
**ELECTROACUPUNCTURE AND ENDOGENOUS STEM/PROGENITOR CELL
MOBILIZATION: A SCOPING REVIEW OF MECHANISMS AND REGENERATIVE
MEDICINE IMPLICATIONS**

**ELETROACUPUNTURA E MOBILIZAÇÃO DE
CÉLULAS-TRONCO/PROGENITORAS ENDÓGENAS: UMA REVISÃO DE
ESCOPO SOBRE MECANISMOS E IMPLICAÇÕES PARA A MEDICINA
REGENERATIVA**

**ELECTROACUPUNTURA Y MOVILIZACIÓN DE CÉLULAS
MADRE/PROGENITORAS ENDÓGENAS: UNA REVISIÓN DE ALCANCE SOBRE
MECANISMOS E IMPLICACIONES PARA LA MEDICINA REGENERATIVA**

DOI: 10.54899/dcs.v23i95.6629

Submitted: 8/14/2026

Approved: 8/17/2026

Published on: 9/2/2026

Maxime Moulins

Bachelor's degree in Physiology

Institution: Université Claude Bernard Lyon 1

Livia Maria Marques Pereira

Bachelor's degree in Biological Sciences

Institution: Universidade Federal Rural de Pernambuco

Anisio Francisco Soares

Doctorate in Biochemistry and Physiology

Institution: Universidade Federal Rural de Pernambuco

ABSTRACT

The Electroacupuncture (EA) is a nonpharmacological neuromodulatory intervention increasingly investigated for its systemic effects, including potential mobilization of endogenous stem and progenitor cells. This scoping review, conducted according to PRISMA-ScR, mapped in vivo animal and human studies reporting EA-induced systemic mobilization and regenerative outcomes across five major databases. Ten studies (nine preclinical, one clinical) showed EA-associated mobilization of mesenchymal stem cells, endothelial progenitor cells, bone marrow-derived interstitial cells of Cajal, and progenitors, with mechanistic convergence on SDF-1/CXCR4 and SCF/c-Kit signaling integrated with sympathetic neuroautonomic activation and context-dependent tissue repair benefits. However, protocol heterogeneity, limited phenotypic standardization, small samples, and scarce causal and clinical designs indicate an emerging field rather than a consolidated therapeutic strategy, suggesting

EA is more plausibly positioned as a low-cost adjuvant to enhance homing and engraftment of transplanted or endogenous cells than as a stand-alone systemic mobilizer in regenerative medicine.

Keywords: electroacupuncture; mesenchymal stem cells; progenitor cells; scoping review; neuromodulation.

RESUMO

A eletroacupuntura (EA) é uma intervenção neuromodulatória não farmacológica cada vez mais investigada por seus efeitos sistêmicos, incluindo o potencial de mobilização de células-tronco e progenitoras endógenas. Esta revisão de escopo, conduzida de acordo com o PRISMA-ScR, mapeou estudos in vivo em animais e humanos que relataram mobilização sistêmica induzida por EA e desfechos regenerativos em cinco importantes bases de dados. Dez estudos (nove pré-clínicos e um clínico) demonstraram mobilização associada à EA de células-tronco mesenquimais, células progenitoras endoteliais, células intersticiais de Cajal derivadas da medula óssea e células progenitoras, com convergência mecanística nas vias de sinalização SDF-1/CXCR4 e SCF/c-Kit, integrada à ativação neuroautônoma simpática e a benefícios de reparo tecidual dependentes do contexto. Contudo, a heterogeneidade dos protocolos, a limitada padronização fenotípica, as pequenas amostras e a escassez de delineamentos causais e clínicos indicam um campo emergente, e não uma estratégia terapêutica consolidada, sugerindo que a EA é mais plausivelmente posicionada como um adjuvante de baixo custo para potencializar o homing e o enxerto de células transplantadas ou endógenas do que como um mobilizador sistêmico independente na medicina regenerativa.

Palavras-chave: eletroacupuntura; células-tronco mesenquimais; células progenitoras; revisão de escopo; neuromodulação.

RESUMEN

La electroacupuntura (EA) es una intervención neuromoduladora no farmacológica cada vez más investigada por sus efectos sistémicos, incluida la posible movilización de células madre y progenitoras endógenas. Esta revisión de alcance, realizada de acuerdo con PRISMA-ScR, mapeó estudios in vivo en animales y seres humanos que informaron sobre la movilización sistémica inducida por EA y los resultados regenerativos en cinco importantes bases de datos. Diez estudios (nueve preclínicos y uno clínico) mostraron una movilización asociada a la EA de células madre mesenquimales, células progenitoras endoteliales, células intersticiales de Cajal derivadas de la médula ósea y células progenitoras, con convergencia mecanística en la señalización SDF-1/CXCR4 y SCF/c-Kit, integrada con la activación neuroautónoma simpática y beneficios de reparación tisular dependientes del contexto. Sin embargo, la heterogeneidad de los protocolos, la limitada estandarización fenotípica, los tamaños muestrales reducidos y la escasez de diseños causales y clínicos indican un campo emergente más que una estrategia terapéutica consolidada, lo que sugiere que la EA se posiciona de manera más plausible como un coadyuvante de bajo costo para mejorar el homing y el injerto de células trasplantadas o endógenas que como un movilizador sistémico independiente en la medicina regenerativa.

Palabras clave: electroacupuntura; células madre mesenquimales; células progenitoras; revisión de alcance; neuromodulación.

1 INTRODUCTION

Endogenous stem and progenitor cells sustain the homeostasis and repair of cardiovascular, neurological, digestive, and musculoskeletal tissues. Pharmacological mobilization strategies, most notably granulocyte colony-stimulating factor (G-CSF) and SDF-1/CXCR4 axis agonists, can expand circulating stem cell pools but rely on costly injectable agents, act predominantly on the hematopoietic lineage, and depend on specialized clinical infrastructure, which restricts their use in broader regenerative practice (Bonig *et al.*, 2012). The mechanistic basis of G-CSF-driven mobilization is now understood to involve remodeling of the bone marrow niche through sympathetic nervous system signaling rather than a direct action on stem cells themselves (Suzuki *et al.*, 2023), underscoring that neural pathways are already recognized regulators of stem cell trafficking independently of pharmacological triggers.

