

## Appendix 1. The search strategy.

Dataset	Search strategy	No.
PubMed	("Spinal Cord Injuries"[MeSH] OR SCI[TIAB] OR (("Spinal Cord"[MeSH] OR (Spine[tiab] OR Spinal*[tiab] OR "Spinal Injuries"[MeSH]) AND Cord*[tiab]) OR spinalcord*[TIAB] OR "Conus Medullari"[tiab] OR "Conus Terminali"[tiab]) AND ("Wounds and Injuries"[MeSH] OR Injuries[Subheading] OR Injur*[tiab] OR Trauma*[tiab] OR reinjury[TIAB] OR Transection*[tiab] OR Laceration*[tiab] OR Contusion*[tiab] OR damag*[tiab] OR hemisection*[tiab] OR compress*[tiab] OR wound*[tiab])) AND (Fishes[MeSH] OR Fish*[tiab] OR Teleosts OR Teleostei OR goldfish[MeSH] OR "Carassius auratus" OR "Carassius carassius" OR guppies OR "Poecilia reticulata" OR "Lebistes reticulatus" OR "Japanese rice minnows" OR "Oryzias latipes" OR zebrafish[MeSH] OR (Danio OR B. OR Brachydanio OR D. OR Fish*) AND (rerio* OR Zebra)) OR minnows OR "Phoxinus phoxinus" OR eels OR eel OR "Anguilla Anguilla" OR Gymnotiformes OR "ghost knifefish" OR "Apteronotus albifrons" OR "ghost knifefish" OR ((black OR brown) AND knifefish) OR "Apteronotus leptorhynchus" )	1044
Embase	('Spinal Cord Injuries'/exp OR SCI:ti,ab OR (('Spinal Cord'/exp OR (Spine:ti,ab OR Spinal*:ti,ab OR 'Spinal Injuries'/exp) AND Cord*:ti,ab) OR spinalcord*:ti,ab OR "Conus Medullari":ti,ab OR "Conus Terminali":ti,ab) AND ('Wounds and Injuries'/exp OR Injuries:ti,ab OR Injur*:ti,ab OR Trauma*:ti,ab OR reinjury:ti,ab OR Transection*:ti,ab OR Laceration*:ti,ab OR Contusion*:ti,ab OR damag*:ti,ab OR hemisection*:ti,ab OR compress*:ti,ab OR wound*:ti,ab))) AND ('Fishes'/exp OR Fish*:ti,ab OR Teleosts OR Teleostei OR 'goldfish'/exp OR "Carassius auratus" OR "Carassius carassius" OR guppies OR "Poecilia reticulata" OR "Lebistes reticulatus" OR "Japanese rice minnows" OR "Oryzias latipes" OR 'zebrafish'/exp OR (Danio OR B. OR Brachydanio OR D. OR Fish*) AND (rerio* OR Zebra)) OR minnows OR "Phoxinus phoxinus" OR eels OR eel OR "Anguilla Anguilla" OR Gymnotiformes OR "ghost knifefish" OR "Apteronotus albifrons" OR "ghost knifefish" OR ((black OR brown) AND knifefish) OR "Apteronotus leptorhynchus" )	1626
Web of science	(TS=("Spinal Cord Injuries" OR SCI OR (("Spinal Cord" OR (Spine OR Spinal* OR "Spinal Injuries") AND Cord*) OR spinalcord* OR "Conus Medullari" OR "Conus Terminali") AND ("Wounds and Injuries" OR Injuries OR Injur* OR Trauma* OR reinjury OR Transection* OR Laceration* OR Contusion* OR damag* OR hemisection* OR compress* OR wound*)))) AND (TS=(Fishes OR Fish* OR Teleosts OR Teleostei OR goldfish OR "Carassius auratus" OR "Carassius carassius" OR guppies OR "Poecilia reticulata" OR "Lebistes reticulatus" OR "Japanese rice minnows" OR "Oryzias latipes" OR zebrafish OR (Danio OR B. OR Brachydanio OR D. OR Fish*) AND (rerio* OR Zebra)) OR minnows OR "Phoxinus phoxinus" OR eels OR eel OR "Anguilla Anguilla" OR Gymnotiformes OR "ghost knifefish" OR "Apteronotus albifrons" OR "ghost knifefish" OR ((black OR brown) AND knifefish) OR "Apteronotus leptorhynchus" )	1444
Scopus	(TITLE-ABS("Spinal Cord Injuries" OR SCI OR (("Spinal Cord" OR (Spine OR Spinal* OR "Spinal Injuries") AND Cord*) OR spinalcord* OR "Conus Medullari" OR "Conus Terminali") AND ("Wounds and Injuries" OR Injuries OR Injur* OR Trauma* OR reinjury OR Transection* OR Laceration* OR Contusion* OR damag* OR hemisection* OR compress* OR wound*)))) AND (TITLE-ABS-KEY(Fishes OR Fish* OR Teleosts OR Teleostei OR goldfish OR "Carassius auratus" OR "Carassius carassius" OR guppies OR "Poecilia reticulata" OR "Lebistes reticulatus" OR "Japanese rice minnows" OR "Oryzias latipes" OR zebrafish OR (Danio OR B. OR Brachydanio OR D. OR Fish*) AND (rerio* OR Zebra)) OR minnows OR "Phoxinus phoxinus" OR eels OR eel OR "Anguilla Anguilla" OR Gymnotiformes OR "ghost knifefish" OR "Apteronotus albifrons" OR "ghost knifefish" OR ((black OR brown) AND knifefish) OR "Apteronotus leptorhynchus" )	1519

