Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada
Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

APLIKASI KOMBINASI SEL PUNCA ALOGENIK ASAL TALI PUSAT DAN SERAT PERANCAH DENGAN DIAMETER NANO PADA MODEL CEDERA MEDULA SPINALIS

Ringkasan Disertasi

Untuk memenuhi sebagian persyaratan mencapai derajat S-3

Diajukan oleh

Yudha Mathan Sakti

NIM: 21/485732/SKU/897

Kepada

Program Doktor Ilmu Kedokteran & Kesehatan

Fakultas Kedokteran, Kesehatan Masyarakat dan Keperawatan

UNIVERSITAS GADJAH MADA

YOGYAKARTA

2024

UNIVERSITAS
GADJAH MADA
**Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada
Model Cedera Medula Spinalis**
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

ABSTRAK

Latar Belakang :

Cedera medula spinalis/*spinal cord injury* (SCI) menyebabkan gangguan fungsi motorik, sensoris, dan otonom. Pemulihan kondisi neurologis pasien pasca cedera masih menjadi sebuah tantangan. Salah satu hambatan terbesar proses penyembuhan medula spinalis adalah neuro-inflamasi serta *debris clearance* yang tidak efektif. Selain intervensi terapetik yang ada, dibutuhkan terobosan intervensi regeneratif yang dapat menggantikan jaringan saraf yang cedera.

Metode Penelitian :

Penelitian ini bertujuan mengetahui pengaruh aplikasi kombinasi sel punca mesenkimal alogenik asal tali pusat dan perancah komposit PVA/Kitosan pada cedera medula spinalis. Pada prosesnya terdapat 3 tahap; uji mekanis berupa uji gugus kimia FTIR, uji kekuatan perancah, uji observasi SEM; uji biologis berupa uji biodegradabilitas perancah, uji viabilitas seluler, dan uji proliferasi seluler; dan uji hewan yang melibatkan anjing (*Canis Lupus Familiaris*) sebagai model cedera tulang belakang. Pengujian dibagi menjadi 3 kelompok yaitu kontrol tanpa perlakuan, perlakuan satu dengan instrumentasi implant dan perlakuan dua kombinasi instrumentasi, perancah PVA/Kitosan dan sel punca. Evaluasi regenerasi medula spinalis dilakukan dengan pengamatan klinis dan uji histopatologis.

Hasil Penelitian :

Hasil penelitian ini menunjukkan perancah PVA/Kitosan memiliki aspek mekanis dan biologis yang baik. Pada uji mekanis proses *elektrospinning* menghasilkan serat perancah dengan gugus kimia PVA (1150 dan 1650 cm^{-1}) dan Kitosan (1152 cm^{-1}) pada pemeriksaan FTIR, ukuran serat nano struktur sesuai SEM dengan rentang 460.25 ± 26.84 nm dan kekuatan mekanis sesuai uji UTM dalam rentang 120- 190 N. Pada uji biologis didapatkan perancah nanostruktur memiliki kemampuan biodegradabilitas 60,48% yang didukung oleh hasil viabilitas seluler

UNIVERSITAS
GADJAH MADA
**Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada
Model Cedera Medula Spinalis**
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Histopathological examination revealed decreased hemorrhage, inflammation, and astrogliosis indicated by GFAP, increased myelination by LFB, and higher number of neuron cells by NeuN.

Keywords : scaffold, stem cell, PVA/Chitosan

UNIVERSITAS
GADJAH MADA
**Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada
Model Cedera Medula Spinalis**
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

RINGKASAN

Pendahuluan

Cedera medula spinalis/*spinal cord injury* (SCI) adalah gangguan neurologis pada sistem motorik, sensoris, dan otonom di level di bawah dari tempat cedera. Secara epidemiologis terjadi sekitar 0.98 juta kasus baru cedera medula spinalis sedunia, dengan prevalensi total 27.04 juta kasus. Kurang dari 1% pasien yang mengalami cedera medula spinalis akan pulih secara sempurna pasca perawatan di rumah sakit.

Epidemiologi menunjukkan tren semakin meningkat pada usia produktif, menekankan kepentingan untuk mengembangkan program terapi dan rehabilitasi yang efektif untuk mengurangi beban nasional secara sosial dan finansial.

Selama beberapa dekade terakhir, pemulihan kondisi neurologis pasien setelah cedera tulang belakang masih menjadi sebuah tantangan. Salah satu hambatan terbesar dalam proses penyembuhan sistem saraf pusat pasca cedera medula spinalis adalah proses neuro-inflamasi serta *debris clearance* yang tidak efektif. Sistem imun tubuh akan berusaha membatasi proses inflamasi untuk melindungi jaringan sehat melalui proses *microglial bordering* pada sekitar lesi cedera, dan *glial scarring* pada lesi cedera tersebut. Namun, hal tersebut mengakibatkan penurunan kapabilitas regenerasi sistem saraf pusat akibat keberadaan *inhibitory growth factor* dan *glial scar*.

Proses regenerasi juga terganggu akibat keberadaan ruang kistik pasca cedera yang menghambat potensi untuk proses migrasi sel. Hal tersebut menekankan pentingnya aspek matriks ekstraseluler dalam mendukung proses penyembuhan pasca cedera medula spinalis. Sebagai pengganti jaringan ekstrseluler yang rusak, keberadaan konsep perancah hadir untuk menjadi jembatan regenerasi sel dalam membentuk jaringan.

Selain jaringan perancah, sel punca atau sel progenitor merupakan platform biologis dengan potensi untuk mendukung perbaikan medula spinalis. Aplikasi dari kombinasi antara sel punca alogenik asal tali pusat dan perancah medula spinalis

UNIVERSITAS
GADJAH MADA
**Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada
Model Cedera Medula Spinalis**
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

serat ukuran nano dapat membantu proses penyembuhan dengan memberikan dukungan mekanis dan biologis pada proses regenerasi medula spinalis pasca cedera.

Penelitian ini memiliki tujuan utama untuk Mengetahui pengaruh aplikasi kombinasi sel punca alogenik asal tali pusat (*umbilical cord-derived mesenchymal stem cells*, UC-MSCs) dan perancah komposit Polivinil Alkohol/Kitosan (PVA/CS) pada cedera medula spinalis di model hewan coba anjing.

Metode Penelitian

Penelitian secara umum dibagi menjadi 3 tahapan:

1. **Tahap 1** – **Karakterisasi mekanis**,
   a. Identifikasi gugus kimia relevan
   b. Pengujian kekuatan mekanis
   c. Analisis morfologi permukaan
2. **Tahap 2 – Properti Biologis**
   a. Uji biodegradabilitas
   b. Uji viabilitas seluler
   c. Uji proliferasi seluler.
3. **Tahap 3 – Uji Hewan**
   a. Evaluasi toksisitas
   b. Perbaikan motoris dan sensoris
   c. Pemeriksaan histopatologis

Variabel penelitian adalah sebagai berikut

1. Variabel independen:
   a. Instrumentasi implan
   b. Intervensi perancah PVA/ kitosan dengan sel punca alogenik asal tali pusat
2. Variabel dependen:

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

a. Derajat toksisitas dengan nilai laboratorium (angka Hb, Hct, Leukosit, Trombosit, SGOT, ALP, BUN, Kreatinin, Ureum)
b. Fungsi klinis motoris dengan menggunakan skoring cBBB dan fungsi klinis sensori dengan menilai reaksi rangsang panas dan dingin
c. Derajat perdarahan dan inflamasi jaringan medula spinalis dari evaluasi patologi anatomi dengan pewarnaan hematoxylin dan eosin
d. Derajat regenerasi jaringan medula spinalis dari evaluasi patologi anatomi dengan pewarnaan *luxol fast blue*, GFAP, dan NeuN

3. Variabel Kontrol:
   a. Volume perancah PVA/CS dari proses *elektrospinning*
   b. Volume sel puncal mesenkimal alogenik asal tali pusat
   c. Induksi kompresi medula spinalis dengan balon kateter forgati

Pada studi hewan, cedera medula spinalis diinduksi menggunakan metode kompresi balon dengan kateter Forgatti pada anjing (*Canis lupus familiaris*) yang kemudian dibagi menjadi 3 grup dengan 4 anjing per grup, yaitu grup kontrol/model cedera (CD), instrumentasi saja (IM), dan kombinasi instrumentasi dengan sel punca-perancah (SC). Observasi dilakukan selama 56 hari, kemudian euthanasia diberikan dan jaringan medula spinalis diambil untuk evaluasi histopatologis.

Skala numerik dianalissi menggunakan *one-way* ANOVA dan Bonferroni *post-hoc test*. Sementara itu, variabel ordinal dianalisis menggunakan Kruskal-Wallis dan Mann Whitney U *post hoc*. Distribusi normalitas dinilai dengan tes Saphiro-Wilk. Analisis statistic dilakukan dengan IBS SPSS Statistics 25.0 2017.

Hasil Penelitian

1. Tahap 1 – Karakterisasi mekanis

a. Identifikasi gugus kimia relevan

   Gugus utama CS (1152 cm^{-1}) dan PVA (1650 cm^{-1} dan 1150 cm^{-1}) dapat teridentifikasi pada perancah.

b. Pengujian kekuatan mekanis

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Kekuatan mekanis perancah 6 mL adalah 159 N dengan kekuatan tarik 41,3 kPa, sementara perancah 8 mL memiliki kekuatan mekanis 191 N dan kekuatan tarik 49,6 kPa

c. Analisis morfologi permukaan

Perancah 6 mL memiliki ketebalan 171.00 ± 4.72 µm, diameter serat 424.67 ± 42.94 nm, dan porositas 21.01 ± 1.58. Sementara itu, volume 8 mL memiliki ketebalan 228.67 ± 6.01 µm, diameter serat 414.33 ± 19.09 nm, dan porositas 21.23 ± 433. Meskipun perancah 8 mL memiliki porositas tinggi, terdapat banyak sumbatan saat produksi sehingga homogenitas seratnya kurang baik.

