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POLYLAMININ IN NEURAL REGENERATION: MOLECULAR MECHANISMS, MODULATION OF NEUROPLASTICITY, AND TRANSLATIONAL POTENTIAL IN CENTRAL NERVOUS SYSTEM INJURIES

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ABSTRACT

The injuries of the central nervous system represent one of the greatest challenges in regenerative neuroscience, due to the limited capacity for repair of neural tissue, the formation of an inhibitory post-injury microenvironment, and the complexity of the mechanisms involved in functional recovery. In this context, poly-L-lysine has emerged as a promising strategy by acting as a bioactive extracellular matrix capable of promoting neural regeneration, adaptive plasticity, and tissue remodeling. The present study aimed to analyze, through an integrative literature review, the scientific evidence on the role of poly-L-lysine in neural regeneration, with an emphasis on its molecular mechanisms, its influence on neuroplasticity, and its translational potential in injuries of the central nervous system. The search was conducted in the PubMed/MEDLINE database, with complementary manual tracking, including experimental and translational studies related to poly-L-lysine and convergent strategies based on laminin, integrins, bioactive peptides, and functionalized biomaterials.The findings demonstrated that polylaminin exhibits superior bioactivity compared to non-polymerized laminin in experimental models, promoting cell adhesion, neuritogenesis, axonal growth, and functional improvement. It was also observed that pathways mediated by β1-integrin, integrin-linked kinase, and modulation of the glial response play a central role in the regenerative effects associated with this matrix. Studies with hydrogels, nanofibers, scaffolds, and bioinspired systems in laminin reinforced the translational potential of these approaches, especially in creating permissive niches for regeneration and functional reorganization of the injured tissue. It is concluded that polylaminin constitutes a biologically plausible and experimentally promising platform for neuroregeneration in the central nervous system, although the literature remains predominantly preclinical and requires more standardized and translational studies for therapeutic validation.

Keywords: Polylaminin; Neural regeneration; Neuroplasticity; Central nervous system.

INTRODUCTION

Injuries to the central nervous system (CNS), especially those affecting the spinal cord and the brain, remain among the greatest challenges of translational neuroscience and regenerative medicine, due to the limited intrinsic capacity for repair of mature nervous tissue, the formation of a hostile post-injury microenvironment, and the structural and functional complexity of the affected neural circuits [1,8, 11]. After the injury, a pathological cascade characterized by inflammation, cell death, demyelination, remodeling of the extracellular matrix, reactive glial activation, and deposition of inhibitory molecules for axonal growth, such as chondroitin sulfate proteoglycans, occurs, which restricts regeneration and compromises functional restoration [8,9,11,20]. In this context, the search for strategies capable of modulating the injury niche, favoring adaptive plasticity, and stimulating structural regeneration has become a scientific priority internationally [12-18].

The neural extracellular matrix plays a central role in this process, not only as structural support but also as a bioactive platform that regulates cell adhesion, migration, differentiation, neuritic survival and extension through interaction with surface receptors, especially integrins [7-10]. Among its components, laminin stands out as an essential glycoprotein of the basement membranes, widely recognized for its ability to promote axonal growth, cytoskeletal organization, and pro-regenerative signaling in different neural populations [7,10,15,21]. Experimental studies demonstrate that laminin-rich substrates or those functionalized with bioactive epitopes derived from this molecule, such as IKVAV, favor the adhesion of neural stem cells, axonal sprouting, neuroblast migration, and remodeling of the post-injury environment, both in brain injury models and spinal cord injury [12-21].

In recent years, polylaminin, a polymeric form of laminin obtained from its supramolecular self-organization, has emerged as a particularly promising approach within this field. Unlike laminin in its non-polymerized form, polylaminin has its own three-dimensional architecture, greater topographic complexity and properties

Bioactive substances that seem to enhance cell-matrix interaction and amplify neuritogenic and regenerative responses [1-4]. Experimental evidence indicates that poly-laminin favors cell spreading, proliferation, neurite formation, and structural stability of the biological substrate, suggesting that its molecular organization not only preserves but also enhances the classical functions of laminin in neural repair [2-4]. In a spinal cord injury model in rodents, the administration of poly-laminin promoted functional improvement and axonal growth through the injured area, representing one of the most relevant direct pieces of evidence of its therapeutic potential in the CNS [1].

From a mechanistic point of view, the regenerative effects associated with poly-laminin and other laminin-based strategies seem to involve the activation of pathways mediated by β1-integrin, integrin-linked kinase, intracellular kinases, and cytoskeletal modulators, influencing everything from the migration of neural stem cells to the control of astrogliosis and the scar response [7-10]. Furthermore, recent studies show that biomaterials functionalized with laminin signals can reduce fibrous scar tissue, favor tissue reorganization, and enhance the plasticity of serotonergic fibers and create permissive niches for cellular integration and neurite extension [11-14, 18-20]. These findings reinforce the notion that neural regeneration depends not only on cellular replacement or the administration of isolated trophic factors but on the intelligent reconstruction of a microenvironment biochemical and biomechanical capable of reorienting the response of the injured tissue [12, 13, 16, 18,20].