## Appendix 2. The predefined data collection sheet was used to extract the following information:

- Study design
- Geographical location of the study species of the fish model used
- Mechanism and level of the induced SCI
- Administration of any drug or supplements—if applicable
- Behavior assessment tests

- **Outcome assessment**

### Appendix 3. Study the characteristics and outcomes of the zebrafish.

Studies	SCI mechanism	The aim of the study	Laboratory test	Drugs administration
Anguita-Salinas et al., 2019 (1)	Electroablation with a tungsten microelectrode	To examine regeneration of the tissue over time after transecting the spinal cord of zebrafish larvae by transgenic lines to follow immune cells, oligodendrocytes, and neurons <i>in vivo</i> during the entire regenerative process.	IHC and optical microscopy	Regenerative cell transplantation
Baumgart et al., 2012 (2)	Transection with a needle	To examine the glia response to injury and the long-term survival of neurons settling at the former injury site in the brain parenchyma of the adult zebrafish.	IHC	N.a.
Becker et al., 1997 (3)	Transection with microscissors	To investigate axonal regrowth of neurons in zebrafish brain nuclei projecting to the spinal cord and investigate the contribution of newly grown axons to the reestablished projection after spinal cord transection and the possible re-establishment of ascending projections.	Optical microscopy	N.a.
Becker et al., 1998 (4)	Transection with microscissors	To detect a regenerative response in axotomized neurons by assessing changes in the expression of Gap-43 mRNA after axotomy.	Optical microscopy and ISH	N.a.
Becker et al., 2001 (5)	Transection with microscissors	To analyze the pathways taken by regenerating axons from brain neurons as well as the changes in the cellular environment caudal to a spinal lesion site.	Optical and electron microscopy, and IHC	N.a.
Becker et al., 2004 (6)	Transection with an incision	To show directly that expression of L1.1 is a necessary component of the regenerative response of brainstem neurons in adult zebrafish.	Visual inspection, IHC, and electron microscopy	N.a.
Becker et al., 2005 (7)	Transection with an incision	To analyze the expression of the growth-related molecules Gap-43 and L1.1 in long-projecting neurons with ascending and descending axons axotomized by a spinal lesion.	ISH and optical microscopy	N.a.
Bhatt et al., 2004 (8)	Transection with a glass pipette	To evaluate the response of the mauthner axon to a lesion and to the subsequent application of camp.	<i>In-vivo</i> calcium imaging and behavioral testing	N.a.
Bormann et al., 1999 (9)	Transection and crushing with forceps	To detect the expression of zFLRR as a neuronal-specific adhesion molecule or soluble ligand binding receptor, primarily during restoration of the nervous system after injury.	ISH and northern blot hybridization	N.a.
Bremer et al., 2019 (10)	Laser injury	To identify the ubiquitin ligase PHR protein and whether it promotes CNS axonal regrowth along the pre-lesional trajectory	IHC and optical microscopy	JNK inhibitor
Briona et al., 2014 (11)	Transection with a glass pipette	To characterize the identity of dbx1a:GFP-expressing cells and their progenitor in the embryonic and larval zebrafish and their response to spinal cord transection.	ISH, IHC, and optical microscopy	N.a.
Briona et al., 2015 (12)	Transection with a glass pipette	To delineate the roles of Hmgb1 in recovery following SCI.	IHC and confocal microscopy	N.a.
Burris et al., 2021 (13)	Transection	To describe a set of behavioral assays to quantify zebrafish motor capacity inside an enclosed swim tunnel.	Behavioral	N.a.
Cavone et al., 2021 (14)	Stab injury	To establish the principle that macrophages directly communicate with spinal progenitor cells via non-developmental signals after injury.	IHC, histology, ISH, western blotting, and PCR	gRNA
Chang et al., 2021 (15)	Transection with a microknife	To determine whether physical activity can induce spinal cord neurogenesis.	Fluorescence staining, microscopy imaging, and IHC	Saline, Nicotine, and Gabazine
Chapela et al., 2019 (16)	Transection with a needle	To evaluate whether riluzole and minocycline, two molecules that are in clinical trials for SCI, promote the rescue of the locomotor function of the transected larvae.	IHC, histology, and behavioral	N.a.
Chen et al., 2016 (17)	Transection with an incision	To investigate the functional role of L1.2, the zebrafish paralog of L1.1, and the ortholog of mammalian L1CAM in adult zebrafish spinal cord regeneration after injury.	RT-PCR, ISH, IHC, western blot analysis, visual inspection, and optical microscopy	L1.2 anti-sense morpholino
Cui et al., 2021 (18)	Longitudinal incision with microscissors	To determine the neuroprotective effect of NPY and NPY1R in zebrafish after SCI.	Immunostaining, ISH, and PCR	N.a.