2. Tahap 2 : Properti biologis

a. Uji Biodegradabilitas

Degradasi paruh waktu (>50%) PVA/CS setelah perendaman dengan UC-MSCs ditemukan pada hari 14 (hari 1=23,01%; hari 3=35,04%; hari 7=42,41%; hari 14=51,81%; hari 21=60,48%).

b. Uji Viabilitas

Perancah PVA/Kitosan aman bagi sel dengan rata-rata viabilitas sel mencapai 59,00 % - 91,48%

c. Uji Proliferasi

Hasil uji proliferasi menunjukkan perancah tipis (6mL) memiliki kemampuan untuk memfasilitasi proliferasi sel yang lebih baik jika dibandingkan dengan perancah tebal (8 mL).

3. Tahap 3 : Uji Hewan

a. Evaluasi toksisitas

Berkurangnya berat badan dan leukositosis ditemukan di semua subjek pasca intervensi. Namun, tidak ada parameter yang berubah secara signifikan dibandingkan dengan pre-intervensi yang mengkonfirmasi bahwa terapi PVA/CS+UC-MSCs bersifat non-toksik.

b. Perbaikan Motoris dan Sensoris

UNIVERSITAS
GADJAH MADA
**Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada
Model Cedera Medula Spinalis**
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Meskipun semua grup menunjukkan perbaikan cBBB, tren perbaikan motoris lebih tinggi secara signifikan pada grup SC dibandingkan grup CD ($p = .012$) dan IM ($p = .037$). Tidak ada perbedaan signifikan dari fungsi sensoris ($p > 0.05$).

c. Pemeriksaan histopatologis

Terdapat perdarahan intralesi yang lebih sedikit secara signifikan pada grup SC dibandingkan grup CD ($p = 0.019$) dan IM ($p = 0.045$) dari pewarnaan HE. Sementara itu, LFB menunjukkan demyelinisasi intralesi yang lebih sedikit pada grup SC dibandingkan grup CD ($p_{anterior}=0.016$; $p_{lateral\text{-}1} = 0.012$; $p_{lateral\text{-}2} = 0.007$) dan IM ($p_{anterior}=0.020$; $p_{lateral\text{-}1} = 0.048$; $p_{lateral\text{-}2} = 0.027$). Pewarnaan GFAP dan NeuN tidak bisa dianalisis secara statistik karena kerusakan pada grup CD.

Analisis

Perbaikan fungsional dari medula spinalis membutuhkan terapi komprehensif untuk menargetkan keempat pilar dari *Diamond Concept*. Terapi sel punca dapat memberikan *cellular platform* dengan sitokin neuroinduktif apabila diberikan bersama dengan terapi operatif rutin yang mempertahankan integritas struktural medula spinalis. Terapi sel saja tidak cukup untuk mempertahankan lingkungan kondusif untuk sel bekerja, sehingga terapi kombinasi sel punca dengan perancah dapat menjembatani keempat aspek dari *Diamond Concept* untuk menghasilkan neuroregenerasi pada area target.

Berbagai macam jenis material telah diteliti untuk menciptakan perancah pada medula spinalis. Bahan perancah yang ideal sebaiknya terdiri dari material yang kuat dengan biokompatibilitas yang baik dengan jaringan sekitar. Hal ini dicapai dari penggunaan polimer PVA dengan bahan biologis Kitosan. Karakterisasi perancah dilakukan untuk memastikan perancah memiliki diameter nano untuk meningkatkan ratio luas permukaan-volume serta memberikan porositas yang cukup untuk difusi biomolekuler sekaligus menghambat infiltrasi sel inflamasi. Selain itu, gabungan PVA/CS juga memiliki property unik berupa

UNIVERSITAS
GADJAH MADA
**Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada
Model Cedera Medula Spinalis**
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

peningkatan kekuatan tarik dan stabilitas structural pada lingkungan cair, sehingga sesuai untuk implantasi intrakanal.

Perbaikan dari cedera medula spinalis yang berat masih susah dicapai dan beban penyakit masih tinggi, diindikasikan dari YLD (*Years Lived with Disability*) yang tidak berubah dari 1990 hingga 2019. Model binatang pada studi ini diberikan paralisis motor total untuk menggambarkan efek terapeutik terapi kombinasi pada pasien dengan cedera berat. Regenerasi saraf yang dicapai ditunjukkan dari perbaikan motoris dan pemeriksaan histopatologis setelah observasi selama 56 hari, di mana fase ini sudah melewati fase akut dan subakut dari patofisiologi cedera medula spinalis. Studi sebelumnya telah melaporkan hasil yang sama menggunakan bahan perancah yang berbeda. Namun, hasil pada penelitian ini juga menekankan pentingnya kombinasi terapi perancah-sel punca dengan terapi mekanis yang merupakan terapi rutin dari cedera medula spinalis.

Sel punca mesenkimal mempromosikan perbaikan saraf dengan efek immunomodulasi yang mengurangi mikroglia pro-inflamatori (M1) dan mengaktivasi fenotipe anti-inflamasi (M2) melalui sekresi IL-4 dan IL-13, sekaligus mengurangi TNF-α dan IL-6. Respon inflamasi pasca cedera medula spinalis ini yang berperan dalam memburuknya kerusakan setelah trauma awal. Pada studi ni, mekanisme terapi sel punca pada cedera adalah menciptakan lingkungan kondusif untuk pertumbuhan akson dan perbaikan fungsional, seperti yang ditunjukkan dari demyelinasi yang lebih sedikit pada hasil uji. Sementara itu, mekanisme kerja perancah adalah mengurangi pembentukan vakuola, jaringan, dan kavitasi untuk meningkatkan densitas sel saraf pada area cidera. Hal ini dicapai dengan menghambat pembentukan glia yang berujung pada jaringan parut. Meskipun awalnya pembentukan jaringan perut glia bersifat protektif pada fase akut cedera, jaringan ini menjadi penhambat utama dari neuroregenerasi di cedera medula spinalis.

Kesimpulan

UNIVERSITAS
GADJAH MADA
**Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada
Model Cedera Medula Spinalis**
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Neuroregenerasi pada cedera medula spinalis dapat tercapai bila semua aspek *Diamond Concept* terpenuhi. Perancah PVA/CS dapat menjadi sistem *homing* untuk terapi seluler di cedera medula spinalis dengan properti mekanis dan biologis yang baik. Aplikasi terapi perancah PVA/CS+UC-MSCs terbukti menghasilkan perbaikan klinis dan histopatologis pada model cedera medula spinalis anjing yang mendukung penggunaannya di masa depan untuk uji klinis di manusia.

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

DAFTAR PUSTAKA

Agarwal, S., Wendorff, J. H., & Greiner, A. (2008). Use of elektrospinning technique for biomedical applications. *Polymer*, *49*(26), 5603–5621. https://doi.org/10.1016/j.polymer.2008.09.014

Agbay, A., Edgar, J. M., Robinson, M., Styan, T., Wilson, K., Schroll, J., Ko, J., Khadem Mohtaram, N., Jun, M. B.-G., & Willerth, S. M. (2016). Biomaterial Strategies for Delivering Stem Cells as a Treatment for Spinal Cord Injury. *Cells Tissues Organs*, *202*(1–2), 42–51. https://doi.org/10.1159/000446474

Ahuja, C. S., Wilson, J. R., Nori, S., Kotter, M. R. N., Druschel, C., Curt, A., & Fehlings, M. G. (2017). Traumatic spinal cord injury. *Nature Reviews Disease Primers*, *3*(1), 17018. https://doi.org/10.1038/nrdp.2017.18

Alexander, J. K., & Popovich, P. G. (2009a). *Neuroinflammation in spinal cord injury: therapeutic targets for neuroprotection and regeneration* (pp. 125–137). https://doi.org/10.1016/S0079-6123(09)17508-8

Alexander, J. K., & Popovich, P. G. (2009b). *Neuroinflammation in spinal cord injury: therapeutic targets for neuroprotection and regeneration* (pp. 125–137). https://doi.org/10.1016/S0079-6123(09)17508-8

Alexander, J. K., & Popovich, P. G. (2009c). *Neuroinflammation in spinal cord injury: therapeutic targets for neuroprotection and regeneration* (pp. 125–137). https://doi.org/10.1016/S0079-6123(09)17508-8

Alisauskaite, N., Spitzbarth, I., Baumgärtner, W., Dziallas, P., Kramer, S., Dening, R., Stein, V. M., & Tipold, A. (2017). Chronic post-traumatic intramedullary lesions in dogs, a translational model. *PloS One*, *12*(11), e0187746. https://doi.org/10.1371/journal.pone.0187746

Alizadeh, A., Dyck, S. M., & Karimi-Abdolrezaee, S. (2019). Traumatic Spinal Cord Injury: An Overview of Pathophysiology, Models and Acute Injury Mechanisms. *Frontiers in Neurology*, *10*. https://doi.org/10.3389/fneur.2019.00282