Electroacupuncture (EA) is a nonpharmacological neuromodulatory technique that couples acupuncture needle insertion with low-intensity electrical stimulation, enabling reproducible control of frequency, intensity, and duration. Beyond its established analgesic and anti-inflammatory actions, EA modulates autonomic tone through mechanisms increasingly characterized at the level of vagal and sympathetic outflow (Li *et al.*, 2013), suggesting a plausible neural route through which EA could influence the bone marrow niche in a manner comparable to pharmacological mobilizers. A limited but growing body of preclinical work suggests that EA may additionally trigger the release of mesenchymal and other endogenous progenitors into the systemic circulation, followed by chemokine-directed homing to injured tissue. These observations remain scattered across heterogeneous animal models and cellular phenotypes and have not previously been synthesized from a stem cell biology perspective.

The broader literature on acupuncture mechanisms has focused mainly on local effects (proliferation, differentiation, and angiogenesis at the needling site) rather than on cellular trafficking between the marrow niche, the circulation, and distant target tissues. Many EA protocols also select acupoint combinations on the basis of

traditional Chinese medicine (TCM) rationales without articulating their relationship to contemporary neuroautonomic and chemokine-mediated mobilization pathways. Given this fragmentation, a synthesis was needed to map, rather than adjudicate, the existing evidence on EA-induced systemic mobilization.

This choice is consistent with current methodological guidance recommending scoping reviews when a field is heterogeneous in populations, interventions, and outcome definitions, and when the primary purpose is to identify knowledge gaps and inform future research priorities rather than to establish a definitive effect estimate (Tricco *et al.*, 2018).

This scoping review aimed to map the available evidence on whether EA induces measurable systemic mobilization of endogenous stem or progenitor cells, followed by increased recruitment to injured tissues, and to characterize the mechanisms proposed to underlie this process. The specific objectives were: (1) to describe the stem/progenitor cell populations reported as mobilized by EA in animal and human studies; (2) to chart the chemokine axes, neuroautonomic pathways, and other mediators proposed to drive this mobilization and homing; (3) to identify the main gaps and limitations of the current evidence base; and (4) to discuss the translational relevance of these findings, including the possibility that EA may be more promising as an adjuvant to cell-based therapies than as a stand-alone mobilizing agent.

2 THEORETICAL FRAMEWORK

2.1 CONCEPTUAL BACKGROUND

Endogenous stem and progenitor cells contribute to tissue homeostasis and repair across cardiovascular, neurological, digestive, and musculoskeletal systems. Although pharmacological strategies targeting the SDF-1/CXCR4 axis or hematopoietic growth factors can increase circulating stem cell pools, their clinical use is constrained by cost, injectable administration, predominant hematopoietic targeting, and dependence on specialized infrastructure (Bonig *et al.*, 2012). These constraints motivate the search for nonpharmacological approaches capable of modulating mobilization and tissue recruitment within a broader regenerative framework.

2.2 ELECTROACUPUNCTURE AS A CANDIDATE SYSTEMIC MODULATOR

EA combines needle insertion with low-intensity electrical stimulation delivered under controlled parameters of frequency, intensity, and waveform. Existing reviews of acupuncture's autonomic effects indicate that stimulation of specific acupoints differentially engages vagal versus sympathetic outflow depending on point location and stimulation parameters (Li *et al.*, 2013; Li *et al.*, 2022)." This body of evidence frames EA not solely as a local intervention but as a potential systemic modulator capable of influencing bone marrow and adipose tissue niches through central and autonomic circuits.

2.3 DEFINING SYSTEMIC MOBILIZATION

For the purposes of this review, systemic mobilization was defined as the egress of endogenous stem or progenitor cells from their niche into the bloodstream, with possible secondary recruitment to distant injured tissue, as distinct from purely local proliferative or differentiative responses. This distinction matters because a substantial fraction of the acupuncture mechanistic literature documents local tissue changes without addressing whether cells first transit through the circulation.

2.4 CANDIDATE MECHANISTIC AXES

Two mechanistic axes recur across the mobilization literature more broadly and provide a framework for interpreting EA-induced cellular trafficking. The SDF-1/CXCR4 axis governs both the retention of hematopoietic stem/progenitor cells within the marrow niche and their chemotactic egress and homing when the gradient is reversed or amplified (Sharma *et al.*, 2011). The SCF/c-Kit axis regulates progenitor survival, proliferation, and differentiation and has been implicated in the restoration of interstitial cell of Cajal networks in gut motility disorders. Independently of these chemokine pathways, sympathetic nervous system activation is now recognized as a direct regulator of hematopoietic stem cell mobilization through its action on the osteoblastic niche (Suzuki *et al.*, 2023), offering a neural route by which EA-induced autonomic engagement could intersect with chemokine-driven trafficking. The convergence on SDF-1/CXCR4 and SCF/c-Kit signaling is mechanistically coherent, and it parallels broader work showing that these axes govern homing and engraftment

of hematopoietic and mesenchymal stem cells (Cheng *et al.*, 2012), but such mechanistic coherence alone does not demonstrate that EA-induced systemic mobilization is robust or clinically meaningful.

2.5 PERSISTENT GAPS IN THE LITERATURE

Despite these convergent conceptual elements, the literature on EA and cellular mobilization remains methodologically and conceptually fragmented: studies differ substantially in acupoints, stimulation parameters, treatment schedules, species, and phenotypic definitions of mobilized cells, and many rely on small sample sizes or correlative evidence. This heterogeneity, combined with the still-limited number of available studies, is itself an informative finding, motivating a scoping approach capable of mapping the field's current boundaries rather than a systematic review structured around a single pooled effect estimate.

3 METHODOLOGY

3.1 STUDY DESIGN

This scoping review was conducted in accordance with the PRISMA Extension for Scoping Reviews (PRISMA-ScR) checklist (Tricco *et al.*, 2018) and informed by the Joanna Briggs Institute methodology for scoping reviews (Peters *et al.*, 2021). A scoping approach was selected because the objective was to map the extent, range, and nature of the available evidence, to characterize study and intervention features, and to identify knowledge gaps, rather than to answer a narrowly defined efficacy question through critical appraisal and quantitative pooling, which is the domain of systematic reviews (Munn *et al.*, 2018).