Cunha et al., 2020 (19)	Demyelination with lyssolecithin	To analyze the underlying molecular mechanisms of the heterogenic intrinsic growth potential of axon regeneration in adult zebrafish by genome analysis.	PCR, IHC, microscopic imaging, and ISH	60 ng TNF- $\alpha$
Dehnisch Ellstrom et al., 2019 (20)	Laser injury	To evaluate the new method to induce SCI in zebrafish by laser light.	Visual inspection, optical microscopy, and fluorescence staining	N.a.
Dias et al., 2012 (21)	Transection with an incision	To show the role of Notch signaling in motor neuron regeneration in the adult zebrafish spinal cord.	PCR, IHC, optical microscopy, and visual inspection	N.a.
Drake et al., 2023 (22)	Transection with a needle	To describe a simple protocol to disrupt gene function in this model using acute injections of highly active synthetic gRNA to rapidly detect loss-of-function phenotypes without the need for breeding	PCR and fluorescence microscopy	CRISPER/Cas9 gRNA
El-Daher et al., 2021 (23)	Laser injury	To develop a protocol used with a semi-automated zebrafish larvae imaging system combined with a spinning disk equipped with a UV laser.	Fluorescence	N.a.
Fang et al., 2014 (24)	Transection	To delineate the roles of HMGB1 in recovery following SCI.	Rt-PCR, ISH, IHC, western blot analysis, visual inspection, and optical microscopy	HMGB1 anti-sense morpholino
Fu et al., 2019 (25)	N.a.	To analyze the underlying molecular mechanisms of the heterogenic intrinsic growth potential of axon regeneration in adult zebrafish by genome analysis.	Genome analysis	N.a.
Gahtan et al., 2001 (26)	Transection with a glass pipette	To propose a lesioning technique in which large numbers of neurons are lesioned but the lesioned neurons are specifically identified by fluorescent labeling and establish a causal relationship between the activity of specific individual nerve cells and the behaviors they produce.	Visual inspection and optical microscopy	N.a.
Goldshmit et al., 2012 (27)	Transection with microscissors	To investigate the importance of LPA modulation in neurotrauma and to provide proof of concept for the blockage of LPA signaling to treat SCI.	visual inspection, optical microscopy, IHC, RT-PCR, ISH, and ELISA	N.a.
Goldshmit et al., 2012 (28)	Transection with microscissors	To investigate whether glial activation and the consequent regeneration-permissive morphology are controlled by FGF signaling.	IHC, visual inspection, ISH, and optical microscopy	BrdU and FGF8
Goldshmit et al., 2018 (29)	Transection with microscissors	To compare the role of distinct FGFs during regeneration and development of ISL1 and C-met motor neurons, as well as across species.	ISH, IHC, and optical microscopy	Heat shock treatment, BrdU, and FGF3 injection
Guo et al., 2011 (30)	Transection	To find damage-induced genes after SCI and upregulation of the Sox11b mRNA.	Microarray analysis, RT-PCR, ISH, IHC, optical microscopy, and visual inspection	N.a.
Gwee et al., 2018 (31)	Laser injury	To observe the localization and distribution of AURKB within neurons and investigate its role in axonal development and regeneration.	IHC and microscopy imaging of AURKB expression	Embryonic genetic manipulation
Hecker et al., 2020 (32)	Electroablation with pulled glass	To use two-photon microscopy in parallel with behavioral assays in zebrafish to show that the mauthner axon can regenerate very rapidly and that the recovery of functionality lags by just days.	Behavioral	N.a.
Herzog et al., 2020 (33)	Transection with scissors	To identify signaling pathways that regulate secondary cell death after acute neural injury in larval zebrafish.	PCR and imaging	CRISPER
Hossainian et al., 2022 (34)	Electroablation with a tungsten microelectrode	To develop and validate new open-source software to measure zebrafish lateral trunk curvature during propulsive and turning movements at high temporal resolution.	Behavioral assessment and video	N.a.
Hosseini et al., 2022 (35)	Transection with a needle	To investigate whether the dopamine receptor expression pattern may be dissimilar in female and male zebrafish SC auto-repair.	H&E staining, immunofluorescent staining, RT-PCR, functional recovery, and swim test	No
Huang et al., 2017 (36)	Transection	To observe whether brain ha signaling could influence the repair of SCI in zebrafish.	Swim-tracking test	Histamine
Huang et al., 2021 (37)	Transection with a stab knife	To study the recovery of locomotor function when the supraspinal connections are dismissed.	Locomotor function, IHC, RT-PCR, EMG and functions imaging, RNA-sequencing, fluorescence-activated cell sorting, and LC-MS analysis	Highly selective 5-HT agonist