Anderson, M. A., Burda, J. E., Ren, Y., Ao, Y., O'Shea, T. M., Kawaguchi, R., Coppola, G., Khakh, B. S., Deming, T. J., & Sofroniew, M. V. (2016). Astrocyte scar

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

formation aids central nervous system axon regeneration. *Nature*, *532*(7598), 195–200. https://doi.org/10.1038/nature17623

Andrzejowski, P., & Giannoudis, P. V. (2019). The 'diamond concept' for long bone non-union management. *Journal of Orthopaedics and Traumatology*, *20*(1), 21. https://doi.org/10.1186/s10195-019-0528-0

Ariestania, V., Hendrijantini, N., Prahasanti, C., Prasetyo, E., Kuntjoro, M., Sari, R. P., & Maharani, A. D. (2022). Cytotoxicity of HA-TCP Scaffold on Human Umbilical Cord Mesenchymal Stem Cells using MTT Assay. *The International Journal of Integrated Engineering*, *14*(2). https://doi.org/10.30880/ijie.2022.14.012

Ashammakhi, N., Kim, H.-J., Ehsanipour, A., Bierman, R. D., Kaarela, O., Xue, C., Khademhosseini, A., & Seidlits, S. K. (2019). Regenerative Therapies for Spinal Cord Injury. *Tissue Engineering Part B: Reviews*, *25*(6), 471–491. https://doi.org/10.1089/ten.teb.2019.0182

Badhiwala, J. H., Wilson, J. R., Witiw, C. D., Harrop, J. S., Vaccaro, A. R., Aarabi, B., Grossman, R. G., Geisler, F. H., & Fehlings, M. G. (2021). The influence of timing of surgical decompression for acute spinal cord injury: a pooled analysis of individual patient data. *The Lancet. Neurology*, *20*(2), 117–126. https://doi.org/10.1016/S1474-4422(20)30406-3

Bansal, H., Verma, P., Agrawal, A., Leon, J., Sundell, I. B., & Koka, P. S. (2016). Autologous Bone Marrow-Derived Stem Cells in Spinal Cord Injury. *Journal of Stem Cells*, *11*(1), 51–61.

Berger, J., Reist, M., Mayer, J. M., Felt, O., Peppas, N. A., & Gurny, R. (2004). Structure and interactions in covalently and ionically crosslinked chitosan hydrogels for biomedical applications. *European Journal of Pharmaceutics and Biopharmaceutics*, *57*(1), 19–34. https://doi.org/10.1016/S0939-6411(03)00161-9

Blando, S., Anchesi, I., Mazzon, E., & Gugliandolo, A. (2022). Can a Scaffold Enriched with Mesenchymal Stem Cells Be a Good Treatment for Spinal Cord Injury? *International Journal of Molecular Sciences*, *23*(14). https://doi.org/10.3390/ijms23147545

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Bowers, C., Kundu, B., & Hawryluk, GregoryW. J. (2016). Methylprednisolone for acute spinal cord injury: An increasingly philosophical debate. *Neural Regeneration Research*, *11*(6). https://doi.org/10.4103/1673-5374.184450

Bradbury, E. J., Moon, L. D. F., Popat, R. J., King, V. R., Bennett, G. S., Patel, P. N., Fawcett, J. W., & McMahon, S. B. (2002). Chondroitinase ABC promotes functional recovery after spinal cord injury. *Nature*, *416*(6881), 636–640. https://doi.org/10.1038/416636a

Bradke, F., Fawcett, J. W., & Spira, M. E. (2012). Assembly of a new growth cone after axotomy: the precursor to axon regeneration. *Nature Reviews Neuroscience*, *13*(3), 183–193. https://doi.org/10.1038/nrn3176

Cengiz, S. L., Kalkan, E., Bayir, A., Ilik, K., & Basefer, A. (2008). Timing of thoracolomber spine stabilization in trauma patients; impact on neurological outcome and clinical course. A real prospective (rct) randomized controlled study. *Archives of Orthopaedic and Trauma Surgery*, *128*(9), 959–966. https://doi.org/10.1007/s00402-007-0518-1

Chedly, J., Soares, S., Montembault, A., von Boxberg, Y., Veron-Ravaille, M., Mouffle, C., Benassy, M.-N., Taxi, J., David, L., & Nothias, F. (2017a). Physical chitosan microhydrogels as scaffolds for spinal cord injury restoration and axon regeneration. *Biomaterials*, *138*, 91–107. https://doi.org/10.1016/j.biomaterials.2017.05.024

Chedly, J., Soares, S., Montembault, A., von Boxberg, Y., Veron-Ravaille, M., Mouffle, C., Benassy, M.-N., Taxi, J., David, L., & Nothias, F. (2017b). Physical chitosan microhydrogels as scaffolds for spinal cord injury restoration and axon regeneration. *Biomaterials*, *138*, 91–107. https://doi.org/10.1016/j.biomaterials.2017.05.024

Chen, L., Wang, W., Lin, Z., Lu, Y., Chen, H., Li, B., Li, Z., Xia, H., Li, L., & Zhang, T. (2022). Conducting molybdenum sulfide/graphene oxide/polyvinyl alcohol nanocomposite hydrogel for repairing spinal cord injury. *Journal of Nanobiotechnology*, *20*(1), 210. https://doi.org/10.1186/s12951-022-01396-8

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Chen, Y., Etxabide, A., Seyfoddin, A., & Ramezani, M. (2023). Fabrication and characterisation of poly(vinyl alcohol)/chitosan scaffolds for tissue engineering applications. *Materials Today: Proceedings*. https://doi.org/10.1016/j.matpr.2023.02.303

Chocholata, P., Kulda, V., & Babuska, V. (2019). Fabrication of Scaffolds for Bone-Tissue Regeneration. *Materials*, *12*(4), 568. https://doi.org/10.3390/ma12040568

Choo, A. M.-T., Liu, J., Liu, Z., Dvorak, M., Tetzlaff, W., & Oxland, T. R. (2009). Modeling spinal cord contusion, dislocation, and distraction: Characterization of vertebral clamps, injury severities, and node of Ranvier deformations. *Journal of Neuroscience Methods*, *181*(1), 6–17. https://doi.org/10.1016/j.jneumeth.2009.04.007

Chudickova, M., Vackova, I., Machova Urdzikova, L., Jancova, P., Kekulova, K., Rehorova, M., Turnovcova, K., Jendelova, P., & Kubinova, S. (2019). The Effect of Wharton Jelly-Derived Mesenchymal Stromal Cells and Their Conditioned Media in the Treatment of a Rat Spinal Cord Injury. *International Journal of Molecular Sciences*, *20*(18), 4516. https://doi.org/10.3390/ijms20184516

Cofano, F., Boido, M., Monticelli, M., Zenga, F., Ducati, A., Vercelli, A., & Garbossa, D. (2019). Mesenchymal Stem Cells for Spinal Cord Injury: Current Options, Limitations, and Future of Cell Therapy. *International Journal of Molecular Sciences*, *20*(11). https://doi.org/10.3390/ijms20112698

Comolli, N., Donaldson, O., Grantier, N., Zhukareva, V., & Tom, V. J. (2012). Polyvinyl alcohol–polyvinyl pyrrolidone thin films provide local short-term release of anti-inflammatory agents post spinal cord injury. *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, *100B*(7), 1867–1873. https://doi.org/10.1002/jbm.b.32754

Coumans, J. V, Lin, T. T., Dai, H. N., MacArthur, L., McAtee, M., Nash, C., & Bregman, B. S. (2001). Axonal regeneration and functional recovery after complete spinal cord transection in rats by delayed treatment with transplants and neurotrophins. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *21*(23), 9334–9344. https://doi.org/10.1523/JNEUROSCI.21-23-09334.2001

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Courtine, G., Bunge, M. B., Fawcett, J. W., Grossman, R. G., Kaas, J. H., Lemon, R., Maier, I., Martin, J., Nudo, R. J., Ramon-Cueto, A., Rouiller, E. M., Schnell, L., Wannier, T., Schwab, M. E., & Edgerton, V. R. (2007). Can experiments in nonhuman primates expedite the translation of treatments for spinal cord injury in humans? *Nature Medicine*, *13*(5), 561–566. https://doi.org/10.1038/nm1595

Crapo, P. M., Tottey, S., Slivka, P. F., & Badylak, S. F. (2014). Effects of Biologic Scaffolds on Human Stem Cells and Implications for CNS Tissue Engineering. *Tissue Engineering Part A*, *20*(1–2), 313–323. https://doi.org/10.1089/ten.tea.2013.0186

Cui, Z., Zheng, Z., Lin, L., Si, J., Wang, Q., Peng, X., & Chen, W. (2018). Elektrospinning and crosslinking of polyvinyl alcohol/chitosan composite nanofiber for transdermal drug delivery. *Advances in Polymer Technology*, *37*(6), 1917–1928. https://doi.org/10.1002/adv.21850

Dao, T. T.-T., Nguyen, C. T.-H., Vu, N. B., Le, H. T.-N., Nguyen, P. D.-N., & Van Pham, P. (2019). *Evaluation of Proliferation and Osteogenic Differentiation of Human Umbilical Cord-Derived Mesenchymal Stem Cells in Porous Scaffolds* (pp. 207–220). https://doi.org/10.1007/5584_2019_343