Concurrently, the advancement of biomaterials engineering has increased interest in translational platforms that incorporate laminin, poly-laminin, or laminin peptides in hydrogels, nanofibers, films, and multifunctional scaffolds, aimed at enhancing cell retention, guiding migration, supporting neuronal survival, and stimulating reconnection of injured circuits [5, 12-18,21-26]. Experimental models in the brain and spinal cord have demonstrated that these systems can act as instructive matrices, favoring tissue repair, axonal sprouting, and functional performance to varying degrees [12-18,21-25]. Particularly relevant is the application of a laminin-based therapy in dogs with chronic spinal cord injury, represents an important step

towards translation, by bringing research closer to more complex biological scenarios and clinically challenging situations [6].

Despite these advances, the literature still appears fragmented. Evidence directly centered on polylaminin remains more restricted compared to the broader volume of studies on laminin, bioactive epitopes, and bioinspired biomaterials. This necessitates an integrative analysis capable of gathering, comparing, and critically interpreting the available findings, clarifying both the molecular mechanisms involved and the true extent of the translational potential of this strategy in the treatment of CNS injuries [1-6,12-26]. In this sense, the present integrative review aims to analyze the scientific evidence regarding the role of polylaminin in neural regeneration, emphasizing its molecular mechanisms of action, its influence on neuroplasticity, and its translational prospects in central nervous system injuries.

METHODOLOGY

This is an integrative literature review, descriptive and analytical in nature, conducted with the aim of critically synthesizing the scientific evidence on the role of poly-laminin in neural regeneration, with an emphasis on its molecular mechanisms, its influence on neuroplasticity, and its translational potential in central nervous system injuries. The methodological conduct was based on the integrative review framework proposed by Whittemore and Knafl, which includes the stages of problem identification, literature search, data evaluation, study analysis, and presentation of the synthesis, and the process of selecting and describing the findings was structured in a manner compatible with the PRISMA 2020 recommendations for greater transparency in reporting. [27,28]

The guiding question of the review was defined as follows: what is the available evidence regarding poly-laminin and laminin-based strategies in neural regeneration, the molecular mechanisms related to the modulation of neuroplasticity, and the translational perspectives for the treatment of central nervous system injuries? The formulation of the question considered the conceptual axis.

composed of neural extracellular matrix, polymerized laminin, neural repair, spinal cord injury, brain injury, axonal plasticity, and bioinspired biomaterials. [27]

The structured bibliographic search was primarily conducted in the **PubMed/ MEDLINE** database, due to its relevance for indexing biomedical and neuroscientific literature, and was complemented by manual tracking of the reference lists of eligible studies, in order to identify additional articles of high thematic relevance. Descriptors and boolean combinations in English were used, compatible with the predominant terminology of the international literature, including: “polylaminin”, “polyLM”, “polymerized laminin”, “laminin”, “laminin-derived peptide”, “IKVAV”, “neural regeneration”, “neuroplasticity”, “spinal cord injury”, “brain injury”, “central nervous system”, “neural stem cells”, “integrin”, “hydrogel”, and “scaffold”. The search strategies were adjusted to enhance sensitivity and specificity, prioritizing experimental, translational, and mechanistic studies directly related to the central theme of the review. [28]

Eligible articles considered were original experimental, translational, or mechanistic studies published in indexed scientific journals, with traceable text and content directly related to poly-L-lysine or, convergently, to laminin and its bioactive epitopes in neural regeneration processes in the CNS. Studies involving in vitro, ex vivo, and in vivo models were included, provided they addressed at least one of the following outcomes: neuritic growth, axonal sprouting, cell migration, neural differentiation, modulation of the glial response, scar reduction, reorganization of the post-injury microenvironment, or functional recovery associated with neural regeneration. Translational studies with biomaterials functionalized with laminin signals were also accepted when they had unequivocal relevance to the conceptual axis of the review. [27]

Articles that did not adhere thematically to the neuroregenerative focus, exclusively peripheral studies without conceptual applicability to the CNS, non-traceable publications, reports without sufficient methodological description, duplicate documents, and works whose content was restricted to biochemical or structural aspects dissociated from any interface with neural repair, neuroplasticity, or therapeutic translation were excluded. When peripheral studies presented mechanistic or biomaterial engineering relevance clearly related to the rationale of poly-L-lysine, their inclusion was

considered in a complementary manner and critically interpreted in the final synthesis, without equating them to the same level of evidence as the central studies in CNS. [27,28]