Huang et al., 2022 (38)	Transection with a microsurgical stab knife	To show that V2a interneurons regrow their axon to bridge the spinal segment lesion in a subclass-specific and chronological order.	IHC, PCR, sequencing, electrophysiology, and behavioral assessment	CRISPER
Hui et al., 2010 (39)	Transection	To observe the beneficial role of apoptotic cell death and injury-induced proliferation, the presence of radial glia cells, and their role as progenitors, which contribute to cellular replacement and successful neurogenesis after injury in adult zebrafish.	N.a.	N.a.
Hui et al., 2014 (40)	Transection	To report a comprehensive genome-wide expression analysis of the regenerating zebrafish spinal cord after a complete transection injury.	IHC	N.a.
Hui et al., 2015 (41)	Transection	To show the expression of several markers associated with dedifferentiation and reprogramming during CNS regeneration in zebrafish.	IHC, transmission electron microscopy, immunoblotting, and ELISA	BrdU solution
Hui et al., 2020 (42)	Transection with forceps	To report ultrastructural and cell biological analyses of regeneration processes after SCI.	PCR, IHC, and microscopy	N.a.
Jensen et al., 2023 (43)	Transection with scissors	To explore connections between functional and cellular regeneration measurements during spinal cord regeneration in adult zebrafish.	Swimming behavior	N.a.
Ji et al., 2021 (44)	Transection with microscissors	To explore the effects of ATF6 on neuroregeneration following SCI in zebrafish.	PCR, ISH, IHC, and locomotor activity	N.a.
John et al., 2022 (45)	Transection with a needle	Protocol for mechanical transection of zebrafish SCI.	ISH and IHC	N.a.
Keatinge et al., 2021 (46)	Transection with a needle	To find a very rapid screening method for the function of inflammation-related genes in zebrafish larvae after SCI.	PCR, sequencing, IHC, and behavioral analysis	CRISPER
Klatt Shaw et al., 2021 (47)	Transection with scissors	To identify seven single- or duplicate-gene crispants with reduced functional recovery after SCI.	Next-generation sequencing and IHC	CRISPER
Klatt Shaw et al., 2021 (48)	Surgery	To identify the mechanisms that regulate differential regenerative capacity between mammals and zebrafish.	Histology, PCR, locomotor, next-generation sequencing, and RNA sequencing	CRISPER
Kroehne et al., 2017 (49)	Transection	To describe how zebrafish spinal OPCs can be isolated and used in cell culture to test underlying pathways that could explain their resilience and remyelinating abilities.	IHC	N.a.
Kuscha et al., 2012 (50)	Transection	To determine the plastic changes of th1p and serotonergic terminals and cells during successful spinal cord regeneration in adult zebrafish.	Swim-tracking test	Cyclopamine and BrdU
Lee et al., 2022 (51)	Transection with tweezers	To determine the role of zebrafish ANP32a in the neuronal regeneration of SCI embryos.	Locomotor activity, western blot, and IHC	ANP32a mRNA
Li et al., 2018 (52)	Transection	To examine the restorative potential of phenelzine in a zebrafish model of SCI.	Swim-tracking test	Phenelzine
Lieberoth et al., 2003 (53)	Transection	To provide a relatively simple procedure for non-radioactive ISH in sections of adult zebrafish brains in combination with retrograde axonal tracing.	Combined tracing and ISH	N.a.
Lin et al., 2012 (54)	Transection	To test the functions of contactin-2 in spinal cord regeneration.	IHC	N.a.
Liu et al., 2014 (55)	Transection	To investigate the function of PTEN-a and b in adult zebrafish after SCI with the aim of assessing the contribution of the two zebrafish genes to functional recovery in an animal species that spontaneously recovers from central nervous system injury.	Swim-tracking test	Morpholino
Liu et al., 2016 (56)	Transection	To investigate the effects of MCAM on SCI and subsequent recovery in adult zebrafish.	Swim-tracking test	Morpholino
Ma et al., 2012 (57)	Transection	To identify CRP1 as a key component of functional spinal cord regeneration in adult zebrafish.	Microarray analysis with laser-capture micro-dissected NMLF	N.a.
Ma et al., 2014 (58)	Transection	To observe the novel function of legumain in the nervous system, and in particular, the regeneration of the adult zebrafish CNS.	A two-tailed student's t-test and a two-way and one-way ANOVA, followed by Tukey's post hoc test	N.a.

Ma et al., 2017 (59)	Transection	To evaluate Hnk-1's role in the recovery of function after SCI in adult zebrafish.	Two-way and one-way ANOVA, followed by Tukey's post hoc test	N.a.
Mokalled et al., 2016 (60)	N.a.	To observe a genome-wide profiling screen for secreted factors that are upregulated during zebrafish spinal cord regeneration.	N.a.	N.a.
Mollmert et al., 2020 (61)	N.a.	To determine the spatial distributions of apparent elastic moduli of living spinal cord tissue sections obtained from uninjured zebrafish and at distinct time points after complete spinal cord transection.	Hertz model for a spherical indenter	N.a.
Morris et al., 2021 (62)	Demyelination with lysolecithin	To create and characterize a focal lysolecithin injection model in zebrafish that allows us to investigate the temporal dynamics underlying lysolecithin-induced damage <i>in vivo</i> .	<i>In-vivo</i> imaging and IHC	Lysolecithin
Morsch et al., 2015 (63)	laser injury	To describe a live imaging approach that uses UV laser ablation to selectively stress and kill spinal neurons and visualize the clearance of neuronal remnants by microglia in the zebrafish spinal cord.	<i>In-vivo</i> live-imaging of spinal motor neurons and microglia	N.a.
Moya-Diaz et al., 2014 (64)	Electroablation with a tungsten microelectrode	To develop an electrical-based method for neurectomy and tissue ablation, which allowed us to precisely sever nerves and to ablate small areas of tissue in a simple and reproducible way in both larvae and adult fish.	Two-way ANOVA, followed by Bonferroni's post-hoc test	N.a.
Nelson et al., 2019 (65)	Transection	To report that glucocorticoids, used in the clinical management of SCI, directly inhibit neural repair by targeting ependymal glia independently of hematogenous cells and microglia.	Student's t-test	Dexamethasone
Ogai et al., 2012 (66)	Transection with microscissors	To investigate the cell survival of axotomized upper motor neurons and their molecular machinery in the zebrafish brain.	Swim-tracking test	BrdU solution
Ogai et al., 2014 (67)	Transection with microscissors	To investigate the expression and function of Sox2 after SCI in zebrafish.	RT-PCR and IHC	N.a.
Ohnmacht et al., 2016 (68)	Transection	To show that pharmacological suppression of the cellular response of the innate immune system inhibits motor neuron regeneration.	T-tests, Mann-Whitney U-tests, Bonferroni's test, and Kruskal-Wallis's test, followed by Dunn's test	5-Ethynyl-2'-deoxyuridine and Dexamethasone
Oprişoreanu et al., 2023 (69)	Transection with a needle	To find pharmacological modulators of the inflammation response, we designed a rapid drug screening paradigm in larval zebrafish, followed by testing of hit compounds in a mouse SCI model.	PCR, fluorescence, hybridization, and behavioral	N.a.
Pan et al., 2013 (70)	Transection	To examine whether major vault protein mRNA and protein expression levels would increase in ependymal cells in the spinal cord caudal to the lesion site	Swim-tracking test	Morpholino and a major vault protein
Paramos-de-Carvalho et al., 2021 (71)	Transection with forceps	To investigate whether the accumulation of satellite cells contributes to the failure of spinal cord regeneration observed in mammals.	Behavioral assessment, histology, and IHC	ABT-263, Dasatinib, and Quercetin
Peng et al., 2017 (72)	Transection with an incision	To study the role of sema4d in a zebrafish spinal cord transection model.	Swim-tracking test	Morpholino
Pietri et al., 2009 (73)	Transection with an incision	To demonstrate that the kinetics of spontaneous coiling and touch-evoked responses show distinct developmental time courses and that the touch response is dependent on AMPA-type glutamate receptor activation.	Two-tailed unpaired t-tests	N.a.
Reimer et al., 2008 (74)	Transection with an incision	To demonstrate that adult zebrafish, which show functional spinal cord regeneration, are capable of motor neuron regeneration.	Mann-Whitney U-test, ANOVA with Bonferroni's and Dunn's post-hoc tests	N.a.
Reimer et al., 2009 (75)	Transection with an incision	To show that genes involved in motor neuron development, i.e., the ventral morphogen Shh-a, as well as the transcription factors nkx6.1 and pax6, and Tg (olig2:EGFP) transgene.	Behavioral assays of functional recovery	N.a.
Ribeiro et al., 2017 (76)	Transection with an incision	To show that cells surrounding the ependymal canal in the adult zebrafish spinal cord express Foxj1a.	N.a.	N.a.
Ribeiro et al., 2022 (77)	Transection with scissors	To describe the zebrafish spinal cord vasculature.	PCR, IHC, and microscopy	N.a.