3.2 ELIGIBILITY CRITERIA (POPULATION, CONCEPT, CONTEXT)

The review question was structured using the Population, Concept, Context (PCC) framework recommended for scoping reviews. Population: animal models and human subjects exposed to EA in physiological or pathological contexts. Concept: systemic mobilization of endogenous stem or progenitor cells, defined as their egress

from the originating niche into the bloodstream, with possible secondary recruitment to an injured site, documented as long-distance trafficking rather than local proliferation or differentiation. Context: any experimental or clinical setting reporting at least one outcome compatible with this definition, particularly an increase in circulating stem or progenitor cells in peripheral blood and/or convincing evidence of cells originating from a distinct bone marrow or tissue niche within a target compartment.

Eligible sources were original in vivo animal or human investigations of EA, with full text available in English, French, or Portuguese. Marked autologous or allogeneic bone marrow graft models were included when EA demonstrably modulated systemic mobilization of bone marrow-derived cells into a target compartment; in these cases, grafted cells were treated, in the functional sense adopted here, as endogenous bone marrow-derived cells. Exclusion criteria comprised exclusively in vitro studies, manual acupuncture without an EA arm, exogenous cell transplantation without specific assessment of endogenous cells, studies reporting only local proliferation or differentiation without evidence of systemic mobilization, and secondary publications (systematic or narrative reviews, meta-analyses, editorials, letters, and conference abstracts without extractable primary data).

Admissible comparators included no treatment, the pathological model alone, sham EA, manual acupuncture, or any other comparator judged relevant by the original authors.

3.3 INFORMATION SOURCES AND SEARCH STRATEGY

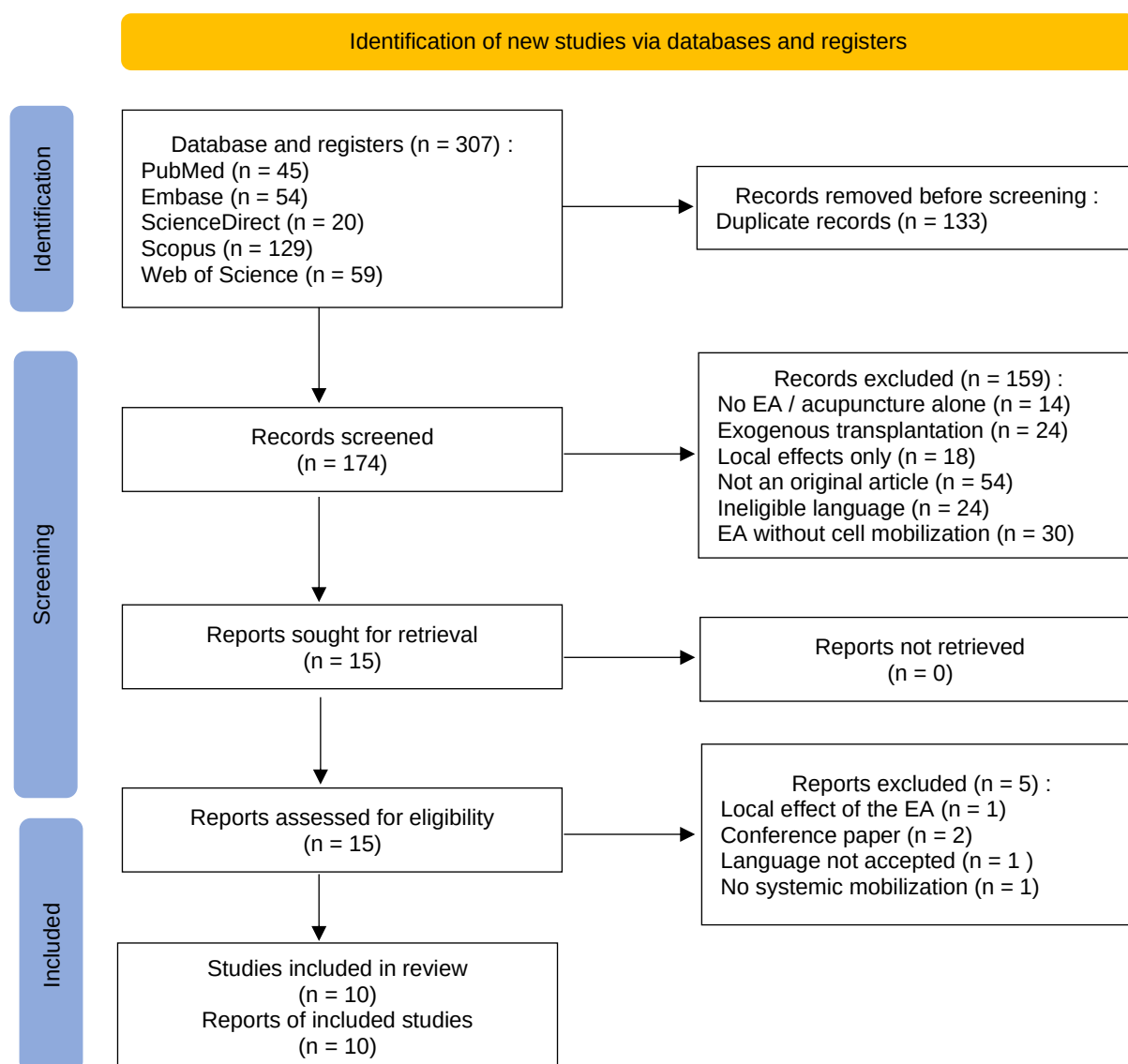
The literature search covered PubMed, Embase, ScienceDirect, Scopus, and Web of Science up to June 26, 2026, without an initial date limit, and was complemented by screening the reference lists of included studies and relevant reviews. The strategy combined free terms and, when appropriate, controlled vocabulary across three keyword blocks: terms for electroacupuncture, terms for stem and progenitor cells, and terms for mobilization, trafficking, or systemic release, combined with Boolean operators and adapted to each database syntax. Full search equations are available from the corresponding author on request. Although searching had no date restriction, inclusion was limited to studies published from 2009 onward, corresponding, to our knowledge, to the earliest reports suggesting systemic

mobilization of endothelial progenitor cells by EA in cerebral ischemia models (Cai *et al.*, 2009).