David, S., & Aguayo, A. J. (1981). Axonal Elongation into Peripheral Nervous System "Bridges" After Central Nervous System Injury in Adult Rats. *Science*, *214*(4523), 931–933. https://doi.org/10.1126/science.6171034

de Barros Filho, T. E. P., & Molina, A. E. I. S. (2008). Analysis of The Sensitivity and Reproducibility Of The Basso, Beattie, Bresnahan (BBB) Scale in Wistar Rats. *Clinics*, *63*(1), 103–108. https://doi.org/10.1590/S1807-59322008000100018

Deng, W.-S., Ma, K., Liang, B., Liu, X.-Y., Xu, H.-Y., Zhang, J., Shi, H.-Y., Sun, H.-T., Chen, X.-Y., & Zhang, S. (2020). Collagen scaffold combined with human umbilical cord-mesenchymal stem cells transplantation for acute complete spinal cord injury. *Neural Regeneration Research*, *15*(9), 1686. https://doi.org/10.4103/1673-5374.276340

Dietz, V., & Fouad, K. (2014). Restoration of sensorimotor functions after spinal cord injury. *Brain*, *137*(3), 654–667. https://doi.org/10.1093/brain/awt262

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Ding, W., Hu, S., Wang, P., Kang, H., Peng, R., Dong, Y., & Li, F. (2022). Spinal Cord Injury: The Global Incidence, Prevalence, and Disability From the Global Burden of Disease Study 2019. *Spine*, *47*(21), 1532–1540. https://doi.org/10.1097/BRS.0000000000004417

Donnelly, C. J., Fainzilber, M., & Twiss, J. L. (2010). Subcellular Communication Through RNA Transport and Localized Protein Synthesis. *Traffic*, *11*(12), 1498–1505. https://doi.org/10.1111/j.1600-0854.2010.01118.x

Duchen, M. R. (2012). Mitochondria, calcium-dependent neuronal death and neurodegenerative disease. *Pflugers Archiv : European Journal of Physiology*, *464*(1), 111–121. https://doi.org/10.1007/s00424-012-1112-0

Dumont, R. J., Okonkwo, D. O., Verma, S., Hurlbert, R. J., Boulos, P. T., Ellegala, D. B., & Dumont, A. S. (2001). Acute Spinal Cord Injury, Part I: Pathophysiologic Mechanisms. *Clinical Neuropharmacology*, *24*(5), 254–264. https://doi.org/10.1097/00002826-200109000-00002

Dunai, Z., Bauer, P. I., & Mihalik, R. (2011). Necroptosis: Biochemical, Physiological and Pathological Aspects. *Pathology & Oncology Research*, *17*(4), 791–800. https://doi.org/10.1007/s12253-011-9433-4

Erwin, H. (n.d.). *Medical Advantages of Allogeneic vs Autologous Stem Cell Transplants as Treatment in Blood Related Cancer Patients*. https://digitalcommons.sacredheart.edu/acadfest

Fathi, A., Khanmohammadi, M., Goodarzi, A., Foroutani, L., Mobarakeh, Z. T., Saremi, J., Arabpour, Z., & Ai, J. (2020). Fabrication of chitosan-polyvinyl alcohol and silk electrospun fiber seeded with differentiated keratinocyte for skin tissue regeneration in animal wound model. *Journal of Biological Engineering*, *14*(1), 27. https://doi.org/10.1186/s13036-020-00249-y

Fawcett, J. W., Curt, A., Steeves, J. D., Coleman, W. P., Tuszynski, M. H., Lammertse, D., Bartlett, P. F., Blight, A. R., Dietz, V., Ditunno, J., Dobkin, B. H., Havton, L. A., Ellaway, P. H., Fehlings, M. G., Privat, A., Grossman, R., Guest, J. D., Kleitman, N., Nakamura, M., … Short, D. (2007). Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: spontaneous

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

recovery after spinal cord injury and statistical power needed for therapeutic clinical trials. *Spinal Cord*, *45*(3), 190–205. https://doi.org/10.1038/sj.sc.3102007

Fehlings, M. G., & Arvin, B. (2009). The timing of surgery in patients with central spinal cord injury. *Journal of Neurosurgery. Spine*, *10*(1), 1–2. https://doi.org/10.3171/2008.10.SPI0822

Fehlings, M. G., Smith, J. S., Kopjar, B., Arnold, P. M., Yoon, S. T., Vaccaro, A. R., Brodke, D. S., Janssen, M. E., Chapman, J. R., Sasso, R. C., Woodard, E. J., Banco, R. J., Massicotte, E. M., Dekutoski, M. B., Gokaslan, Z. L., Bono, C. M., & Shaffrey, C. I. (2012). Perioperative and delayed complications associated with the surgical treatment of cervical spondylotic myelopathy based on 302 patients from the AOSpine North America Cervical Spondylotic Myelopathy Study. *Journal of Neurosurgery: Spine*, *16*(5), 425–432. https://doi.org/10.3171/2012.1.SPINE11467

Fehlings, M. G., Tetreault, L. A., Wilson, J. R., Kwon, B. K., Burns, A. S., Martin, A. R., Hawryluk, G., & Harrop, J. S. (2017). A Clinical Practice Guideline for the Management of Acute Spinal Cord Injury: Introduction, Rationale, and Scope. *Global Spine Journal*, *7*(3_suppl), 84S-94S. https://doi.org/10.1177/2192568217703387

Fehlings, M. G., Vaccaro, A., Wilson, J. R., Singh, A., W. Cadotte, D., Harrop, J. S., Aarabi, B., Shaffrey, C., Dvorak, M., Fisher, C., Arnold, P., Massicotte, E. M., Lewis, S., & Rampersaud, R. (2012). Early versus Delayed Decompression for Traumatic Cervical Spinal Cord Injury: Results of the Surgical Timing in Acute Spinal Cord Injury Study (STASCIS). *PLoS ONE*, *7*(2), e32037. https://doi.org/10.1371/journal.pone.0032037

Fehlings, M. G., Wilson, J. R., Harrop, J. S., Kwon, B. K., Tetreault, L. A., Arnold, P. M., Singh, J. M., Hawryluk, G., & Dettori, J. R. (2017). Efficacy and Safety of Methylprednisolone Sodium Succinate in Acute Spinal Cord Injury: A Systematic Review. *Global Spine Journal*, *7*(3 Suppl), 116S-137S. https://doi.org/10.1177/2192568217706366

Frankel, H. L., Hancock, D. O., Hyslop, G., Melzak, J., Michaelis, L. S., Ungar, G. H., Vernon, J. D. S., & Walsh, J. J. (1969). The value of postural reduction in the initial

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

management of closed injuries of the spine with paraplegia and tetraplegia. *Spinal Cord*, *7*(3), 179–192. https://doi.org/10.1038/sc.1969.30

Fukuda, S., Nakamura, T., Kishigami, Y., Endo, K., Azuma, T., Fujikawa, T., Tsutsumi, S., & Shimizu, Y. (2005). New canine spinal cord injury model free from laminectomy. *Brain Research. Brain Research Protocols*, *14*(3), 171–180. https://doi.org/10.1016/j.brainresprot.2005.01.001

Galtrey, C. M., & Fawcett, J. W. (2007). The role of chondroitin sulfate proteoglycans in regeneration and plasticity in the central nervous system. *Brain Research Reviews*, *54*(1), 1–18. https://doi.org/10.1016/j.brainresrev.2006.09.006

Gao, L., Peng, Y., Xu, W., He, P., Li, T., Lu, X., & Chen, G. (2020). Progress in Stem Cell Therapy for Spinal Cord Injury. *Stem Cells International*, *2020*, 1–16. https://doi.org/10.1155/2020/2853650

Garg, T., Singh, O., Arora, S., & Murthy, R. (2012). Scaffold: a novel carrier for cell and drug delivery. *Critical Reviews in Therapeutic Drug Carrier Systems*, *29*(1), 1–63. https://doi.org/10.1615/critrevtherdrugcarriersyst.v29.i1.10

Ge, J., Guo, L., Wang, S., Zhang, Y., Cai, T., Zhao, R. C. H., & Wu, Y. (2014). The Size of Mesenchymal Stem Cells is a Significant Cause of Vascular Obstructions and Stroke. *Stem Cell Reviews and Reports*, *10*(2), 295–303. https://doi.org/10.1007/s12015-013-9492-x

Ghiasi, B., Sefidbakht, Y., & Rezaei, M. (2019). *Hydroxyapatite for Biomedicine and Drug Delivery* (pp. 85–120). https://doi.org/10.1007/978-3-030-10834-2_4

Ghiasi, M., Kalhor, N., Tabatabaei Qomi, R., & Sheykhhasan, M. (2016). The effects of synthetic and natural scaffolds on viability and proliferation of adipose-derived stem cells. *Frontiers in Life Science*, *9*(1), 32–43. https://doi.org/10.1080/21553769.2015.1077477

Giannoudis, P. V., Einhorn, T. A., & Marsh, D. (2007). Fracture healing: The diamond concept. *Injury*, *38*, S3–S6. https://doi.org/10.1016/S0020-1383(08)70003-2

Gwam, C., Mohammed, N., & Ma, X. (2021). Stem cell secretome, regeneration, and clinical translation: a narrative review. *Annals of Translational Medicine*, *9*(1), 70. https://doi.org/10.21037/atm-20-5030

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Hachem, L. D., Ahuja, C. S., & Fehlings, M. G. (2017). Assessment and management of acute spinal cord injury: From point of injury to rehabilitation. *The Journal of Spinal Cord Medicine*, *40*(6), 665–675. https://doi.org/10.1080/10790268.2017.1329076

Hammarlund, M., Nix, P., Hauth, L., Jorgensen, E. M., & Bastiani, M. (2009). Axon Regeneration Requires a Conserved MAP Kinase Pathway. *Science*, *323*(5915), 802–806. https://doi.org/10.1126/science.1165527

Hejcl, A., Urdzikova, L., Sedy, J., Lesny, P., Pradny, M., Michalek, J., Burian, M., Hajek, M., Zamecnik, J., Jendelova, P., & Sykova, E. (2008). Acute and delayed implantation of positively charged 2-hydroxyethyl methacrylate scaffolds in spinal cord injury in the rat. *Journal of Neurosurgery. Spine*, *8*(1), 67–73. https://doi.org/10.3171/SPI-08/01/067

Hellenbrand, D. J., Quinn, C. M., Piper, Z. J., Morehouse, C. N., Fixel, J. A., & Hanna, A. S. (2021). Inflammation after spinal cord injury: a review of the critical timeline of signaling cues and cellular infiltration. *Journal of Neuroinflammation*, *18*(1), 284. https://doi.org/10.1186/s12974-021-02337-2

Hermanson, J. W., & Lahunta, A. de. (2020). *Miller's Anatomy of the Dog* (5th ed.). Elsevier.

