EDITORIAL



Most-read articles 2019: A year of noteworthy research



Anthony Atala
Editor-in-Chief, STEM CELLS Translational Medicine

We wish the very best to you and yours in 2020! At STEM CELLS Translational Medicine (SCTM), we look forward to continuing our mission of publishing trailblazing research that will move the field closer to broader and more widespread use of stem cell therapies. But first, we want to look back and congratulate the outstanding research teams that submitted the most-read articles for 2019.

These selections include a wide range of exciting clinical trials, noteworthy basic science research that is paving the way for future therapies, and review articles highlighting the current state of the science, as well as an article on model criteria for the regulation of cord blood banks and cord blood banking.¹

Focusing first on clinical findings, two research teams reported on the potential application of mesenchymal stromal/stem cells (MSCs) for knee arthritis, a growing concern with the aging population. Chahal et al,² in the #1 most-read paper, established that a single intra-articular injection of bone marrow-derived MSCs improved pain and symptoms and reduced inflammation. And Lee et al,³ described how the intra-articular injection of autologous adipose-derived MSCs fostered functional improvements and pain relief without any apparent adverse effects.

In the second most-read paper, Campbell et al⁴ reported on the first randomized controlled trial of allogeneic corneal epithelial stem cells cultured on amniotic membrane in the treatment of severe bilateral limbal stem cell deficiency, demonstrating the feasibility and safety of this approach.

Potential new treatments for autism were also reported, with Riordan et al⁵ conducting what is believed to be the first single-arm phase I/II clinical trial of repeated dose umbilical cord MSCs in children

diagnosed with autism spectrum disorder. Forty percent of participants showed notable improvement of symptoms. In addition, Carpenter et al⁶ found improvements in social communication skills and a reduction in symptoms in children treated with autologous cord blood infusion.

Mazzini et al,⁷ on behalf of the ALS-NSCs Trial Study Group, reported the first account of the reproducible and stable ex vivo expansion of human fetal neural stem cells (NSCs) and a description of the long-term outcomes of patients with amyotrophic lateral sclerosis (ALS) receiving intraspinal NSC administrations in a phase I clinical trial.

For the treatment of stroke, Zhang et al⁸ provided evidence that a neural stem cell line that differentiates, matures, and integrates into central nervous system tissue formed stable allogeneic neural tissue, suggesting statistically significant clinical benefits in chronic stroke patients.

The most-read papers also included important laboratory research findings, such as the third most-read paper from Mellough et al, ⁹ which compared retinal organoid differentiation from human pluripotent stem cells and revealed stage specific, cell line, and methodological differences.

A report by Shojaati et al¹⁰ may lead to a rapid and inexpensive means of treating corneal blindness due to corneal scarring. The team found that the regenerative potential of stem cells from human cornea can be duplicated by delivery of microRNA to ocular tissues by extracellular vesicles (EVs).

In a rat model, Fernandes-Cunha et al¹¹ discovered that the reconstitution of the lyophilized secretome of MSCs within a viscoelastic gel allowed for enhanced corneal epithelial wound healing both in vitro and in vivo in a study that highlights the ever-growing trend toward cell-free regenerative approaches.

In another basic science finding that may lead to more effective clinical treatments, Vawda et al¹² compared human umbilical cordderived fetal cells of distinct ages with the goal of optimizing MSC therapy for traumatic spinal cord injury.

In another example, Zhu et al¹³ found, for the first time, that diabetes mellitus impairs the bone regenerative effect of exosomes derived from bone marrow MSCs, suggesting that the autologous transplantation of these cells to promote bone regeneration may be inadequate in these patients.

Narbute et al¹⁴ provided the first report showing therapeutic efficacy of intranasally administered EVs derived from human exfoliated deciduous teeth stem cells in a rat model of Parkinson's disease.

Rounding out the most-read articles of 2019 were reviews by noted experts, including three articles focused on MSCs. Baek et al^{15}

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2020 The Author. Stem Cells Translational Medicine published by Wiley Periodicals, Inc. on behalf of AlphaMed Press

summarized the enormous potential and current obstacles faced in the application of exosomes and EVs derived from MSCs as next-generation drug delivery systems. Mastrolia et al 16 discussed the current challenges to the clinical development of MSCs, and Hoogduijn and Lombardo 17 provided an excellent overview of the therapeutic mechanisms of action of MSCs and the current status of MSC therapeutics.