3.4 SELECTION OF SOURCES OF EVIDENCE

A total of 307 records were imported into the Zotero reference management software and deduplicated, yielding 133 exclusions and 174 unique records. These underwent title/abstract screening followed by full-text assessment of studies considered relevant or uncertain. At the title/abstract stage, records were classified as included, excluded, or uncertain according to the predefined PCC criteria, resulting in 15 retained references and 159 exclusions. All 15 retained or uncertain articles were assessed in full text; the main reason for exclusion was recorded for each discarded study, allowing construction of a PRISMA flow diagram (Figure 1). Ten studies were ultimately included. Study selection was performed by the principal author, with discussion of ambiguous cases with the project supervisor to maintain consistency within a small team framework.

Figure 1 PRISMA-ScR flow diagram of source selection process.



Source : Adapted from Page *et al.*, 2021.

3.5 DATA CHARTING PROCESS AND DATA ITEMS

Data from included studies were charted using a standardized extraction form developed from the review question and eligibility criteria. Variables comprised author and year, species/population and experimental or clinical model, EA parameters and comparator, stem/progenitor cell type evaluated, method used to measure mobilization, and key findings related to systemic mobilization and, when reported, tissue or functional effects. Charting was conducted by the principal author, with verification of ambiguous points through discussion with the supervisor. When

information was incomplete, non-standardized, or difficult to interpret, it was recorded as not reported or uncertain to preserve transparency.

3.6 CRITICAL APPRAISAL OF INDIVIDUAL SOURCES OF EVIDENCE

Consistent with PRISMA-ScR guidance, formal critical appraisal of risk of bias was not performed, as it is not a mandatory component of the scoping review methodology and would not have altered the descriptive, mapping-oriented purpose of this synthesis (Tricco *et al.*, 2018). Methodological features relevant to the interpretation of each study (sample size, comparator type, blinding) were nonetheless recorded during data charting and are discussed narratively as limitations of the evidence base.

3.7 SYNTHESIS OF RESULTS

Given the heterogeneity of models, populations, EA parameters, measurement methods, and outcome criteria, no meta-analysis was planned or would have been appropriate. Results were synthesized descriptively and narratively, with studies charted into separate tables addressing distinct dimensions of the evidence (species/model, EA protocol and comparator, mobilized cell type, measurement method, and key mobilization findings) to improve the clarity and interpretability of a heterogeneous evidence base. The analysis focused primarily on demonstrating measurable systemic mobilization of endogenous stem or progenitor cells after EA, secondarily on associated tissue repair, and explicitly on identifying gaps that could inform future research priorities.

4 RESULTS AND DISCUSSIONS

4.1 THE SELECTION OF SOURCES OF EVIDENCE

A total of 307 records were identified in PubMed, Embase, ScienceDirect, Scopus, and Web of Science. After deduplication, 174 unique records were submitted to title and abstract screening. At this stage, 159 references were excluded (absence of EA, manual acupuncture alone, no cell mobilization, ineligible language, non-original

article, strictly local effects, or exogenous transplantation), and 15 articles were retained for full-text assessment. All full-text reports were obtained, and 10 studies were ultimately included (Figure 1). The small number of eligible studies, despite an exhaustive five-database search without date restriction, is itself a first substantive finding of this scoping review: it indicates that EA-induced systemic mobilization is an emerging research question rather than an established sub-field of acupuncture research.

4.2 CHARACTERISTICS OF SOURCES OF EVIDENCE: SPECIES, MODELS, AND STUDY DESIGN

The 10 included studies covered a range of animal models (rat, mouse, dog, horse) and one clinical study in humans (Table 1). They explored diverse physiological and pathological contexts, including healthy subjects, and models of diabetes, cerebral infarction, myocardial infarction, and tendon injury. Nine of the ten sources were preclinical, and only one (Lee *et al.*, 2015) involved a human clinical population, indicating a marked predominance of animal evidence over clinical translation.

Table 1 Species, experimental/clinical model, and study design of included sources.

Author, year	Species/ population	Model/condition	Sample size
Lee, 2015	Human	Cerebral infarction (stroke)	n = 20
Liu, 2016	Rat	Healthy	n = 60
Xie, 2016	Rat	Middle cerebral artery occlusion/reperfusion	n = 250
Salazar, 2017	Rat, human, mouse, horse	Healthy; Achilles tendon partial lesion (rat)	n = 6-6-4-6
Zhao, 2018	Mouse	Diabetic gastric neuromuscular dysfunction	n = 66
An, 2019	Mouse	Diabetic colonic dysmotility	n = 60
Vieira, 2021	Horse	Healthy	n = 3
Zhao, 2022	Mouse	Myocardial infarction	n = 12
Xuan, 2023	Rat	Myocardial infarction	n = 40
Phanwanich, 2026	Dog	Healthy	n = 4

Source: authors

4.3 EA PROTOCOLS AND COMPARATOR

EA protocols differed markedly in acupoints, stimulation frequency, intensity, waveform, session duration, and number of sessions (Table 2). Comparators ranged from sham needling without electrical stimulation, to non-acupoint stimulation,

manual acupuncture without electrical current, or pharmacological blockade of the sympathetic nervous system (propranolol), reflecting varying degrees of control for the specific contribution of electrical stimulation and neuroautonomic pathways.

Table 2 Electroacupuncture parameters and comparator groups.

Author, year	Acupoints	Frequency/ intensity	Session protocol	Comparator/sham
Lee, 2015	PC5, PC6, ST36, ST37	2 Hz, continuous wave	20 min, 2 sessions, 7 days	Superficial puncture, no electrical stimulation
Liu, 2016	GV4, GV6	50/2 Hz, dense- disperse wave	30 min/day, 14 days	Needling beside points, connected but not stimulated
Xie, 2016	GV20, LI4, LIV3	2/20 Hz, 1 mA	30 min/day, 7 days	Model without EA
Salazar, 2017	LI4, LI11, GV14, GV20, ST36, LIV3	4 Hz (mouse); variable	1 session to 2 week	Non-acupoint stimulation; EA + propranolol
Zhao, 2018	ST36	Low 10 Hz, High 100 Hz, 1 mA	30 min/day, 8 weeks	Manual acupuncture, same points, no manipulation
An, 2019	ST36	Low 10 Hz, High 100 Hz, 1 mA	30 min/day, 8 weeks	Manual acupuncture, same points, no manipulation
Vieira, 2021	LI4, LI11, GV14, GV20	20 Hz	45 min, single session	In vitro human iPSC- derived MSC comparator
Zhao, 2022	PC6, BL15	2-15 Hz, alternative current, 1 mA	30 min, single session	Infarction model without EA
Xuan, 2023	PC6, BL15	20 Hz, 1 mA	30 min/day, 4 weeks	Manual acupuncture, same points
Phanwanich, 2026	GV4, GV6, SP10, GB39, LIV3	Sequential low then high frequency	10 min/week, 3 weeks	No EA sham; in vitro AD- MSC comparator