Sahu et al., 2018 (78)	Laser injury	To investigate the possibility that tacrine promotes regeneration in a larval zebrafish SCI model and then validate its action in an adult zebrafish SCI model.	Video tracking and western blot analysis	Tacrine
Sahu et al., 2019 (79)	Transection with an incision	To observe the effect of <i>c4st-1/chst-11</i> and <i>d4st-1/chst-14</i> down-regulation on spinal cord regeneration in larval and adult zebrafish.	N.a.	Morpholino and biocytin
Saraswathy et al., 2022 (80)	Transection with scissors	To uncover the dynamic expression of zebrafish Myostatin-b in a niche of dorsal SC progenitors after injury. Myostatin-b mutants show impaired functional recovery, normal glial and axonal bridging across the lesion, and an increase in the profiles of newborn neurons.	Histology, PCR, and swim behavior	N.a.
Sasagawa et al., 2016 (81)	Transection with an incision	To demonstrate that genes related to cell cycle were significantly enriched in the genes specifically dysregulated in zebrafish SCI.	ANOVA followed by Sidak's multiple comparison test and Welch's t-test	N.a.
Shao et al., 2023 (82)	Transection	To investigate whether knocking out <i>DUSP2</i> promotes the regeneration of zebrafish mauthner axons.	Behavioral, western blot analysis, and PCR	gRNA
Shen et al., 2022 (83)	Transection with scissors	To identify the key genes and pathways involved in zebrafish recovery after SCI.	PCR, protein-to-protein interaction, swimming pattern, and gene ontology	N.a.
Stone et al., 2022 (84)	Laser injury	To track neurons after dendrite injury.	Imaging	Dual-insert plasmids
Strand et al., 2016 (85)	Transection with an incision	To observe the role of Wnt/ $\beta$ -catenin signaling after SCI.	Free-swim analysis, locomotor analysis, image acquisition and processing, cell counting, and RT-PCR	N.a.
Tsarouchas et al., 2018 (86)	Transection with an incision	To show that inhibiting inflammation reduces and promotes axonal regeneration in spinal-lesioned zebrafish larvae.	Fluorescence-activated cell sorting, RT-PCR, and Mann-Whitney U-test	Dexamethasone and ac-YVAD-cmk
Tsata et al., 2020 (87)	Transection	To provide novel insight into OPC responses in a regenerative context.	Histology, IHC, ISH, and imaging	N.a.
Tsata et al., 2021 (88)	Transection with a needle	To show that an injury to the zebrafish spinal cord triggers recruitment of PDGFR+ myoseptal and perivascular cells in a PDGFR signaling-dependent manner.	ISH, IHC, histology, and PCR	CRISPER
Vajn et al., 2014 (89)	Transection with an incision	To determine the exact temporal relationship between swimming ability and regenerated cerebrospinal axon number in adult zebrafish with a complete spinal cord transection.	Kolmogorov-Smirnov, Shapiro-Wilk's tests, and Levene's test	N.a.
Vandestadt et al., 2021 (90)	Electroablation with a tungsten microelectrode	To show that RNA released from damaged and dying cells is necessary for the recruitment of PNS and repair during spinal cord regeneration.	IHC, imaging, and swimming behavior	Olomoucine and Ryuvudine for CDK blocking
Vasudevan et al., 2021 (91)	Transection with a steel pin	To show that multiple interneuron subtypes known to play a role in locomotor circuitry are regenerated in injured spinal cord segments during the period of functional recovery.	IHC, behavioral, and electrophysiological	N.a.
Wahlstrom-Helgren et al., 2019 (92)	Demyelination with $\alpha$ -bungarotoxin	To induce locomotor activity in spinalized transgenic zebrafish larvae that expressed channelrhodopsin-2 in all subtypes of spinal Vglut2a.	High-speed video acquisition and pharmacology	Blue light
Wang et al., 2017 (93)	Transection with an incision	To investigate the role of ATF3 in regeneration following SCI.	Swim tracking	Morpholino
Wehner et al., 2018 (94)	Transection with an incision	To assess the restoration of anatomical continuity of the spinal cord after complete transection and without inhibition of the Wnt/ $\beta$ -catenin pathway.	Fluorescence microscopy	DMSO-treated and IWR-1
Xing et al., 2021 (95)	Transection with a needle	To study the effect of aging on optic nerve regeneration.	Behavioral analysis of locomotor function, m <sup>6</sup> A RNA sequence analysis, RT-PCR, and imaging	N.a.
Yu et al., 2011 (96)	Transection with an incision	To assess the often-disparate functions of the extracellular matrix glycoprotein tenascin-c molecule under <i>in vivo</i> conditions in the zebrafish SCI model.	N.a.	N.a.