After the initial search, the retrieved records were subjected to screening by reading titles and abstracts, followed by eligibility analysis of the full content when necessary. Subsequently, a final selection was made guided by adherence to the review's objective, resulting in an analytical database composed of core studies on poly-laminin and convergent studies on laminin, laminin epitopes, integrins, and bioinspired scaffolds applied to CNS repair. This strategy was adopted because the literature strictly focused on poly-laminin is still quantitatively more restricted than the mechanistic and translational literature on the laminin-neural regeneration axis, making it scientifically more appropriate to interpret the topic from a direct core surrounded by converging supporting evidence. [27]

The data extraction was carried out in a standardized manner, encompassing author, year of publication, experimental model, type of intervention, main biological target, investigated molecular mechanisms, structural and functional outcomes, main results, and the contribution of the study to the review topic. Subsequently, the articles were organized into thematic axes for interpretative synthesis: direct evidence of poly-laminin in neural repair; molecular mechanisms associated with laminin-integrin interaction and modulation of the glial response; neuroplasticity and axonal growth in an inhibitory microenvironment; and the translational potential of laminin-based biomaterials in CNS injuries. [27]

The analysis of the studies occurred through integrative narrative synthesis, with critical comparison between models, interventions, molecular pathways, and observed outcomes. In interpreting the findings, the relative hierarchy of evidence was considered, distinguishing studies directly centered on poly-laminin from those providing mechanistic or indirect translational support through laminin, IKVAV, hydrogels, nanofibers, and functional scaffolds. This differentiation was adopted in order to preserve conceptual rigor and avoid overestimating the volume of direct evidence available on poly-laminin in the CNS. [27,28]

RESULTS

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A Synthesis of the Included Studies

The literature on polylaminin applied to neural regeneration in the central nervous system is shown to be organized around four main scientific axes: direct evidence of polylaminin in neural repair; molecular mechanisms related to extracellular matrix-integrin interaction and modulation of the glial response; neuroplasticity and axonal growth in an inhibitory post-lesional environment; and the translational potential of biomaterials.

laminin and bioinspired scaffolds for brain and spinal cord injuries. Taken together, the findings show that polylaminin occupies a promising position as a bioactive matrix, but that the greatest density of evidence is still concentrated in studies converging with laminin, laminin peptides, and biomaterial platforms that mimic their biological signals [1-26]. Table 1 shows a summary of the main studies of polylaminin applied to regeneration.

neural system in the central nervous system.

Table 1. Summary of the Main Studies Included in the Review.

Thematic axis	Representative studies	Model	Main Findings	Relevance for the review
Direct evidence of polylaminin	Menezes et al. [1]; Hochman-Mendez et al. [2-4]	Injury medullary in rodents; cultures neural	Functional improvement, axonal growth, increased cell spread, neuritogenesis and bioactivity superior to non-polymerized laminin	It supports polylaminin as a bioactive matrix with direct regenerative potential.
Mechanisms molecular	Pan et al. [7]; North et al. [8]; Tan et al. [9]; Prestoz et al. [10]	Cells stem neural models of SKI and essays in vitro	Involvement of β 1-integrin, ILK, BMP modulation, cell migration, and astrogliosis attenuation.	It explains how laminin-derived signals can reprogram the lesion niche.
Neuroplasticity and axonal sprouting	Hawthorne et al. [11]; Tysseling-Mattiace et al. [12]; Tysseling et al. [13]	Injuries of CNS in rodents	Reduction of gliosis, increase in oligodendrocytes, axonal elongation, and serotonergic fiber plasticity	This demonstrates that the laminin microenvironment favors circuital reorganization.

Thematic axis	Representative studies	Model	Key findings	Relevance for the review
Translational biomaterials based on laminin/ IKVAV	Wei et al. [14]; Hou et al. [15]; Park et al. [16]; Cheng et al. [17] ; Hassannejad et al. [18]; Yin et al. [19]; Jiang et al. [20]	Hydrogels, nanofibers, scaffolds For brain and spinal cord	Tissue repair, adhesion of neural stem cells, reduction of fibrous scar tissue, support for regeneration.	It supports the use of bio-inspired platforms as a translational bridge.
Advanced strategies and more translational models	Ajioka et al. [21]; Ruzicka et al. [22]; Yang et al. [23]; Huang et al. [24]; Yu et al. [25]; Arulmoli et al. [26]	Cortical injury, chronic SCI, electronic scaffolds, and cellular hydrogels.	Neuroblast migration, neural progenitor integration, neuritic orientation, and niche engineering.	It indicates translational maturation of the field, although still predominantly preclinical

The table shows that studies more directly focused on polylaminin are quantitatively less numerous, but biologically consistent, while most of the literature expands and reinforces the rationale of the topic based on laminin-like strategies and functionalized biomaterials.