Source: authors

4.4 MOBILIZED CELL POPULATIONS AND MEASUREMENT METHODS

The stem and progenitor cell types assessed spanned mesenchymal stem cells and related populations, circulating endothelial progenitor cells, bone marrow-derived interstitial cells of Cajal, and bone marrow progenitors expressing CD34, c-Kit, Sca-1, or CXCR4 (Table 3). Measurement methods included flow cytometry of peripheral blood, colony-forming unit assays (CFU-F), Transwell migration assays, transcriptomic profiling, and GFP-chimeric bone marrow tracing.

Table 3 Stem/progenitor cell populations mobilized and methods used to measure mobilization.

Author, year	Cell population mobilized	Measurement method
Lee, 2015	Circulating EPC (CD45 ⁻ CD34 ⁺ KDR ⁺)	Flow cytometry, peripheral blood
Liu, 2016	MSC-like colonies (CFU-F, CD90 ⁺ CD44 ⁺ CD45 ⁻)	CFU-F assay, Transwell migration

Author, year	Cell population mobilized	Measurement method
Xie, 2016	EPC (CD34 ⁺ VEGFR2 ⁺)	Flow cytometry, bone marrow and peripheral blood
Salazar, 2017	MSC-like cells (Lin ⁻ CD90 ⁺ CD44 ^{HL} ; CD34 ⁺ CD45 ⁻ CD31 ⁻ ; Lin ⁻ PDGFR α ⁺ Sca-1 ⁺)	Flow cytometry across four species; DNA microarray
Zhao, 2018	Bone marrow-derived ICC (c-Kit ⁺ GFP ⁺)	GFP-chimeric bone marrow tracing, immunohistochemistry
An, 2019	Bone marrow-derived ICC (c-Kit ⁺ GFP ⁺)	GFP-chimeric bone marrow tracing, protein/mRNA quantification
Vieira, 2021	Circulating MSC (CD90 ⁺ CD105 ⁺ CD73 ⁺)	Colony isolation and culture, flow cytometry
Zhao, 2022	Bone marrow progenitors (CD34 ⁺ CD117 ⁺ Sca-1 ⁺ CD90 ⁺)	Flow cytometry, peripheral blood kinetics
Xuan, 2023	Bone marrow stem/progenitor cells (c-Kit ⁺ Sca-1 ⁺ CXCR4 ⁺)	Immunohistochemistry, infarcted myocardium
Phanwanich, 2026	Circulating MSC-like colonies (PBSCs, CD90 ⁺)	Colony culture from peripheral blood

Source: authors

4.5 KEY FINDINGS ON SYSTEMIC MOBILIZATION AND TISSUE/FUNCTIONAL OUTCOMES

Table 4 summarizes the principal mobilization results and associated tissue or functional findings reported across the ten included sources. In patients with cerebral infarction, a single EA session significantly increased circulating EPC alongside elevated plasma VEGF and improved peripheral endothelial function, although tissue homing was not documented (Lee *et al.*, 2015). In healthy rats, daily EA increased CFU-F colonies and plasma SDF-1 α , with mobilized MSC retaining multipotent differentiation capacity in vitro (Liu *et al.*, 2016). In a rat stroke model, EA increased EPC in both bone marrow and peripheral blood, with an early marrow peak followed by a circulating peak and improvement in neurological deficit scores (Xie *et al.*, 2016). A multi-species study reported a 313% increase in circulating MSC-like cells in rats, with convergent findings across humans, mice, and horses, attributing mobilization to a central nervous system–sympathetic nervous system (CNS/SNS) axis and selective activation of medium- to large-diameter dorsal root ganglion fibers (Salazar *et al.*, 2017). DNA microarray analysis of EA-mobilized MSC in horses in this study shows coordinated regulation of genes linked to migration, adhesion, angiogenesis, immunomodulation, and matrix remodeling, suggesting that systemic mobilization is accompanied by transcriptional reprogramming compatible with tissue repair processes.

Table 4 Key mechanistic and tissue/functional findings related to systemic mobilization.

Author, year	Main mobilization finding	Proposed mechanism	Tissue/functional outcome
Lee, 2015	EPC + 131.8% ¹ vs + 33.0% ⁴ in placebo	VEGF-EPC correlation	Improved peripheral endothelial function after stroke
Liu, 2016	CFU-F colonies increased by 79.6% ⁴ ; circulating MSC-like colonies increased by 186.5% ⁴	SDF-1 α upregulation and SDF-1/CXCR4 axis activation	Mobilized MSC retained multipotent differentiation in vitro
Xie, 2016	EPC increase in marrow and peripheral blood	Marrow to blood SDF-1 α gradient	Improved Modified neurological severity score (mNSS)
Salazar, 2017	Circulating MSC-like cells increased by 313% at 2 h post-EA (rat)	CNS/SNS axis; activation of dorsal root ganglion	Increased IL-10, adipose browning, reduced hyperalgesia
Zhao, 2018	Bone marrow-derived ICC (c-Kit ⁺ GFP ⁺) increased in gastric plexuses	SDF-1/CXCR4 and mSCF/c-Kit–ETV1 pathways	Restoration of gastric motility
An, 2019	Colonic ICC (c-Kit ⁺ GFP ⁺) increased in diabetic colon	SDF-1/CXCR4, TGF- β 1/Smad3, mSCF/c-Kit–ERK–ETV1 axes	Restoration of colonic ICC density
Vieira, 2021	~100 MSC colonies isolated from peripheral blood post-EA	CNS/SNS axis (proposed)	Osteogenic, adipogenic, and angiogenic potential in vitro
Zhao, 2022	Transient increase in bone marrow progenitors at 6 h post-EA	Myocardial SDF-1/CXCR4 signaling (attenuated in CXCR4 ^{-/-} mice)	Reduced infarct size, improved ventricular function
Xuan, 2023	Increased c-Kit ⁺ /Sca-1 ⁺ /CXCR4 ⁺ cells in infarcted myocardium	Local SDF-1 and SCF upregulation	Reduced fibrosis; improved echocardiographic parameters
Phanwanich, 2026	Reproducible PBSC-like colonies isolated from peripheral blood post-EA	Sympathetic and HPA axis activation, SDF-1 release	Not evaluated