Yu et al., 2013 (97)	Transection with an incision	To observe, syntenin-1 expression is upregulated in the adult zebrafish spinal cord caudal to the lesion site after injury.	N.a.	Morpholino
Zeng et al., 2020 (98)	Transection with an incision	To develop a technological platform for transplanting cells into the lesion site of SCI-treated adult zebrafish.	ANOVA, followed by Dunn's multiple	N.a.
Zeng et al., 2021 (99)	Transection with a glass needle	To establish stress-responsive transgenic zebrafish embryos with SCI.	Histology, fluorescence, western blot analysis, and locomotor tests	mRNA
Zhao et al., 2022(100)	Transection	To investigate the role of lesion-site IGF-1 on spinal cord regeneration in zebrafish.	PCR and immunofluorescence	IGF-1 Morpholino
Zhou et al., 2023 (101)	Transection with scissors	To define mechanisms that direct the molecular and cellular responses of glial cells after SCI in adult zebrafish.	Histology, swimming behavior, and IHC	N.a.
Zhu et al., 2023 (102)	Transection with a microinjection pipette	To show that Rassf7a promotes spinal cord regeneration after injury.	ISH, histology, locomotor tests, and IHC	N.a.

ac-YVAD-cmk: acetyl-tyrosyl-valyl-alanyl-aspartyl-chloromethylketone; AMPA:  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; ANP32a: acidic nuclear phosphoprotein 32 family member A; ATF: activating transcription factor; AURKB: aurora kinase B; BrdU: bromodeoxyuridine; c4st-1/chst-11: chondroitin 4-o-sulfotransferase-1/carbohydrate sulfotransferase-11; CDK: cyclin-dependent kinases; c-met: mesenchymal-epithelial transition factor; CNS: central nervous system; CRISPER: clustered regularly interspaced short palindromic repeats; CRP1: cysteine-rich protein 1; d4st-1/chst-14: dermatan 4-*o*-sulfotransferase-1/carbohydrate sulfotransferase-14; DMSO: dimethyl sulfoxide; DUSP2: dual-specificity phosphatase 2; ELISA: enzyme-linked immunoassay; FGF: fibroblast growth factor; Foxj1a: forkhead box protein J1-A; Gap-43: growth-associated protein 43; gRNA: guide RNA; Hmgb1: high mobility group box 1 protein; Hnk-1: human natural killer-1; ICC: immunocytochemistry; IGF-1: insulin-like growth factor 1; IHC: immunohistochemistry; ISH: in situ hybridization; ISL1: ISL LIM homeobox 1; IWR-1: inhibitor of Wnt response; Jnk: Jun N-terminal kinase; L1cam: L1 cell adhesion molecule; LC-MS analysis: liquid chromatography with tandem mass spectrometry; LPA: lysophosphatidic acid; m<sup>6</sup>a: N<sup>6</sup>-methyladenosine; MCAM: methocinnamox; mTOR: mammalian target of rapamycin; N.a.: not accessible, nkx6.1: NK6 homeobox 1; NMDA: N-methyl-D-aspartate; NMLF: nucleus of the medial longitudinal; NPY: neuropeptide Y; OPCs: oligodendrocyte precursor cells; pax6: paired box 6; PDGFR: platelet-derived growth factor receptor; PHR: Pam/Highwire/RPM-1; PNS: peripheral nervous system; PTEN: phosphatase and tensin homolog; Rassf7: Ras association domain family member 7; RT-PCR: reverse transcription-polymerase chain reaction test; SCI: spinal cord injury; sema4d: semaphorin 4d; TNF- $\alpha$ : tumor necrosis factor alpha; UV: ultraviolet; Vglut2a: vesicular glutamate transporter 2a; zfLRR: zebrafish neuronal leucine-rich repeat.