Heumann, R., Korsching, S., Bandtlow, C., & Thoenen, H. (1987). Changes of nerve growth factor synthesis in nonneuronal cells in response to sciatic nerve transection. *The Journal of Cell Biology*, *104*(6), 1623–1631. https://doi.org/10.1083/jcb.104.6.1623

Hiraizumi, Y., Transfeldt, E. E., Fujimaki, E., & Nambu, M. (1995). Application of Polyvinyl Alcohol Hydrogel Membrane as Anti-adhesive Interposition After Spinal Surgery. *Spine*, *20*(21), 2272–2277. https://doi.org/10.1097/00007632-199511000-00002

Hodgetts, S. I., & Harvey, A. R. (2017). *Neurotrophic Factors Used to Treat Spinal Cord Injury* (pp. 405–457). https://doi.org/10.1016/bs.vh.2016.11.007

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Hsieh, W.-C., Liau, J.-J., & Li, Y.-J. (2015). Characterization and Cell Culture of a Grafted Chitosan Scaffold for Tissue Engineering. *International Journal of Polymer Science*, *2015*, 1–7. https://doi.org/10.1155/2015/935305

Huang, L., Fu, C., Xiong, F., He, C., & Wei, Q. (2021a). Stem Cell Therapy for Spinal Cord Injury. *Cell Transplantation*, *30*, 096368972198926. https://doi.org/10.1177/0963689721989266

Huang, L., Fu, C., Xiong, F., He, C., & Wei, Q. (2021b). Stem Cell Therapy for Spinal Cord Injury. *Cell Transplantation*, *30*, 963689721989266. https://doi.org/10.1177/0963689721989266

Hur, J. W., Cho, T.-H., Park, D.-H., Lee, J.-B., Park, J.-Y., & Chung, Y.-G. (2016). Intrathecal transplantation of autologous adipose-derived mesenchymal stem cells for treating spinal cord injury: A human trial. *The Journal of Spinal Cord Medicine*, *39*(6), 655–664. https://doi.org/10.1179/2045772315Y.0000000048

Jung, D.-I., Ha, J., Kang, B.-T., Kim, J.-W., Quan, F.-S., Lee, J.-H., Woo, E.-J., & Park, H.-M. (2009a). A comparison of autologous and allogenic bone marrow-derived mesenchymal stem cell transplantation in canine spinal cord injury. *Journal of the Neurological Sciences*, *285*(1–2), 67–77. https://doi.org/10.1016/j.jns.2009.05.027

Jung, D.-I., Ha, J., Kang, B.-T., Kim, J.-W., Quan, F.-S., Lee, J.-H., Woo, E.-J., & Park, H.-M. (2009b). A comparison of autologous and allogenic bone marrow-derived mesenchymal stem cell transplantation in canine spinal cord injury. *Journal of the Neurological Sciences*, *285*(1–2), 67–77. https://doi.org/10.1016/j.jns.2009.05.027

Karimi, A., Shojaei, A., & Tehrani, P. (2017). Mechanical properties of the human spinal cord under the compressive loading. *Journal of Chemical Neuroanatomy*, *86*, 15–18. https://doi.org/10.1016/j.jchemneu.2017.07.004

Khan, I. U., Yoon, Y., Choi, K. U., Jo, K. R., Kim, N., Lee, E., Kim, W. H., & Kweon, O.-K. (2019). Therapeutic Effects of Intravenous Injection of Fresh and Frozen Thawed HO-1-Overexpressed Ad-MSCs in Dogs with Acute Spinal Cord Injury. *Stem Cells International*, *2019*, 1–15. https://doi.org/10.1155/2019/8537541

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Kim, H., Tator, C. H., & Shoichet, M. S. (2011). Chitosan implants in the rat spinal cord: Biocompatibility and biodegradation. *Journal of Biomedical Materials Research Part A*, *97A*(4), 395–404. https://doi.org/10.1002/jbm.a.33070

Kjell, J., & Olson, L. (2016). Rat models of spinal cord injury: from pathology to potential therapies. *Disease Models & Mechanisms*, *9*(10), 1125–1137. https://doi.org/10.1242/dmm.025833

Kourgiantaki, A., Tzeranis, D. S., Karali, K., Georgelou, K., Bampoula, E., Psilodimitrakopoulos, S., Yannas, I. V., Stratakis, E., Sidiropoulou, K., Charalampopoulos, I., & Gravanis, A. (2020). Neural stem cell delivery via porous collagen scaffolds promotes neuronal differentiation and locomotion recovery in spinal cord injury. *Npj Regenerative Medicine*, *5*(1), 12. https://doi.org/10.1038/s41536-020-0097-0

Kwon, B. K., Stammers, A. M. T., Belanger, L. M., Bernardo, A., Chan, D., Bishop, C. M., Slobogean, G. P., Zhang, H., Umedaly, H., Giffin, M., Street, J., Boyd, M. C., Paquette, S. J., Fisher, C. G., & Dvorak, M. F. (2010). Cerebrospinal Fluid Inflammatory Cytokines and Biomarkers of Injury Severity in Acute Human Spinal Cord Injury. *Journal of Neurotrauma*, *27*(4), 669–682. https://doi.org/10.1089/neu.2009.1080

Lee, J.-H., Chung, W.-H., Kang, E.-H., Chung, D.-J., Choi, C.-B., Chang, H.-S., Lee, J.-H., Hwang, S.-H., Han, H., Choe, B.-Y., & Kim, H.-Y. (2011). Schwann cell-like remyelination following transplantation of human umbilical cord blood (hUCB)-derived mesenchymal stem cells in dogs with acute spinal cord injury. *Journal of the Neurological Sciences*, *300*(1–2), 86–96. https://doi.org/10.1016/j.jns.2010.09.025

Li, J. J., Liu, H., Zhu, Y., Yan, L., Liu, R., Wang, G., Wang, B., & Zhao, B. (2021). Animal Models for Treating Spinal Cord Injury Using Biomaterials-Based Tissue Engineering Strategies. *Tissue Engineering Part B: Reviews*, ten.teb.2020.0267. https://doi.org/10.1089/ten.teb.2020.0267

Li, J. J., Liu, H., Zhu, Y., Yan, L., Liu, R., Wang, G., Wang, B., & Zhao, B. (2022). Animal Models for Treating Spinal Cord Injury Using Biomaterials-Based Tissue

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Engineering Strategies. *Tissue Engineering Part B: Reviews*, *28*(1), 79–100. https://doi.org/10.1089/ten.teb.2020.0267

Li, X., & Dai, J. (2018). Bridging the gap with functional collagen scaffolds: tuning endogenous neural stem cells for severe spinal cord injury repair. *Biomaterials Science*, *6*(2), 265–271. https://doi.org/10.1039/C7BM00974G

Li, X., Li, M., Tian, L., Chen, J., Liu, R., & Ning, B. (2020). Reactive Astrogliosis: Implications in Spinal Cord Injury Progression and Therapy. *Oxidative Medicine and Cellular Longevity*, *2020*, 1–14. https://doi.org/10.1155/2020/9494352

Li, Y., Walker, C. L., Zhang, Y. P., Shields, C. B., & Xu, X.-M. (2014). Surgical decompression in acute spinal cord injury: A review of clinical evidence, animal model studies, and potential future directions of investigation. *Frontiers in Biology*, *9*(2), 127–136. https://doi.org/10.1007/s11515-014-1297-z

Liau, L. L., Looi, Q. H., Chia, W. C., Subramaniam, T., Ng, M. H., & Law, J. X. (2020). Treatment of spinal cord injury with mesenchymal stem cells. *Cell & Bioscience*, *10*(1), 112. https://doi.org/10.1186/s13578-020-00475-3

Liau, L. L., Ruszymah, B. H. I., Ng, M. H., & Law, J. X. (2020). Characteristics and clinical applications of Wharton's jelly-derived mesenchymal stromal cells. *Current Research in Translational Medicine*, *68*(1), 5–16. https://doi.org/10.1016/j.retram.2019.09.001

Lim, J.-H., Jung, C.-S., Byeon, Y.-E., Kim, W. H., Yoon, J.-H., Kang, K.-S., & Kweon, O. (2007). Establishment of a canine spinal cord injury model induced by epidural balloon compression. *Journal of Veterinary Science*, *8*(1), 89. https://doi.org/10.4142/jvs.2007.8.1.89