1. Direct Evidence of Polylaminin in Neural Repair

The most specific core of the review consisted of studies that directly investigated polylaminin as a substrate or regenerative intervention. The work of Menezes et al. demonstrated that polylaminin, unlike laminin, does not...

Polymerized polylaminin promoted functional improvement after spinal cord injury in rats, associated with greater axonal growth through the injured area and a biological profile compatible with neural regeneration [1]. In parallel, HochmanMendez et al. showed that polylaminin favored cell spreading, proliferation, and neuritogenesis in retinal cells, reinforcing that polymerization qualitatively alters the bioactivity of laminin [2]. Other studies by the same group showed that polylaminin has structural stability compatible with biotechnological use and organization.

distinct supramolecular structure with a fractal pattern, which helps to explain its

the ability to offer a more efficient cell-matrix interface than laminin in non-polymerized form [3,4]. These results, together, position polylaminin as a matrix extracellular biomimetic

promising for applications neuroregenerative, although direct evidence still remains concentrated in few research groups [1-4].

2. Molecular Mechanisms: integrins, ILK, BMP, and glial modulation

The converging studies indicated that a significant part of the regenerative effects associated with polylaminin and other laminin-based strategies is mediated by cell-matrix recognition pathways, especially those dependent on β1-integrin. Pan et al. demonstrated that β1-integrin and integrin-linked kinase participate in the regulation of astrocytic differentiation of neural stem cells [7], while North et al. showed that β1-integrin alters the localization of the BMP receptor in ependymal stem cells and attenuates astrogliosis after spinal cord injury [8]. These findings suggest that signaling triggered by laminin substrates not only acts on neuritic growth but also reprograms central components of the glial response and cell fate in the post-injury niche. Complementarily, studies such as those by Tan et al. and Prestoz et al. showed that signaling through integrins favors axonal growth in inhibitory environments and is associated with the migratory capacity of transplanted neural cells, expanding the

biological plausibility of using laminin-inspired matrices as regulators of regeneration [9, 10].

3. Neuroplasticity and Growth axonal in an inhibitory environment

Another recurring axis in the foundation was the demonstration that the microenvironment enriched with laminin signals can favor adaptive plasticity even in biologically hostile scenarios. Hawthorne et al. observed that serotonergic neurons exhibit increased sprouting capability in the injured CNS and better performance on substrates containing laminin, even in the presence of inhibitory components, indicating the involvement of β1-integrin in this behavior [11]. Convergently, Tysseling-Mattiace et al. demonstrated that self-organizing nanofibers with bioactive epitopes reduced gliosis, increased oligodendroglia, and favored the regeneration of motor fibers.

Descending and ascending sensory fibers after spinal cord injury [12]. In a subsequent study, Tysseling et al. showed that bioactive peptide amphiphiles also increased the plasticity of serotonergic fibers after SCI [13]. These data indicate that functional regeneration in the CNS may depend less on complete anatomical regeneration and more on a combination of axonal elongation, compensatory sprouting, and permissive remodeling of the injured tissue [11-13].

4. Laminin-Based Biomaterials, IKVAV and reduction of post-injury scar

The largest mass of translational evidence from the review focused on hydrogels, nanofibers, and scaffolds functionalized with laminin or derived epitopes, especially IKVAV. Studies in injured brain demonstrated that hyaluronic acid hydrogels modified with laminin or IKVAV favor tissue repair, axonal regeneration, and adhesion of neural cells [14, 15, 19]. In spinal cord, platforms biofunctionalized

showed the ability to improve regeneration, increase cell retention, and modulate the post-injury niche [16-18]. A particularly relevant finding was that of Jiang et al., who demonstrated that a Hydrogel containing IKVAV reduced fibrous scarring after SCI by inhibiting the migration and activation of fibroblasts, enhancing the understanding that the scar response is not limited to astrocytic gliosis [20]. Together, these studies indicate that laminin signals organized in three-dimensional matrices not only function as a permissive substrate but also as instructive elements capable of modulating adhesion, migration, differentiation, and tissue architecture in regeneration [14-20].

5. Translational Potential In advanced models of brain and spinal cord injury

The latest studies have pointed to a progressive advancement in the field towards more sophisticated platforms and biological scenarios closer to clinical application. Ajioka et al. demonstrated that a porous sponge rich in laminin increased the migration of neuroblasts to cortical injury, functioning as a cellular orientation scaffold [21]. In a model of chronic spinal cord injury, Ruzicka et al. evaluated neural progenitors derived from iPS in laminin-coated hydrogel, suggesting that the scaffold + cell combination may favor integration into the injured tissue.

in late stages [22]. Yang et al. went further by developing electronic scaffolds coated with laminin and with vascular topography, capable of promoting and tracking the migration of brain cells after injury [23]. These data converge with other recent works based on functionalized scaffolds and Janus platforms for spinal repair [24,25], in addition to composite systems aimed at human neural cells [26]. The set suggests that the translational application of polylaminin and related strategies tends to consolidate not as isolated monotherapy, but as a component of multifunctional systems that combine matrix bioactivity, structural guidance, cellular support, and, in some cases, release of bioactive factors [21-26].