#### Appendix 4. Study the characteristics and outcomes of the lamprey.

Studies	SCI mechanism	The aim of the study	Laboratory test	Drugs discovery
Cai et al., 2022 (103)	Transection with a blade	To identify the members of BRINP and ASTN of lampreys by bioinformatics.	PCR	N.a.
Fies et al., 2021 (104)	Transection with scissors	To examine how swimming performance is related to the degree of axon regeneration in lampreys recovering from spinal cord transection by quantifying the relationship between swimming performance and the percent axon regeneration of transected lampreys after 11 weeks of recovery.	Behavioral assessment	N.a.
Gonzalez-Llera et al., 2022 (105)	Longitudinal incision with scissors	To study the regeneration of CRH descending axons after a complete SCI at the level of the 5 <sup>th</sup> gill in larval sea lampreys.	Immunofluorescence and microscopic imaging	peptide-KLH and anti-SRH peptide antibodies
Hough et al., 2021 (106)	Transection with scissors	To include additional large, identified injured lamprey reticulospinal neurons and additional recovery times, as well as to test possible mechanisms for the differences in properties of uninjured and injured reticulospinal neurons.	Locomotor assessment, sensory and motor-evoked responses, and Grubb's test	N.a.
Hu et al., 2021 (107)	Transection with scissors	To explore the role of Akt in mediating the axon regeneration and suppression of retrograde neuronal death produced by ChABC treatment after SCI in the lamprey.	ISH, Western blot analysis, and IHC	ChABC
Jin et al., 2022 (108)	Transection with scissors	To gain insight into the role of local protein synthesis in selecting regenerative vs. degenerative responses to axotomy in the lamprey spinal cord.	RNA sequencing, IHC, PCR, Western blot analysis, and histologic	N.a.
Katz et al., 2020 (109)	Transection with scissors	To investigate the recovery of burrowing behavior after SCI in larval lampreys.	Locomotor tests	N.a.
Parker et al., 2022 (110)	Transection with scissors	To compare the properties of synapses made by regenerated axons with unlesioned axons using the lamprey, a model system for spinal injury research in which functional locomotor recovery after spinal cord lesions is associated with axonal regeneration across the lesion site.	Electrophysiological recording	N.a.
Romaus-Sanjurjo, 2018 (111)	Transection with an incision	To analyze the recovery of the spinal GABAergic system after SCI in lampreys.	GABA immunofluorescence	N.a.
Sobrido-Camean et al., 2020 (112)	Transection with scissors	To reveal the possible role for taurine in the modulation of axonal regeneration following a complete SCI using lampreys as an animal model.	High-performance liquid chromatography	N.a.
Sun et al., 2022 (113)	N.a.	To screen four genes encoding progranulins from the genomes and perform a phylogenetic tree.	PCR, IHC, microscopy, western blotting, and RNA extraction	N.a.
Zhang et al., 2020 (114)	Transection	To identify the neurons giving rise to axon regeneration as early as two weeks post-transection, combine the higher clarity of benzyl alcohol or benzyl benzoate with anterograde and retrograde tracing.	IHC, histology, and immunostaining	N.a.
Zhang et al., 2022 (115)	Transection with scissors	To investigate the expression patterns of these lamprey lecticans during development and after SCI.	PCR and ISH	N.a.

BRINPs and ASTNs: bone morphogenic protein and retinoic acid-inducible neural-specific proteins and astrotactins; ChABC: chondroitinase ABC; CRH: corticotropin-releasing hormone; GABA: gamma-aminobutyric acid; IHC: immunohistochemistry; ISH: in situ hybridization; KLH: keyhole limpet hemocyanin; N.a.: not accessible; PCR: polymerase chain reaction test; SCI: spinal cord injury.

### Appendix 5. Study the characteristics and outcomes of the goldfish.

Studies	SCI mechanism	The aim of the study	Laboratory test	Drugs discovery
Bentley et al., 1993 (116)	Crushing with forceps	To determine whether novel pathway choices were made by regenerating CNS neurons in adult goldfish.	Optical microscopy	N.a.
Koganti et al., 2020 (117)	Surgery	To evaluate the invasion of reactive cells that occurs after damage to the mauthner axon by spinal cord crush.	Histology, PCR, and IHC	N.a.
Nona et al., 1995 (118)	Transection with an incision	To observe the glial repair in the regenerated goldfish spinal cord.	Swim-tracking test	N.a.
Takeda et al., 2007 (119)	Transection with an incision	To examine whether regenerated axons re-innervate the appropriate targets.	N.a.	Rhodamine dextran
Takeda et al., 2008 (120)	Transection with an incision	To examine whether neurogenesis is involved in posttraumatic regeneration in the goldfish spinal cord.	N.a.	BrdU solution
Takeda et al., 2017 (121)	Transection with an incision	To examine the chondroitin sulfate immunoreactivity to determine whether chondroitin sulfates are expressed at the lesion site.	N.a.	N.a.
Takeda et al., 2018 (122)	Transection with an incision	To examine cs expression in perineuronal nets in the ventral horn of a goldfish-hemisected spinal cord in which descending axons regenerate beyond the lesion to connect with distal spinal neurons.	Mann-Whitney U-test	N.a.
Takeda et al., 2021 (123)	Transection with scissors	To investigate the expression of matrix metalloproteinases that might play a role in the degradation of the extracellular matrix in fibrous scar tissue and in the remodeling of tubular structures.	Fluorescence and histology	N.a.
Takeda et al., 2023 (124)	Transection with scissors	To investigate whether multiple serotonin receptors are involved in remodeling the injured site during the regenerative process following spinal cord transection.	Immunostaining	N.a.
Zottoli et al., 2003 (125)	Transection with an incision	To provide a quantitative analysis of the recovery of c-starts that occur in adult goldfish after SCI.	N.a.	N.a.
Zottoli et al., 2021 (126)	Transection with forceps	To investigate whether the aberrant pathway choice of the Mauthner neuron may limit its role in the recovery of behavior.	Behavior and electromyography	N.a.