Liu, R., Chen, X.-P., & Tao, L.-Y. (2008). Regulation of axonal regeneration following the central nervous system injury in adult mammalian. *Neuroscience Bulletin*, *24*(6), 395–400. https://doi.org/10.1007/s12264-008-0218-z

Liu, S., Li, Y., Choi, H. M. C., Sarkar, C., Koh, E. Y., Wu, J., & Lipinski, M. M. (2018). Lysosomal damage after spinal cord injury causes accumulation of RIPK1 and RIPK3 proteins and potentiation of necroptosis. *Cell Death & Disease*, *9*(5), 476. https://doi.org/10.1038/s41419-018-0469-1

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Menezes, K., Rosa, B. G., Freitas, C., da Cruz, A. S., de Siqueira Santos, R., Nascimento, M. A., Alves, D. V. L., Bonamino, M., Rossi, M. I., Borojevic, R., & Coelho-Sampaio, T. (2020). Human mesenchymal stromal/stem cells recruit resident pericytes and induce blood vessels maturation to repair experimental spinal cord injury in rats. *Scientific Reports*, *10*(1), 19604. https://doi.org/10.1038/s41598-020-76290-0

Middleton, J. W., Dayton, A., Walsh, J., Rutkowski, S. B., Leong, G., & Duong, S. (2012). Life expectancy after spinal cord injury: a 50-year study. *Spinal Cord*, *50*(11), 803–811. https://doi.org/10.1038/sc.2012.55

Moreno-López, Y., & Hollis, E. R. (2021). Sensory Circuit Remodeling and Movement Recovery After Spinal Cord Injury. *Frontiers in Neuroscience*, *15*. https://doi.org/10.3389/fnins.2021.787690

Mozafari, M., Moztarzadeh, Jalali, Alhosseini, N., Asgari, Dodel, Samadikuchaksaraei, & Kargozar. (2012). Synthesis and characterization of electrospun polyvinyl alcohol nanofibrous scaffolds modified by blending with chitosan for neural tissue engineering. *International Journal of Nanomedicine*, 25. https://doi.org/10.2147/IJN.S25376

Nagappan, P. G., Chen, H., & Wang, D.-Y. (2020). Neuroregeneration and plasticity: a review of the physiological mechanisms for achieving functional recovery postinjury. *Military Medical Research*, *7*(1), 30. https://doi.org/10.1186/s40779-020-00259-3

Nagel, S. J., Reddy, C. G., Frizon, L. A., Chardon, M. K., Holland, M., Machado, A. G., Gillies, G. T., Howard, M. A., & Wilson, S. (2018). Spinal dura mater: biophysical characteristics relevant to medical device development. *Journal of Medical Engineering & Technology*, *42*(2), 128–139. https://doi.org/10.1080/03091902.2018.1435745

Nandoe Tewarie, R. S., Hurtado, A., Bartels, R. H., Grotenhuis, A., & Oudega, M. (2009). Stem Cell-Based Therapies for Spinal Cord Injury. *The Journal of Spinal Cord Medicine*, *32*(2), 105–114. https://doi.org/10.1080/10790268.2009.11760761

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Nathan, K. G., Genasan, K., & Kamarul, T. (2023). Polyvinyl Alcohol-Chitosan Scaffold for Tissue Engineering and Regenerative Medicine Application: A Review. *Marine Drugs*, *21*(5), 304. https://doi.org/10.3390/md21050304

Niu, J., Yue, W., Le-Le, Z., Bin, L., & Hu, X. (2017). Mesenchymal stem cells inhibit T cell activation by releasing TGF-β1 from TGF-β1/GARP complex. *Oncotarget*, *8*(59), 99784–99800. https://doi.org/10.18632/oncotarget.21549

Onifer, S. M., Smith, G. M., & Fouad, K. (2011). Plasticity After Spinal Cord Injury: Relevance to Recovery and Approaches to Facilitate It. *Neurotherapeutics*, *8*(2), 283–293. https://doi.org/10.1007/s13311-011-0034-4

Pajer, K., Bellák, T., & Nógrádi, A. (2021). Stem Cell Secretome for Spinal Cord Repair: Is It More than Just a Random Baseline Set of Factors? *Cells*, *10*(11), 3214. https://doi.org/10.3390/cells10113214

Park, J. S., Chu, J. S., Tsou, A. D., Diop, R., Tang, Z., Wang, A., & Li, S. (2011). The effect of matrix stiffness on the differentiation of mesenchymal stem cells in response to TGF-β. *Biomaterials*, *32*(16), 3921–3930. https://doi.org/10.1016/j.biomaterials.2011.02.019

Pattison, M. A., Wurster, S., Webster, T. J., & Haberstroh, K. M. (2005). Three-dimensional, nano-structured PLGA scaffolds for bladder tissue replacement applications. *Biomaterials*, *26*(15), 2491–2500. https://doi.org/10.1016/j.biomaterials.2004.07.011

Penolazzi, L., Mazzitelli, S., Vecchiatini, R., Torreggiani, E., Lambertini, E., Johnson, S., Badylak, S. F., Piva, R., & Nastruzzi, C. (2012). Human mesenchymal stem cells seeded on extracellular matrix-scaffold: viability and osteogenic potential. *Journal of Cellular Physiology*, *227*(2), 857–866. https://doi.org/10.1002/jcp.22983

Perry, V. H., Lunn, E. R., Brown, M. C., Cahusac, S., & Gordon, S. (1990). Evidence that the Rate of Wallerian Degeneration is Controlled by a Single Autosomal Dominant Gene. *European Journal of Neuroscience*, *2*(5), 408–413. https://doi.org/10.1111/j.1460-9568.1990.tb00433.x

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Pittenger, M. F., Discher, D. E., Péault, B. M., Phinney, D. G., Hare, J. M., & Caplan, A. I. (2019). Mesenchymal stem cell perspective: cell biology to clinical progress. *NPJ Regenerative Medicine*, *4*, 22. https://doi.org/10.1038/s41536-019-0083-6

Pivovarova, N. B., & Andrews, S. B. (2010). Calcium-dependent mitochondrial function and dysfunction in neurons. *The FEBS Journal*, *277*(18), 3622–3636. https://doi.org/10.1111/j.1742-4658.2010.07754.x

Pryjmaková, J., Kaimlová, M., Hubáček, T., Švorčík, V., & Siegel, J. (2020). Nanostructured Materials for Artificial Tissue Replacements. *International Journal of Molecular Sciences*, *21*(7), 2521. https://doi.org/10.3390/ijms21072521

Purdy, P. D., White, C. L., Baer, D. L., Frawley, W. H., Reichard, R. R., Pride, G. L., Adams, C., Miller, S., Hladik, C. L., & Yetkin, Z. (2004). Percutaneous translumbar spinal cord compression injury in dogs from an angioplasty balloon: MR and histopathologic changes with balloon sizes and compression times. *AJNR. American Journal of Neuroradiology*, *25*(8), 1435–1442.

Qu, J., & Zhang, H. (2017). Roles of Mesenchymal Stem Cells in Spinal Cord Injury. *Stem Cells International*, *2017*, 1–12. https://doi.org/10.1155/2017/5251313

Qu, W., Chen, B., Shu, W., Tian, H., Ou, X., Zhang, X., Wang, Y., & Wu, M. (2020). Polymer-Based Scaffold Strategies for Spinal Cord Repair and Regeneration. *Frontiers in Bioengineering and Biotechnology*, *8*. https://doi.org/10.3389/fbioe.2020.590549

Rizwan, M., Tse, J. W., Nori, A., Leong, K. W., & Yim, E. K. F. (2019). Cell–Substrate Interactions. In *Principles of Regenerative Medicine* (pp. 437–468). Elsevier. https://doi.org/10.1016/B978-0-12-809880-6.00027-8

Rodriguez, G., Berri, M., Lin, P., Kamdar, N., Mahmoudi, E., & Peterson, M. D. (2021). Musculoskeletal morbidity following spinal cord injury: A longitudinal cohort study of privately-insured beneficiaries. *Bone*, *142*, 115700. https://doi.org/10.1016/j.bone.2020.115700

Rowland, J. W., Hawryluk, G. W. J., Kwon, B., & Fehlings, M. G. (2008). Current status of acute spinal cord injury pathophysiology and emerging therapies: promise on the

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

horizon. *Neurosurgical Focus*, *25*(5), E2. https://doi.org/10.3171/FOC.2008.25.11.E2

Russo, G. S., Mangan, J. J., Galetta, M. S., Boody, B., Bronson, W., Segar, A., Kepler, C. K., Kurd, M. F., Hilibrand, A. S., Vaccaro, A. R., & Schroeder, G. D. (2020). Update on Spinal Cord Injury Management. *Clinical Spine Surgery: A Spine Publication*, *33*(7), 258–264. https://doi.org/10.1097/BSD.0000000000000956

RYU, H.-H., KANG, B.-J., PARK, S.-S., KIM, Y., SUNG, G.-J., WOO, H.-M., KIM, W. H., & KWEON, O.-K. (2012). Comparison of Mesenchymal Stem Cells Derived from Fat, Bone Marrow, Wharton's Jelly, and Umbilical Cord Blood for Treating Spinal Cord Injuries in Dogs. *Journal of Veterinary Medical Science*, *74*(12), 1617–1630. https://doi.org/10.1292/jvms.12-0065