Interpretative Synthesis of the Results

The integrated analysis of the studies revealed three central conclusions. First, The polylaminin shows direct experimental evidence of regenerative bioactivity in the CNS, with functional and structural superiority compared to non-polymerized laminin in the models tested [1-4]. Second, the biological rationale for this strategy is strongly supported by mechanistic studies that connect laminin, β1-integrin, ILK, BMP modulation, reduction of astrogliosis, and axonal plasticity [7-13]. Third, the translational potential of the field is strengthened with laminin-based biomaterials, peptides like IKVAV, and increasingly sophisticated scaffolds capable of reducing scarring, guiding cell migration, and promoting repair in brain and spinal cord models [14-26]. Nevertheless, the literature remains predominantly preclinical, heterogeneous in models and interventions, and more robust for the laminin/biomaterial axis than for polylaminin in the strict sense, which should be considered in the interpretation of the findings.

DISCUSSION

The findings of this integrative review indicate that polylaminin constitutes a biologically promising strategy for neural regeneration in the central nervous system, especially for acting as a bioactive extracellular matrix capable of modifying the interaction between neural cells and the post-lesional microenvironment [1-4]. The main merit of the analyzed set lies in the

convergence between direct evidence of the regenerative effect of polylaminin and a broader mechanistic basis, supported by studies on laminin, integrins, bioactive epitopes, and functionalized biomaterials [1-4,7-26]. Conceptually, this convergence suggests that the therapeutic value of polylaminin is not limited to its molecular composition but involves its supramolecular organization and its ability to more efficiently reproduce structural and functional signals characteristic of the neural matrix [3,4].

One of the most relevant aspects observed was the superiority of polylaminin compared to non-polymerized laminin in the models where both were compared [1,2]. This data shifts the discussion from a quantitative perspective, focused solely on the presence of laminin, to a qualitative perspective, based on the architecture of the matrix. Polymerization seems to confer to the molecule a three-dimensional configuration closer to that found in organized biological environments, favoring more stable cell-matrix interactions, greater adhesion, cell spreading, and stimulation of neuritogenesis [2-4]. This interpretation is consistent with the structural studies included, which indicate that the Polylaminin has its own organization and greater topographical complexity, possibly enhancing the functional exposure of binding sites and potentiating cellular mechanotransduction [3,4].

From a molecular perspective, the review reinforces that integrin-mediated signaling, especially β1-integrin, occupies a central position in the laminin-neural regeneration axis [7-10]. The activation of these pathways seems to influence fundamental processes for CNS repair, including migration of neural stem cells, orientation of axonal growth, control of glial differentiation, and attenuation of astrogliosis [7-10]. This point is highly relevant because one of the main barriers to repair in the CNS does not solely arise from the initial neuronal loss, but from the rapid consolidation of an inhibitory post-lesional niche, marked by reactive gliosis, alterations in the extracellular matrix, and deposition of molecules that restrict axonal elongation [8,9,11,20]. In this scenario, polylaminin and laminin-like systems seem to act not only as permissive substrates but also as active modulators of the biology of the injured tissue [1,7,8].

The analysis of the studies also points to a contemporary view of neural regeneration, less dependent on complete anatomical restitution and more related to the combination of axonal growth, compensatory sprouting, tissue reorganization, and adaptive plasticity [11-13]. Studies demonstrating increased plasticity of serotonergic fibers, reduced gliosis, and greater permissiveness of the lesion environment support this interpretation [11-13]. In functional terms, this means that the recovery observed in some models may result not only from the precise reconstruction of the original circuit, but also from the nervous system's ability to reorganize remaining connections when the microenvironment is adequately modulated [11-13]. From this perspective, polylaminin acquires strategic value by functioning as an element of biological permissiveness in a context where residual plasticity and partial regeneration already have significant clinical relevance [1, 11-13].

Another important point is that the translational potential of the field seems to depend strongly on the integration between bioactive matrix components and tissue engineering platforms [14-26]. Hydrogels, nanofibers, scaffolds Porous materials, functional films, and injectable matrices emerge as vehicles capable of enhancing the local stability of treatment, increasing cell retention, guiding neuritic growth, and modulating post-lesional scarring [14-20,21-26]. This observation is particularly relevant because the clinical translation of regenerative therapies to the CNS is unlikely to occur through a single isolated molecule. The most plausible scenario involves systems multifunctional, in which bioactive matrix elements act in synergy with structural support, therapeutic cells, trophic factors and controlled release strategies [16-18,22-26].