Source: authors

Across the corpus, EA mobilized bone marrow-derived interstitial cells of Cajal and restored their density in diabetic gastric and colonic dysmotility models, with activation of SDF-1/CXCR4, TGF- β 1/Smad3, and SCF/c-Kit–ERK–ETV1 pathways (Zhao *et al.*, 2018; An *et al.*, 2019). In myocardial infarction models, transient or sustained increases in bone marrow-derived progenitors were accompanied by reduced infarct size, fibrosis, and apoptosis, and improved ventricular function, with attenuation of these effects in CXCR4-deficient mice supporting a mechanistic role for this axis (Zhao *et al.*, 2022; Xuan *et al.*, 2023). In healthy horses and dogs, single or repeated EA sessions allowed isolation of MSC-like colonies from peripheral blood with

⁴ Note: Percentage derived by the authors from the primary data reported in the original studies.

in vitro trilineage differentiation potential, without quantification of mobilization kinetics or homing (Vieira *et al.*, 2021; Phanwanich *et al.*, 2026).

4.6 DIVERSITY OF MOBILIZED CELL POPULATIONS

The included sources indicate that EA can mobilize several major families of stem and progenitor cells, spanning mesenchymal, endothelial, and neuromuscular progenitor compartments across rat, mouse, dog, horse, and human models. This phenotypic diversity reflects both the use of multispecies models with marker combinations adapted to each organism, and the absence of a harmonized minimal phenotyping panel within a given species. It is therefore plausible that distinct or partially overlapping sub-populations are mobilized without being systematically detected, a limitation that mirrors challenges already documented in the broader mesenchymal stem cell homing literature, where phenotypic heterogeneity complicates cross-study comparison (Sajjad *et al.*, 2024). Standardization of phenotypic definitions and the use of high-throughput technologies such as multiparametric cytometry and single-cell RNA sequencing would help refine the mapping of EA-mobilized populations.

4.7 NICHE OF ORIGIN, CIRCULATION, AND HOMING

The evidence reveals a continuum between studies documenting a clear circulating mobilization peak and studies inferring mobilization indirectly from bone marrow chimerism and tissue-level labeling. Circulating mobilization is most robustly demonstrated for MSC-related populations and bone marrow progenitors after myocardial infarction, with kinetics compatible with egress from the marrow niche. Conversely, several digestive-tract studies document increased bone marrow-derived cells within target tissues without detailed quantification of the circulating phase, so that systemic mobilization is plausible but not directly confirmed. Even when marrow origin is supported by CD34, c-Kit, or Sca-1 expression, or by GFP-chimeric models, a contribution from other niches, such as adipose tissue or resident vascular stroma, is not formally excluded. This ambiguity illustrates a broader challenge in the stem cell homing field, where distinguishing true long-distance trafficking from local niche

expansion remains methodologically demanding even outside the EA literature (Sajjad *et al.*, 2024).

4.8 MECHANISTIC CONVERGENCE: SDF-1/CXCR4, SCF/C-KIT, AND THE CNS/SNS AXIS

The SDF-1/CXCR4 axis emerges recurrently as a candidate mediator of EA-induced mobilization, consistent with its well-established role in retaining hematopoietic stem/progenitor cells within the bone marrow niche and directing their chemotactic egress and homing when the gradient is perturbed (Sharma *et al.*, 2011). In infarction models, attenuation of EA effects in CXCR4-deficient animals provides more direct evidence for this axis's participation in EA-mediated cardioprotection. The SCF/c-Kit axis is similarly implicated, particularly in restoring digestive interstitial cell of Cajal networks, suggesting that EA may influence progenitor survival and differentiation in target tissues beyond mobilization alone. A second mechanistic pillar concerns a CNS/SNS axis. Electrophysiological and molecular data indicate that electrical stimulation of certain acupoints preferentially activates medium and large diameter sensory fibers, engages central networks, and produces systemic sympathetic activation, consistent with contemporary characterizations of acupuncture's differential effects on sympathetic versus vagal tone depending on stimulation site (Li *et al.*, 2022). This route parallels, at a conceptual level, the demonstrated role of sympathetic signaling in G-CSF-induced hematopoietic stem cell mobilization, in which catecholaminergic tone remodels the osteoblastic niche independently of a direct action of the mobilizing agent on stem cells (Suzuki *et al.*, 2023). This parallel strengthens the biological plausibility of EA as a neurally mediated mobilizing stimulus, even though direct causal evidence specific to EA remains limited to correlative transcriptomic and pharmacological blockade data in a single multi-species study (Salazar *et al.*, 2017).

4.9 TISSUE AND FUNCTIONAL EFFECTS

Beyond hematological and phenotypic changes, several included studies report tissue and functional benefits, including restoration of digestive motility, improved peripheral endothelial function after stroke, reduced hyperalgesia and

collagen remodeling after tendon injury, and reduced infarct size and improved ventricular function after myocardial infarction. These associations support the plausibility that EA-induced mobilization contributes to reparative tissue responses, but a direct causal link between mobilized cells and repair is rarely established formally. Studies combining long-term cell tracing, targeted depletion, or specific homing blockade remain scarce; at this stage, most data support temporally and mechanistically plausible associations rather than complete causal demonstrations.

4.10 LIMITATIONS OF THE AVAILABLE LITERATURE

The central limitation revealed by this scoping review is quantitative before it is qualitative: only ten eligible studies were identified across five databases spanning more than fifteen years without a date restriction, indicating that EA-induced systemic mobilization remains a nascent research question. This scarcity constrains every subsequent inference. Beyond sample size, protocols are markedly heterogeneous in acupoints, stimulation frequency, waveform, and treatment duration, which precludes identification of an optimal EA parameter set. Phenotypic definitions of mobilized cells vary across species and studies without a harmonized minimal marker panel, limiting cross-study comparability. Comparator groups also differ substantially, from sham needling to pharmacological sympathetic blockade, which affects the specificity with which neuroautonomic contributions can be isolated. Clinical evidence is confined to a single study, so that virtually all mechanistic inference currently rests on animal models whose translational relevance to human physiology remains unverified. Finally, because critical appraisal of risk of bias was not undertaken, consistent with PRISMA-ScR guidance for scoping reviews, no formal grading of the certainty of the underlying evidence could be provided; this should be considered when interpreting the mechanistic convergences described above as hypothesis-generating rather than confirmatory.