Safdarian, M., Trinka, E., Rahimi-Movaghar, V., Thomschewski, A., Aali, A., Abady, G. G., Abate, S. M., Abd-Allah, F., Abedi, A., Adane, D. E., Afzal, S., Ahinkorah, B. O., Ahmad, S., Ahmed, H., Amanat, N., Angappan, D., Arabloo, J., Aryannejad, A., Athari, S. S., … Zhang, Z.-J. (2023). Global, regional, and national burden of spinal cord injury, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet Neurology*, *22*(11), 1026–1047. https://doi.org/10.1016/S1474-4422(23)00287-9

Sajeev, U. S., Anoop Anand, K., Menon, D., & Nair, S. (2008). Control of nanostructures in PVA, PVA/chitosan blends and PCL through elektrospinning. *Bulletin of Materials Science*, *31*(3), 343–351. https://doi.org/10.1007/s12034-008-0054-9

Sakiyama-Elbert. (2008). Combining stem cells and biomaterial scaffolds for constructing tissues and cell delivery. *StemBook*. https://doi.org/10.3824/stembook.1.1.1

Sakti, Y. M., Malueka, R. G., Dwianingsih, E. K., Kusumaatmaja, A., Mafaza, A., & Emiri, D. M. (2021a). Diamond Concept as Principle for the Development of Spinal Cord Scaffold: A Literature Review. *Open Access Macedonian Journal of Medical Sciences*, *9*(F), 754–769. https://doi.org/10.3889/oamjms.2021.7438

Sakti, Y. M., Malueka, R. G., Dwianingsih, E. K., Kusumaatmaja, A., Mafaza, A., & Emiri, D. M. (2021b). Diamond Concept as Principle for the Development of Spinal

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Cord Scaffold: A Literature Review. *Open Access Macedonian Journal of Medical Sciences*, *9*(F), 754–769. https://doi.org/10.3889/oamjms.2021.7438

Sandean, D. (2020). Management of acute spinal cord injury: A summary of the evidence pertaining to the acute management, operative and non-operative management. *World Journal of Orthopedics*, *11*(12), 573–583. https://doi.org/10.5312/wjo.v11.i12.573

Schaub, N. J., Johnson, C. D., Cooper, B., & Gilbert, R. J. (2016a). Electrospun Fibers for Spinal Cord Injury Research and Regeneration. *Journal of Neurotrauma*, *33*(15), 1405–1415. https://doi.org/10.1089/neu.2015.4165

Schaub, N. J., Johnson, C. D., Cooper, B., & Gilbert, R. J. (2016b). Electrospun Fibers for Spinal Cord Injury Research and Regeneration. *Journal of Neurotrauma*, *33*(15), 1405–1415. https://doi.org/10.1089/neu.2015.4165

Sekhon, L. H. S., & Fehlings, M. G. (2001). Epidemiology, Demographics, and Pathophysiology of Acute Spinal Cord Injury. *Spine*, *26*(Supplement), S2–S12. https://doi.org/10.1097/00007632-200112151-00002

Sharif-Alhoseini, M., Khormali, M., Rezaei, M., Safdarian, M., Hajighadery, A., Khalatbari, M. M., Safdarian, M., Meknatkhah, S., Rezvan, M., Chalangari, M., Derakhshan, P., & Rahimi-Movaghar, V. (2017). Animal models of spinal cord injury: a systematic review. *Spinal Cord*, *55*(8), 714–721. https://doi.org/10.1038/sc.2016.187

Sheng, S.-R., Wang, X.-Y., Xu, H.-Z., Zhu, G.-Q., & Zhou, Y.-F. (2010). Anatomy of large animal spines and its comparison to the human spine: a systematic review. *European Spine Journal : Official Publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*, *19*(1), 46–56. https://doi.org/10.1007/s00586-009-1192-5

Siddiqi, S. A., Manzoor, F., Jamal, A., Tariq, M., Ahmad, R., Kamran, M., Chaudhry, A., & Rehman, I. U. (2016). Mesenchymal stem cell (MSC) viability on PVA and PCL polymer coated hydroxyapatite scaffolds derived from cuttlefish. *RSC Advances*, *6*(39), 32897–32904. https://doi.org/10.1039/C5RA22423C

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Soderblom, C., Luo, X., Blumenthal, E., Bray, E., Lyapichev, K., Ramos, J., Krishnan, V., Lai-Hsu, C., Park, K. K., Tsoulfas, P., & Lee, J. K. (2013). Perivascular Fibroblasts Form the Fibrotic Scar after Contusive Spinal Cord Injury. *The Journal of Neuroscience*, *33*(34), 13882–13887. https://doi.org/10.1523/JNEUROSCI.2524-13.2013

Song, R. B., Basso, D. M., da Costa, R. C., Fisher, L. C., Mo, X., & Moore, S. A. (2016). Adaptation of the Basso–Beattie–Bresnahan locomotor rating scale for use in a clinical model of spinal cord injury in dogs. *Journal of Neuroscience Methods*, *268*, 117–124. https://doi.org/10.1016/j.jneumeth.2016.04.023

Stamnitz, S., & Klimczak, A. (2021). Mesenchymal Stem Cells, Bioactive Factors, and Scaffolds in Bone Repair: From Research Perspectives to Clinical Practice. *Cells*, *10*(8). https://doi.org/10.3390/cells10081925

Sterner, R. C., & Brooks, N. P. (2022). Early Decompression and Short Transport Time After Traumatic Spinal Cord Injury are Associated with Higher American Spinal Injury Association Impairment Scale Conversion. *Spine*, *47*(1), 59–66. https://doi.org/10.1097/BRS.0000000000004121

Stevens, M. M., & George, J. H. (2005). Exploring and engineering the cell surface interface. *Science (New York, N.Y.)*, *310*(5751), 1135–1138. https://doi.org/10.1126/science.1106587

Stirling, D. P., Liu, S., Kubes, P., & Yong, V. W. (2009). Depletion of Ly6G/Gr-1 leukocytes after spinal cord injury in mice alters wound healing and worsens neurological outcome. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *29*(3), 753–764. https://doi.org/10.1523/JNEUROSCI.4918-08.2009

Sulaiman, O. A., & Gordon, T. (2000). Effects of short- and long-term Schwann cell denervation on peripheral nerve regeneration, myelination, and size. *Glia*, *32*(3), 234–246. https://doi.org/10.1002/1098-1136(200012)32:3<234::aid-glia40>3.0.co;2-3

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Sulaiman, W., & Gordon, T. (2013). Neurobiology of peripheral nerve injury, regeneration, and functional recovery: from bench top research to bedside application. *Ochsner Journal*, *13*(1), 100–108.

Šulla, I., Balik, V., Horňák, S., & Ledecký, V. (2018). Spinal Cord Injuries in Dogs Part I: A Review of Basic Knowledge. *Folia Veterinaria*, *62*(2), 35–44. https://doi.org/10.2478/fv-2018-0015

Suzuki, H., Imajo, Y., Funaba, M., Ikeda, H., Nishida, N., & Sakai, T. (2023). Current Concepts of Biomaterial Scaffolds and Regenerative Therapy for Spinal Cord Injury. *International Journal of Molecular Sciences*, *24*(3). https://doi.org/10.3390/ijms24032528

TARLOV, I. M. (1954). Spinal cord compression studies. III. Time limits for recovery after gradual compression in dogs. *A.M.A. Archives of Neurology and Psychiatry*, *71*(5), 588–597.

Tator, C. H., & Koyanagi, I. (1997). Vascular mechanisms in the pathophysiology of human spinal cord injury. *Journal of Neurosurgery*, *86*(3), 483–492. https://doi.org/10.3171/jns.1997.86.3.0483

Teixeira, M. A., Amorim, M. T. P., & Felgueiras, H. P. (2019a). Poly(Vinyl Alcohol)-Based Nanofibrous Electrospun Scaffolds for Tissue Engineering Applications. *Polymers*, *12*(1), 7. https://doi.org/10.3390/polym12010007

Teixeira, M. A., Amorim, M. T. P., & Felgueiras, H. P. (2019b). Poly(Vinyl Alcohol)-Based Nanofibrous Electrospun Scaffolds for Tissue Engineering Applications. *Polymers*, *12*(1), 7. https://doi.org/10.3390/polym12010007

Tran, A. P., Warren, P. M., & Silver, J. (2018). The Biology of Regeneration Failure and Success After Spinal Cord Injury. *Physiological Reviews*, *98*(2), 881–917. https://doi.org/10.1152/physrev.00017.2017

Ulndreaj, A., Chio, J. C. T., Ahuja, C. S., & Fehlings, M. G. (2016). Modulating the immune response in spinal cord injury. *Expert Review of Neurotherapeutics*, *16*(10), 1127–1129. https://doi.org/10.1080/14737175.2016.1207532

Vaccaro, A. R., Daugherty, R. J., Sheehan, T. P., Dante, S. J., Cotler, J. M., Balderston, R. A., Herbison, G. J., & Northrup, B. E. (1997). Neurologic outcome of early

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

versus late surgery for cervical spinal cord injury. *Spine*, *22*(22), 2609–2613. https://doi.org/10.1097/00007632-199711150-00006