In this context, studies with IKVAV and other laminin-inspired biomaterials offer a substantial contribution to the interpretation of the results [12-20]. Although they cannot be considered direct equivalents of polylaminin, these studies validate the biological principle that laminin signals organized in a functional matrix are capable of critically influencing cellular behavior in the injured CNS [12-20]. This finding strengthens the rationale for polylaminin by demonstrating that the regenerative effect depends not only on the presence of an isolated protein, but also on its presentation.

spatial, functional density, and the ability of the matrix to interact with specific cellular pathways [3,4,7-10, 12-20]. Nevertheless, conceptual rigor requires a clear distinction between direct evidence on poly-laminin and that derived from laminin peptides, scaffolds with laminin, or related biomimetic systems [1-4, 12-20].

The review also highlighted that the modulation of post-lesion scarring is one of the most promising points for the translational application of these strategies [8, 12,20]. Traditionally, the discussion on healing in the CNS has focused on astrocytic gliosis. The included studies show that fibrous scarring and the interaction between fibroblasts, matrix components, and glial cells should also be considered relevant therapeutic targets [20]. The ability of biomaterials containing laminin signals to reduce fibroblast migration and activation suggests that the reorganization of the scar niche may be as important as the direct stimulus for axonal growth [20]. Thus, poly-laminin can be understood not only as a promoter of neuritogenesis but also as a potential tool for the global remodeling of the lesion environment [1-4,20].

Despite the relevance of the findings, some limitations need to be acknowledged. The first is the still limited number of studies directly focused on poly-L-lysine in the CNS [1-4,6]. This limitation restricts the generalization of the results and prevents definitive conclusions about the ideal dose, therapeutic window, route of administration, duration of effect, and superiority over other regenerative strategies [1,6]. The second limitation refers to the methodological heterogeneity among the included studies, with significant differences between experimental models, types of injury, materials used, outcomes analyzed, and follow-up times [1-26]. This variability enhances the interpretive richness of the field but complicates direct comparisons and limits the possibility of more robust quantitative syntheses.

Another critical aspect is that most of the available evidence remains at the preclinical level [1-26]. Even the most advanced translational studies, including veterinary models and sophisticated biomaterial platforms, still do not equate to validation in human clinical trials [6, 21-26]. Questions related to immunogenicity, production scalability, and stability remain open.

in clinical conditions, long-term safety, and reproducibility in human chronic lesions [6,22-26]. There is also the fact that several analyzed approaches combine multiple therapeutic components, such as scaffolds, cells, and trophic factors, which complicates the precise identification of the isolated effect of laminin or polylaminin [16-18,22,26].

Even in the face of these limitations, the review allows us to support that polylaminin occupies a strategic position in development of regenerative therapies for the CNS [1-4]. Its main potential advantage lies in bringing together neural bioactivity, matrix organization, and compatibility with translational platforms [1-4, 14-26]. Instead of being understood merely as another biomaterial, polylaminin can be interpreted as a bioinstructive interface capable of simultaneously influencing adhesion, migration, plasticity, and tissue remodeling [1-4, 7-10]. This characteristic makes it particularly attractive for future applications in spinal cord injury, traumatic brain injury, ischemic lesions, and potentially in neurodegenerative contexts where the extracellular matrix plays a relevant regulatory role [1,6, 14-26].

In light of this panorama, future studies should prioritize standardized comparisons between polylaminin, soluble laminin, and other ECM-like biomaterials, as well as protocols that evaluate long-term functional outcomes, tissue integration biomarkers, and interaction with cell therapies [1,6,22,26]. It will also be necessary to deepen the characterization of the molecular pathways involved, including integrin-dependent signaling, inflammatory response, scar remodeling, and interaction with oligodendrocytes and neural progenitors [7-10,20]. The advancement of the field will depend not only on demonstrating experimental efficacy but also on building a solid translational pathway, with progressive validation in biologically more complex models that are closer to clinical practice [6,21-26].

In summary, the analyzed results support that polylaminin represents a promising platform for neural repair in the CNS, with encouraging initial direct evidence and strong coherence with a broader body of literature on laminin and neuroplasticity. and regenerative biomaterials [1-4,7-26]. Its greatest potential seems to lie in the ability to partially reconstruct a microenvironment.

permissive to regeneration and functional reorganization, overcoming a of the central barriers of CNS injuries: the persistence of a biologically unfavorable post-traumatic matrix for repair [1,8, 11,20].

CONCLUSION

This integrative review evidenced that polylaminin emerges as a promising strategy for neural regeneration in central nervous system injuries, especially due to its ability to act as a bioactive extracellular matrix with structural and functional properties superior to non-polymerized laminin in the models in which it was compared [1-4]. The studies analyzed indicate that this platform favors cell adhesion, spreading, neuritogenesis, axonal growth, and functional improvement, while also being compatible with applications in tissue engineering and more complex regenerative approaches [1-4].

