrative Medicine* 8.1 (2023): 77-85.
7. Gurtner G., et al. "Wound repair and regeneration". *Nature* 453 (2008): 314-321.
8. Kinberg JG. Newly cancelled. Translated from the proceedings of the Royal Academy of Sciences, Stockholm 23 (1867): 97-103, 356-357.

9. Linnaeus C. "The system of nature through the three kingdoms of nature, according to classes, orders, genera, and species, with characters, differences, and synonyms., locis, Edition tenth, reformatted". Tom I. Laurentius Salvius, of Holm, (1758): 824.
10. Müller MCM and AE Bely. "Regeneration in annelids: A comparative overview of developmental processes and molecular mechanisms". *Development Genes and Evolution* 229.1 (2019): 1-18.
11. Myohara M. "Differential tissue regeneration in *Eisenia fetida*". *Developmental Dynamics* 231.3 (2004): 396-403.
12. Perrier E. "Research Contributing to the History of Terrestrial Earthworms". *New Archives of the Natural History Museum, Paris* 8 (1872): 5-198.
13. Reynolds JW. "Earthworm community structure and species co-occurrence patterns across Prince Edward Island, Canada". *Megadrilologica* 30.2 (2026): 13-31.
14. Rosa D. "The exotic terrestrial animals of the Imperial-Royal Natural History Court Museum". *Annals of the Imperial-Royal Natural History Court Museum, Vienna* 6 (1891): 399-406.
15. Rossan Mathews MG., et al. "De novo transcriptome of anterior epimorphic regeneration in *Perionyx excavates*". *Scientific Data* 11 (2024): 1093.
16. Savigny JC. "Analyses of the work of the Royal Academy of Sciences during the year 1821, physics section". Baron G. Cuvier (ed.), *Memoirs of the Royal Academy of Sciences of the Imperial Institute of France* 5 (1826): 176-184.
17. Shi G., et al. "Isolation and characterization of earthworm peptides with neuroprotective effects in Parkinson's disease models". *Molecules* 30.9 (2025): 1952.
18. Wu L., et al. "Piezoelectric materials for neuroregeneration: a review". *Biomaterials Science* 11 (2023): 7296-7310.