4.11 IS THE EVIDENCE PROMISING, OR IS IT SIMPLY SCARCE?

An important interpretive question raised by this mapping exercise is whether the consistent direction of effects across ten heterogeneous studies indicates a genuinely promising biological phenomenon, or whether the small number of eligible

sources instead reflects a limited and possibly modest true effect of EA on systemic mobilization specifically, as distinct from its better-documented local anti-inflammatory and analgesic actions. Publication bias toward positive findings cannot be excluded given the near-total absence of studies reporting a null mobilization result, and several included sources used underpowered designs ($n = 3$ to $n = 12$) that would be unlikely to detect small effects even if present. The convergence on SDF-1/CXCR4 and SCF/c-Kit signaling is mechanistically coherent, and it parallels broader work showing that these axes govern homing and engraftment of hematopoietic and mesenchymal stem cells (Cheng *et al.*, 2012), but such mechanistic coherence alone does not demonstrate that EA-induced systemic mobilization is robust or clinically meaningful. A cautious reading of the evidence favors describing EA's mobilizing potential as biologically plausible and worth further investigation, rather than as an established or clinically actionable effect.

4.12 PERSPECTIVES: ELECTROACUPUNCTURE AS AN ADJUVANT AND METHODOLOGICAL REORIENTATION

Given this uncertainty, an alternative and arguably more defensible translational avenue emerges from the data themselves. Because the SDF-1/CXCR4 and SCF/c-Kit axes govern not only endogenous mobilization but also the homing and engraftment of transplanted stem cells (Sharma *et al.*, 2011), EA could plausibly be repositioned as an adjuvant strategy that enhances the efficacy of exogenous cell therapies rather than as a stand-alone mobilizing intervention. This hypothesis is directly supported by recent work showing that acupuncture combined with bone marrow-derived stem cell transplantation improves engraftment efficiency through the same SDF-1/CXCR4 pathway identified across the sources included in this review (Ma *et al.*, 2025), and it aligns with the broader literature on strategies to enhance MSC homing through modulation of chemokine receptor expression or target-tissue chemokine release (Sajjad *et al.*, 2024). Framed this way, future research would test EA not as a therapy expected to mobilize a clinically sufficient endogenous cell pool on its own, but as a low-cost, nonpharmacological adjuvant capable of potentiating the recruitment and retention of co-administered or transplanted cells at the injury site.

A further methodological consideration concerns how mechanistic hypotheses are generated in this field. Across the included studies and the broader EA literature, most designs test predefined downstream consequences (SDF-1/CXCR4, SCF/c-Kit, sympathetic activation) rather than deriving hypotheses from the systemic logic underlying acupoint selection itself. This confirmatory approach risks observing only what investigators already expect to find, rather than mapping the full physiological network engaged by EA. Traditional Chinese medicine's empirical rationale for acupoint combinations may offer an underused heuristic for generating novel, systemically framed hypotheses, rather than serving only as a historical justification for point choice. Future protocols could productively test candidate mechanisms suggested by TCM meridian logic alongside, rather than exclusively within, established biomedical pathways.

5 CONCLUSION

This scoping review mapped ten studies, predominantly preclinical, addressing whether electroacupuncture induces systemic mobilization of endogenous stem or progenitor cells. Available evidence indicates that EA is associated with mobilization or tissue recruitment of several progenitor populations across multiple animal species and in one clinical context, most consistently through the SDF-1/CXCR4 and SCF/c-Kit axes together with sympathetic-mediated neuroautonomic activation. The most consequential finding of this review, however, is methodological rather than mechanistic: the small number of eligible studies, their preclinical predominance, marked protocol heterogeneity, and the absence of formal causal designs indicate that this field remains at an early, exploratory stage rather than a mature area of evidence capable of supporting therapeutic claims. Rather than concluding that EA holds a demonstrated regenerative potential through endogenous mobilization, this review supports a more circumspect interpretation: the biological plausibility is real and mechanistically coherent, but current data cannot yet distinguish a genuinely promising nonpharmacological mobilization strategy from a modest or context-dependent effect that has simply not yet been rigorously tested. This ambiguity itself constitutes a central rationale for future research, and it reorients the most promising near-term application of EA toward its use as an adjuvant to cell-based regenerative therapies rather than as an independent mobilization strategy. Future

studies should prioritize standardized EA parameters, harmonized phenotypic marker panels, cell tracing and homing-blockade designs to establish causality, adequately powered clinical trials, and explicit testing of EA as a combination strategy with transplanted cell therapies.