The integrated analysis of the literature also demonstrated that the potential of polylaminin cannot be understood in isolation, but within a broader biological axis that involves laminin, β1-integrin, integrin-linked kinase, modulation of the glial response, reorganization of the extracellular matrix, and induction of neural plasticity [7-13]. In this sense, the data suggest that the Polylaminin may contribute to the repair of the CNS not only as a permissive substrate for neuronal growth but also as a bio-instructive element capable of remodeling the post-lesional microenvironment and favoring cellular responses more compatible with regeneration and functional reorganization [1,7-10].

The results also reinforce that the most consistent translational perspectives tend to emerge from the association between laminin signals and bioengineering platforms, such as hydrogels, nanofibers, porous scaffolds, functional films, and hybrid systems for cellular support [12-26]. These biomaterials enhance the local stability of the intervention, promote cellular retention, reduce components of the post-lesional scar, and create niches more permissive to neural integration [14-26]. Thus, the future clinical application of polylaminin is likely to be more associated with the composition of multifunctional therapeutic systems than with the isolated use of the molecule [16-18,22-26].

Despite the promising nature of these findings, the review also demonstrated that evidence directly focused on polylaminin in the CNS is still limited compared to the broader body of convergent studies on laminin, bioactive peptides, and related biomaterials [1-4, 12-26]. The predominance of preclinical models, methodological heterogeneity, and the scarcity of standardized comparative studies necessitate caution in extrapolating the results to the human context [1-26]. For this reason, it is not yet possible to definitively state the magnitude of its therapeutic benefit, its best method of administration, or its clinical superiority compared to other regenerative strategies [1,6].

In Em synthesis, a polylaminin represents one platform biologically plausible, experimentally promising and translationally relevant to the field of neuroregeneration [1-4,6]. Its main distinguishing feature seems to lie in its ability to reconstruct, at least partially, a matrix interface that is permissive to neuronal growth, adaptive plasticity, and remodeling of injured tissue [1-4, 11-13]. Further knowledge in this area will depend on the development of more standardized, comparative, and translational studies capable of consolidating polylaminin as an effective therapeutic tool in the treatment of nervous system injuries.
central [6,21-26].

REFERENCES

1. Menezes K, et al. Polylaminin, a polymeric form of laminin, promotes regeneration after spinal cord injury. FASEB J. 2010;24(11):4513-22. doi:10. 1096/fj.10-157628. PMID: 20643907.
2. Hochman-Mendez C, et al. Polylaminin recognition by retinal cells. J Neurosci Res. 2014;92(1):24-34. doi:10. 1002/jnr.23298. PMID: 24265135.
3. Freire E, et al. Biocompatibility and structural stability of a laminin biopolymer. Macromol Biosci. 2012;12(1):67-74. doi:10. 1002/mabi.201100125. PMID: 21994040.
4. Hochman-Mendez C, Cantini M, Moratal D, Salmeron-Sanchez M, Coelho-Sampaio T. A fractal nature for polymerized laminin. PLoS One. 2014;9(10):e109388. doi:10. 1371/journal.pone.0109388. PMID: 25296244.
5. of Siqueira-Santos R, et al. Biological activity of laminin/polylaminin-coated poly-ε-caprolactone filaments on the regeneration and tissue replacement of the rat sciatic nerve. Mater Today Bio. 2019;3:100021. doi:10. 1016/j.mtbio.2019.100021. PMID: 32159152.