Vaquero, J., Zurita, M., Rico, M. A., Aguayo, C., Bonilla, C., Marin, E., Tapiador, N., Sevilla, M., Vazquez, D., Carballido, J., Fernandez, C., Rodriguez-Boto, G., Ovejero, M., Vaquero, J., Zurita, M., Bonilla, C., Rico, M. A., Aguayo, C., Rodríguez, A., … Rodríguez, B. (2018). Intrathecal administration of autologous mesenchymal stromal cells for spinal cord injury: Safety and efficacy of the 100/3 guideline. *Cytotherapy*, *20*(6), 806–819. https://doi.org/10.1016/j.jcyt.2018.03.032

Varadarajan, S. G., Hunyara, J. L., Hamilton, N. R., Kolodkin, A. L., & Huberman, A. D. (2022). Central nervous system regeneration. *Cell*, *185*(1), 77–94. https://doi.org/10.1016/j.cell.2021.10.029

Vargas, M. E., & Barres, B. A. (2007). Why Is Wallerian Degeneration in the CNS So Slow? *Annual Review of Neuroscience*, *30*(1), 153–179. https://doi.org/10.1146/annurev.neuro.30.051606.094354

Vawda, R., Badner, A., Hong, J., Mikhail, M., Lakhani, A., Dragas, R., Xhima, K., Barretto, T., Librach, C. L., & Fehlings, M. G. (2019). Early Intravenous Infusion of Mesenchymal Stromal Cells Exerts a Tissue Source Age-Dependent Beneficial Effect on Neurovascular Integrity and Neurobehavioral Recovery After Traumatic Cervical Spinal Cord Injury. *Stem Cells Translational Medicine*, *8*(7), 639–649. https://doi.org/10.1002/sctm.18-0192

Vijayaprakash, K. M., & Sridharan, N. (2013). An experimental spinal cord injury rat model using customized impact device: A cost-effective approach. *Journal of Pharmacology & Pharmacotherapeutics*, *4*(3), 211–213. https://doi.org/10.4103/0976-500X.114607

Vijayaraghavan, K., & Seyed, M. (2018). Physicochemical Characterization and Bioactivity of an Improved Chitosan Scaffold Cross-Linked With Polyvinyl Alcohol for Corneal Tissue Engineering Applications. *Annual Research & Review in Biology*, *24*(6), 1–16. https://doi.org/10.9734/ARRB/2018/39648

von Leden, R. E., Yauger, Y. J., Khayrullina, G., & Byrnes, K. R. (2017). Central Nervous System Injury and Nicotinamide Adenine Dinucleotide Phosphate

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Oxidase: Oxidative Stress and Therapeutic Targets. *Journal of Neurotrauma*, *34*(4), 755–764. https://doi.org/10.1089/neu.2016.4486

Wakasa, S., Shiiya, N., Tachibana, T., Ooka, T., & Matsui, Y. (2009). A semiquantitative analysis of reactive astrogliosis demonstrates its correlation with the number of intact motor neurons after transient spinal cord ischemia. *The Journal of Thoracic and Cardiovascular Surgery*, *137*(4), 983–990. https://doi.org/10.1016/j.jtcvs.2008.10.002

Willerth, S. M., & Sakiyama-Elbert, S. E. (2019). Combining Stem Cells and Biomaterial Scaffolds for Constructing Tissues and Cell Delivery. *StemJournal*, *1*(1), 1–25. https://doi.org/10.3233/STJ-180001

Xia, Y., Zhu, J., Yang, R., Wang, H., Li, Y., & Fu, C. (2023). Mesenchymal stem cells in the treatment of spinal cord injury: Mechanisms, current advances and future challenges. *Frontiers in Immunology*, *14*. https://doi.org/10.3389/fimmu.2023.1141601

Xie, X., Chen, Y., Wang, X., Xu, X., Shen, Y., Khan, A. ur R., Aldalbahi, A., Fetz, A. E., Bowlin, G. L., El-Newehy, M., & Mo, X. (2020). Elektrospinning nanofiber scaffolds for soft and hard tissue regeneration. *Journal of Materials Science & Technology*, *59*, 243–261. https://doi.org/10.1016/j.jmst.2020.04.037

Xin, Q., Zhu, W., He, C., Liu, T., & Wang, H. (2023). The effect of different sources of mesenchymal stem cells on microglia states. *Frontiers in Aging Neuroscience*, *15*. https://doi.org/10.3389/fnagi.2023.1237532

Xue, J., Wu, T., Dai, Y., & Xia, Y. (2019a). Elektrospinning and Electrospun Nanofibers: Methods, Materials, and Applications. *Chemical Reviews*, *119*(8), 5298–5415. https://doi.org/10.1021/acs.chemrev.8b00593

Xue, J., Wu, T., Dai, Y., & Xia, Y. (2019b). Elektrospinning and Electrospun Nanofibers: Methods, Materials, and Applications. *Chemical Reviews*, *119*(8), 5298–5415. https://doi.org/10.1021/acs.chemrev.8b00593

Yang, T., Dai, Y., Chen, G., & Cui, S. (2020). Dissecting the Dual Role of the Glial Scar and Scar-Forming Astrocytes in Spinal Cord Injury. *Frontiers in Cellular Neuroscience*, *14*. https://doi.org/10.3389/fncel.2020.00078

UNIVERSITAS GADJAH MADA
Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada Model Cedera Medula Spinalis
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Yang, Z., Wu, Y., Li, C., Zhang, T., Zou, Y., Hui, J. H. P., Ge, Z., & Lee, E. H. (2012). Improved Mesenchymal Stem Cells Attachment and In Vitro Cartilage Tissue Formation on Chitosan-Modified Poly(l -Lactide- co -Epsilon-Caprolactone) Scaffold. *Tissue Engineering Part A*, *18*(3–4), 242–251. https://doi.org/10.1089/ten.tea.2011.0315

Zarepour, A., Hooshmand, S., Gökmen, A., Zarrabi, A., & Mostafavi, E. (2021). Spinal Cord Injury Management through the Combination of Stem Cells and Implantable 3D Bioprinted Platforms. *Cells*, *10*(11). https://doi.org/10.3390/cells10113189

Zhang, C., Zhang, C., Xu, Y., Li, C., Cao, Y., & Li, P. (2020). Exosomes derived from human placenta-derived mesenchymal stem cells improve neurologic function by promoting angiogenesis after spinal cord injury. *Neuroscience Letters*, *739*, 135399. https://doi.org/10.1016/j.neulet.2020.135399

Zhang, H., Zhou, L., & Zhang, W. (2014). Control of Scaffold Degradation in Tissue Engineering: A Review. *Tissue Engineering Part B: Reviews*, *20*(5), 492–502. https://doi.org/10.1089/ten.teb.2013.0452

Zhang, J., Lu, X., Feng, G., Gu, Z., Sun, Y., Bao, G., Xu, G., Lu, Y., Chen, J., Xu, L., Feng, X., & Cui, Z. (2016). Chitosan scaffolds induce human dental pulp stem cells to neural differentiation: potential roles for spinal cord injury therapy. *Cell and Tissue Research*, *366*(1), 129–142. https://doi.org/10.1007/s00441-016-2402-1

Zhang, Y., Al Mamun, A., Yuan, Y., Lu, Q., Xiong, J., Yang, S., Wu, C., Wu, Y., & Wang, J. (2021). Acute spinal cord injury: Pathophysiology and pharmacological intervention (Review). *Molecular Medicine Reports*, *23*(6), 417. https://doi.org/10.3892/mmr.2021.12056

Zhao, Y., Tang, F., Xiao, Z., Han, G., Wang, N., Yin, N., Chen, B., Jiang, X., Yun, C., Han, W., Zhao, C., Cheng, S., Zhang, S., & Dai, J. (2017). Clinical Study of NeuroRegen Scaffold Combined with Human Mesenchymal Stem Cells for the Repair of Chronic Complete Spinal Cord Injury. *Cell Transplantation*, *26*(5), 891–900. https://doi.org/10.3727/096368917X695038

UNIVERSITAS
GADJAH MADA
**Aplikasi Kombinasi Sel Punca Alogenik Asal Tali Pusat dan Serat Perancah dengan Diameter Nano pada
Model Cedera Medula Spinalis**
Yudha Mathan Sakti, Prof. Dr. dr. Teguh Aryandono, Sp.B. Subsp. Onk (K).; dr. Rusdy Ghazali Malueka, Ph.D., Sp.S
Universitas Gadjah Mada, 2024 | Diunduh dari http://etd.repository.ugm.ac.id/

Zheng, B., & Tuszynski, M. H. (2023). Regulation of axonal regeneration after mammalian spinal cord injury. *Nature Reviews Molecular Cell Biology*, *24*(6), 396–413. https://doi.org/10.1038/s41580-022-00562-y

Zhong, D., Cao, Y., Li, C.-J., Li, M., Rong, Z.-J., Jiang, L., Guo, Z., Lu, H.-B., & Hu, J.-Z. (2020). Neural stem cell-derived exosomes facilitate spinal cord functional recovery after injury by promoting angiogenesis. *Experimental Biology and Medicine*, *245*(1), 54–65. https://doi.org/10.1177/1535370219895491

Zhou, T., Zheng, Y., Sun, L., Badea, S. R., Jin, Y., Liu, Y., Rolfe, A. J., Sun, H., Wang, X., Cheng, Z., Huang, Z., Zhao, N., Sun, X., Li, J., Fan, J., Lee, C., Megraw, T. L., Wu, W., Wang, G., & Ren, Y. (2019). Microvascular endothelial cells engulf myelin debris and promote macrophage recruitment and fibrosis after neural injury. *Nature Neuroscience*, *22*(3), 421–435. https://doi.org/10.1038/s41593-018-0324-9