REFERENCES

- AN, Jing *et al.* Bone marrow-derived interstitial cells of Cajal are increased by electro-acupuncture in the colon of diabetic mice. *Journal of Gastroenterology and Hepatology*, v. 34, n. 8, p. 1357–1367, 2019. DOI: <https://doi.org/10.1111/jgh.14579>. Acesso em: 2 set. 2026.
- BONIG, Halvard; PAPAYANNOPOULOU, Thalia. Mobilization of hematopoietic stem/progenitor cells: general principles and molecular mechanisms. In: KOLONIN, M. G.; SIMMONS, P. J. (ed.). *Stem Cell Mobilization*. v. 904. Totowa: Humana Press, 2012. p. 1–14. DOI: https://doi.org/10.1007/978-1-61779-943-3_1. Acesso em: 2 set. 2026.
- CAI, S. X. *et al.* The mechanism of electro-acupuncture (EA) treating cerebral ischemia: whether EA administered to mobilization of EPCs. *IFMBE Proceedings*, v. 25, n. 9, p. 529–532, 2009. DOI: https://doi.org/10.1007/978-3-642-03889-1_142. Acesso em: 2 set. 2026.
- CHENG, Mine; QIN, Gangjian. Progenitor cell mobilization and recruitment: SDF-1, CXCR4, α 4-integrin, and c-kit. *Progress in Molecular Biology and Translational Science*, v. 111, p. 243–264, 2012. DOI: <https://doi.org/10.1016/B978-0-12-398459-3.00011-3>. Acesso em: 2 set. 2026.
- LEE, Sanghoon *et al.* Effects of electroacupuncture on endothelial function and circulating endothelial progenitor cells in patients with cerebral infarction. *Clinical and Experimental Pharmacology & Physiology*, v. 42, n. 8, p. 822–827, 2015. DOI: <https://doi.org/10.1111/1440-1681.12413>. Acesso em: 2 set. 2026.
- LI, Qian-Qian *et al.* Acupuncture effect and central autonomic regulation. *Evidence-Based Complementary and Alternative Medicine*, v. 2013, p. 267959, 2013. DOI: <https://doi.org/10.1155/2013/267959>. Acesso em: 2 set. 2026.
- LI, Yan-Wei *et al.* The autonomic nervous system: a potential link to the efficacy of acupuncture. *Frontiers in Neuroscience*, v. 16, p. 1038945, 2022. DOI: <https://doi.org/10.3389/fnins.2022.1038945>. Acesso em: 2 set. 2026.
- LIU, Lizhen *et al.* Electro-acupuncture promotes endogenous multipotential mesenchymal stem cell mobilization into the peripheral blood. *Cellular Physiology and Biochemistry*, v. 38, n. 4, p. 1605–1617, 2016. DOI: <https://doi.org/10.1159/000443101>. Acesso em: 2 set. 2026.
- MA, Wei-Gang *et al.* Combining acupuncture and mesenchymal stem cell therapy offers promise as a treatment for inflammatory bowel disease. *World Journal of Stem Cells*, v. 17, n. 7, p. 105371, 2025. DOI: <https://doi.org/10.4252/wjsc.v17.i7.105371>. Acesso em: 2 set. 2026.
- MUNN, Zachary *et al.* Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. *BMC Medical Research Methodology*, v. 18, n. 1, p. 143, 2018. DOI: <https://doi.org/10.1186/s12874-018-0611-x>. Acesso em: 2 set. 2026.

PAGE, Matthew J. *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *PLOS Medicine*, v. 18, n. 3, e1003583, 2021. DOI: <https://doi.org/10.1371/journal.pmed.1003583>. Acesso em: 2 set. 2026.

PHANWANICH, Warangkhan *et al.* Characterization of canine peripheral blood stem cells after electroacupuncture stimulation. *Innovations in Acupuncture Medicine*, v. 19, n. 1, 2026. DOI: <https://doi.org/10.1186/s44424-025-00044-w>. Acesso em: 2 set. 2026.

PETERS, Micah D. J. *et al.* Updated methodological guidance for the conduct of scoping reviews. *JBIM Evidence Implementation*, 2021. DOI: <https://doi.org/10.1097/XEB.0000000000000277>. Acesso em: 2 set. 2026.

SAJJAD, Umar *et al.* Exploring mesenchymal stem cells homing mechanisms and improvement strategies. *Stem Cells Translational Medicine*, v. 13, n. 12, p. 1161–1177, 2024. DOI: <https://doi.org/10.1093/stcltm/szae045>. Acesso em: 2 set. 2026.

SALAZAR, Tatiana E. *et al.* Electroacupuncture promotes central nervous system-dependent release of mesenchymal stem cells. *Stem Cells*, v. 35, n. 5, p. 1303–1315, 2017. DOI: <https://doi.org/10.1002/stem.2613>. Acesso em: 2 set. 2026.

SHARMA, Menka *et al.* Stromal-derived factor-1/CXCR4 signaling: indispensable role in homing and engraftment of hematopoietic stem cells in bone marrow. *Stem Cells and Development*, v. 20, n. 6, p. 933–946, 2011. DOI: <https://doi.org/10.1089/scd.2010.0263>. Acesso em: 2 set. 2026.

SUZUKI, Tomohide *et al.* Regulation of granulocyte colony-stimulating factor-induced hematopoietic stem cell mobilization by the sympathetic nervous system. *Current Opinion in Hematology*, v. 30, n. 4, p. 124–129, 2023. DOI: <https://doi.org/10.1097/MOH.0000000000000764>. Acesso em: 2 set. 2026.

TRICCO, Andrea C. *et al.* PRISMA Extension for Scoping Reviews (PRISMA-ScR): checklist and explanation. *Annals of Internal Medicine*, 2018. Disponível em: <https://www.acpjournals.org/doi/full/10.7326/M18-0850>. Acesso em: 2 set. 2026.

VIEIRA, Cristiano P. *et al.* Novel methods to mobilize, isolate, and expand mesenchymal stem cells. *International Journal of Molecular Sciences*, v. 22, n. 11, 2021. DOI: <https://doi.org/10.3390/ijms22115728>. Acesso em: 2 set. 2026.

XIE, Chenchen *et al.* Electroacupuncture modulates stromal cell-derived factor-1 α expression and mobilization of bone marrow endothelial progenitor cells in focal cerebral ischemia/reperfusion model rats. *Brain Research*, v. 1648, pt. A, p. 119–126, 2016. DOI: <https://doi.org/10.1016/j.brainres.2016.07.038>. Acesso em: 2 set. 2026.

XUAN, Shou-song *et al.* Electroacupuncture improves cardiac function after myocardial infarction by regulating the mobilization and migration of endogenous stem cells. *Acupuncture in Medicine: Journal of the British Medical Acupuncture Society*, v. 41, n. 6, p. 354–363, 2023. DOI: <https://doi.org/10.1177/09645284231169485>. Acesso em: 2 set. 2026.

ZHAO, Jiao *et al.* Electroacupuncture at ST36 increases bone marrow-derived interstitial cells of Cajal via the SDF-1/CXCR4 and mSCF/Kit-ETV1 pathways in the stomach of diabetic mice. *Evidence-Based Complementary and Alternative Medicine*, v. 2018, p. 7878053, 2018. DOI: <https://doi.org/10.1155/2018/7878053>. Acesso em: 2 set. 2026.

ZHAO, Tian-tian *et al.* SDF-1/CXCR4-mediated stem cell mobilization involved in cardioprotective effects of electroacupuncture on mouse with myocardial infarction. *Oxidative Medicine and Cellular Longevity*, v. 2022, p. 4455183, 2022. DOI: <https://doi.org/10.1155/2022/4455183>. Acesso em: 2 set. 2026.