6. of Miranda Chize C, et al. A laminin-based therapy for dogs with chronic spinal cord injury: promising results of a longitudinal trial. Front Vet Sci. 2025;12:1592687. doi:10.3389/fvets.2025.1592687. PMID: 40881640.
7. Pan L, et al. β1-Integrin and integrin linked kinase regulate astrocytic differentiation of neural stem cells. PLoS One. 2014;9:e104335. doi:10. 1371/journal.pone.0104335. PMID: 25098415.
8. North HA, Pan L, McGuire TL, Brooker S, Kessler JA. β1-Integrin alters ependymal stem cell BMP receptor localization and attenuates astrogliosis after spinal cord injury. J Neurosci. 2015;35(9):3725 -33. doi:10. 1523/JNEUROSCI.4546-14.2015. PMID: 25740503.
9. Tan CL, Andrews MR, Kwok JCF, Heintz TGP, Gumy LF, Fässler R, et al. Kindlin-1 enhances axon growth on inhibitory chondroitin sulfate proteoglycans and promotes sensory axon regeneration. J Neurosci. 2012;32(21):7325-35. doi:10. 1523/JNEUROSCI.5472-11.2012. PMID: 22623678.
10. Prestoz L, Relvas JB, Hopkins K, Patel S, Sowinski P, Price J, ffrench-Constant C. Association between integrin-dependent migration capacity of neural stem cells in vitro and anatomical repair following transplantation. Mol Cell Neurosci. 2001;18(5):473-84. doi:10. 1006/mcne.2001.1037. PMID: 11922139.
11. Hawthorne AL, et al. The unusual response of serotonergic neurons after CNS injury: lack of axonal dieback and enhanced sprouting within the inhibitory environment of the glial scar. J Neurosci. 2011;31(15):5605-16. doi:10. 1523/JNEUROSCI.6663-10.2011. PMID: 21490201.
12. Tysseling-Mattiace VM, et al. Self-assembling nanofibers inhibit glial scar formation and promote axon elongation after spinal cord injury. J Neurosci. 2008;28(14):3814-23. doi: 10. 1523/JNEUROSCI.0143-08.2008. PMID: 18385339.
13. Tysseling VM, et al. Self-assembling peptide amphiphile promotes plasticity of serotonergic fibers following spinal cord injury. J Neurosci Res. 2010;88(14):3161-70. doi:10. 1002/jnr.22472. PMID: 20818775.
14. Wei YT, et al. Hyaluronic acid hydrogels with IKVAV peptides for tissue repair and axonal regeneration in an injured rat brain. Biomed Mater. 2007;2(3):S142-6. doi:10. 1088/1748-6041/2/3/S11. PMID: 18458459.
15. Hou S, Xu Q, Tian W, Cui F, Cai Q, Ma J, Lee IS. The repair of brain lesion by implantation of hyaluronic acid hydrogels modified with laminin. J Neurosci Methods. 2005;148(1):60-70. doi:10. 1016/j.jneumeth.2005.04.016. PMID: 15978668.
16. Park J, Lim E, Back S, Na H, Park Y, Sun K. Nerve regeneration following spinal cord injury using matrix metalloproteinase-sensitive, hyaluronic acid-based biomimetic hydrogel scaffold containing brain-derived neurotrophic factor. J Biomed Mater Res A. 2010;93(3):1091-9. doi:10. 1002/jbm. a.32519. PMID: 19768787.
17. Cheng TY, Chen MH, Chang WH, Huang MY, Wang TW. Neural stem cells encapsulated in a functionalized self-assembling peptide hydrogel for brain tissue engineering. Biomaterials. 2013;34(8):2005-16. doi:10. 1016/j.biomaterials.2012.11.043. PMID: 23237515.
18. Hassannejad Z, Zadegan SA, Vaccaro AR, Rahimi-Movaghar V, Sabzevari O. Biofunctionalized

peptide-based hydrogel as an injectable scaffold for BDNF delivery can improve regeneration after spinal cord injury. Injury. 2019;50(2):278-85. doi:10.1016/j.injury.2018.12.027. PMID: 30595411.

19. Yin Y, et al. Pentapeptide IKVAV engineered hydrogels for neural stem cell attachment. Biomater Sci. 2021;9(8):2887-92. PMID: 33514963.
20. Jiang T, et al. IKVAV peptide-containing hydrogel decreases fibrous scar after spinal cord injury by inhibiting fibroblast migration and activation. Behav Brain Res. 2023;451:114683. doi:10.1016/j.bbr.2023.114683. PMID: 37751807.
21. Ajioka I, Jinnou H, Okada K, Sawada M, Saitoh S, Sawamoto K. Enhancement of neuroblast migration into the injured cerebral cortex using laminin-containing porous sponge. Tissue Eng Part A. 2015;21(1-2):193-201. doi:10.1089/ten.TEA.2014.0080. PMID: 25010638.
22. Ruzicka J, et al. The effect of iPS derived neural progenitors seeded on laminin-coated pHEMA-MOETACl hydrogel with dual porosity in a rat model of chronic spinal cord injury. Cell Transplant. 2019;28(4):400-412. doi:10.1177/0963689718823705. PMID: 30654639.
23. Yang X, et al. Laminin-coated electronic scaffolds with vascular topography for tracking and promoting the migration of br aincells after injury. Nat Biomed Eng.2023;7(10):1261-1274. doi:10.1038/s41551-023-01101-6. PMID: 37814007.
24. Huang T, et al. A functionalized scaffold facilitates neurites extension for spinal cord injury repair. Small. 2024;20(28):e2401020. doi:10.1002/smll.202401020. PMID: 39012061.
25. Yu L, et al. Polylactic acid/chitosan-IKVAV Janus film serving as a dual functional platform for spinal cord injury repair. Nanoscale. 2024;16(47):21991-22000. doi:10.1039/D4NR02248C. PMID: 39513718.
26. Arulmoli J, et al. Combination scaffolds of salmon fibrin, hyaluronic acid, and laminin for human neural stem cell and vascu lar tissue engineering. Acta Bio mater.2016;43:122-138. doi:10.1016/j.actbio.2016.07.043. PMID: 27475528.