BrdU: bromodeoxyuridine; CNS: central nervous system; IHC: immunohistochemistry; N.a.: not accessible; PCR: polymerase chain reaction; SCI: spinal cord injury.

## Appendix 6. Study the characteristics and outcomes of the European eel.

Studies	SCI mechanism	The aim of the study	Laboratory test	Drugs discovery
Dalton et al., 2009 (127)	Transection with microscissors	To focus on the expression of BDNF and its high-affinity receptor, TrkB, following eel spinal cord transection in neuronal regeneration.	RT-PCR, one-way ANOVA, ISH, and optical microscopy	N.a.
De Heus et al., 1996 (128)	Transection with microscissors	To examine whether associated changes could be detected in G6PD and NADH-TR.	Enzyme histochemistry	N.a.
Dervan et al., 2003 (129)	Transection with microscissors	To determine whether in the eel, as in the mammal, proliferating ependyma contributes to glial scar formation, central canal cells can provide a source of new neural components for regenerating structures.	IHC	N.a.
Dervan et al., 2003 (130)	Transection with microscissors	To describe the organization of the meningeal sheath of the uninjured spinal cord of the eel before assessing its structure and significance during regeneration.	Electron microscopy	N.a.
Doyle et al., 2001 (131)	Transection with microscissors	To establish the relative importance of functional recovery of neural regeneration across the site of a complete spinal cord lesion, as opposed to any role for caudal plasticity.	Visual inspection and histology	N.a.
Doyle et al., 2004 (132)	Transection with microscissors	To establish that levodopa injections can be used to elevate locomotory activity and explore the possibility that eel's recovery from spinal cord transection can be influenced by levodopa-induced activity.	Visual inspection and electron microscopy	Levodopa
Doyle et al., 2004 (133)	Transection with microscissors	To assess whether APV, an antagonist of the NMDA receptor, may contribute to functional recovery.	Visual inspection, electrophysiological investigation, and optical microscopy	APV
Doyle et al., 2006 (134)	Transection with microscissors	To examine whether the axonal regeneration of spontaneously regenerating systems can be modified by exercise.	Visual inspection and optical microscopy	Exercise
Flight et al., 1993 (135)	Transection	To test whether completely separated eel heads can be considered dead.	Visual inspection	N.a.

APV: d-2-amino-5-phosphonovaleric acid; BDNF: brain-derived neurotrophic factor; G6PD: glucose-6-phosphate dehydrogenase; IHC: immunohistochemistry; ISH: in situ hybridization; N.a.: not accessible; NADH-TR: nicotinamide adenine dinucleotide dehydrogenase-tetrazolium reductase; NMDA: N-methyl-D-aspartate; RT-PCR: reverse transcription-polymerase chain reaction; SCI: spinal cord injury; TrkB: tropomyosin receptor kinase B.

**Appendix 7. Study the characteristics and outcomes of other teleost types of fish.**

Studies	Fish species	SCI mechanism	The aim of the study	Laboratory test	Drugs discovery
Anderson et al., 1993 (136)	Black ghost knifefish	Tail amputation	To study regeneration of CNS neurons, including nerve fiber regrowth and neurogenesis from adult vertebrate spinal cord tissue.	Electron microscopy	N.a.
Cornbrooks et al., 1991 (137)	Sailfin molly	Transection with a probe	To determine which, if any, of these sources contribute to the sexually dimorphic galanin-like immunoreactive fiber system found in the male of this teleost fish.	IHC	N.a.
Lou et al., 2023 (138)	African turquoise killifish	Transection with an incision	To provide a convenient and reproducible spinal cord transection protocol for adult and larval killifish.	Immunofluorescence	N.a.
Sirbulescu et al., 2009 (139)	Brown ghost knifefish	Tail amputation	To examine the spatiotemporal dynamics of apoptosis and its relationship to the generation and differentiation of new cells during this cell replacement phase.	Active-caspase-3, BrdU, and Hu triple labeling	BrdU solution
Sirbulescu et al., 2009 (140)	Brown ghost knifefish	Transection with an incision	To analyze the major processes underlying structural and functional regeneration after amputation of the caudal portion of the spinal cord in a weakly electric teleost.	N.a.	N.a.
Sirbulescu et al., 2010 (141)	Brown ghost knifefish	Transection with an incision	To examine the effect of temperature on both structural and functional regeneration after SCI.	N.a.	N.a.
Sirbulescu et al., 2022 (142)	Brown ghost knifefish	Transection with scissors	To clarify the molecular mechanisms underlying high regenerative capacity in teleost fish.	IHC and microscopy	N.a.
Vanhunsel et al., 2022 (143)	African turquoise killifish	Contusion with forceps	To study the effect of aging on optic nerve regeneration and neurorepair.	RNA isolation, RT-PCR, IHC, anterograde tracing of re-innervation, and dorsal light reflex	N.a.
Vitalo et al., 2016 (144)	Brown ghost knifefish	Tail amputation	To investigate the absence of glial scar formation and the role of radial glia in spinal cord regeneration.	Split-plot ANOVA	N.a.

BrdU: bromodeoxyuridine; CNS: central nervous system; IHC: immunohistochemistry; N.a.: not accessible; RT-PCR: reverse transcription-polymerase chain reaction; SCI: spinal cord injury.

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