Zarbin et al¹⁸ provided a fascinating review on the transplantation of retinal pigment epithelium as a means to combat age-related macular degeneration, one of the principal causes of vision loss.

In his review article, Cesario V. Borlongan¹⁹ suggests that failed clinical trials in stroke patients may be due to a loss in translation of optimal laboratory stem cell transplantation protocols to clinical trial designs and suggests that a concerted effort between basic scientists and clinicians—with NIH and FDA guidance—is key to successful translation.

Xu et al²⁰ summarized the recent progress regarding the potential mechanisms of MSC therapy, with an emphasis on MSC-secreted cytokines and miRNAs as a safe and effective cell-free therapy for radiation-induced lung injury.

Please join me in congratulating these research teams for their outstanding work. We are grateful for these and other fine research submissions, as well as to our loyal readers, a combination that has helped SCTM attain a leadership role in the field.

We are also thankful to founding editor Martin Murphy, executive editor Ann Murphy, and their dedicated staff for their vision in launching SCTM and for the work they do daily to bring these high-quality publications to our readers. A special thanks to our senior associate editor Paolo De Coppi; associate editors Geoffrey Gurtner, Douglas Losordo, Alan Trounson, and Rocky Tuan; and our distinguished editorial board members who work to ensure that the best papers can be accepted.

CONFLICT OF INTEREST

The author indicated no potential conflicts of interest.

Anthony Atala, MD Wake Forest Institute for Regenerative Medicine, Wake Forest School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27101. Email: aatala@wakehealth.edu

REFERENCES

- Cord Blood Association. Model criteria for regulation of cord blood banks and cord blood banking: adopted by the Cord Blood Association, Board of Directors, January 29, 2019. Stem Cells Translational Medicine. 2019;8:340-343.
- Chahal J, Gómez-Aristizábal A, Shestopaloff K, et al. Bone marrow mesenchymal stromal cell treatment in patients with osteoarthritis results in overall improvement in pain and symptoms and reduces synovial inflammation. Stem Cells Translational Medicine. 2019;8: 746-757.
- Lee WS, Kim HJ, Kim KI, Kim GB, Jin W. Intra-articular injection of autologous adipose tissue-derived mesenchymal stem cells for the treatment of knee osteoarthritis: a phase Ilb, randomized, placebo-controlled clinical trial. Stem Cells Translational Medicine. 2019;8(8):504-511.

- Campbell JDM, Ahmad S, Agrawal A, et al. Allogeneic ex vivo expanded corneal epithelial stem cell transplantation: a randomized controlled clinical trial. Stem Cells Translational Medicine. 2019;8: 323-331.
- Riordan NH, Hincapié ML, Morales I, et al. Allogeneic human umbilical cord mesenchymal stem cells for the treatment of autism spectrum disorder in children: safety profile and effect on cytokine levels. Stem Cells Translational Medicine. 2019;8:1008-1016.
- Carpenter KLH, Major S, Tallman C, et al. White matter tract changes associated with clinical improvement in an open-label trial assessing autologous umbilical cord blood for treatment of young children with autism. Stem Cells Translational Medicine. 2019;8:138-147.
- Mazzini L, Gelati M, Profico DC, et al. Results from phase I clinical trial with intraspinal injection of neural stem cells in amyotrophic lateral sclerosis: a long-term outcome. Stem Cells Translational Medicine. 2019;8:887-897.
- Zhang G, Li Y, Reuss JL, et al. Stable intracerebral transplantation of neural stem cells for the treatment of paralysis due to ischemic stroke. Stem Cells Translational Medicine. 2019;8:999-1007.
- Mellough CB, Collin J, Queen R, et al. Systematic comparison of retinal organoid differentiation from human pluripotent stem cells reveals stage specific, cell line, and methodological differences. Stem Cells Translational Medicine. 2019;8:694-706.
- Shojaati G, Khandaker I, Funderburgh ML, et al. Mesenchymal stem cells reduce corneal fibrosis and inflammation via extracellular vesicle-mediated delivery of miRNA. Stem Cells Translational Medicine. 2019;8:1192-1201.
- Fernandes-Cunha GM, Na KS, Putra I, et al. Corneal wound healing effects of mesenchymal stem cell secretome delivered within a viscoelastic gel carrier. Stem Cells Translational Medicine. 2019;8: 478-489.
- Vawda R, Badner A, Hong J, et al. 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. 2019:8:639-649.
- Zhu Y, Jia Y, Wang Y, Xu J, Chai Y. Impaired bone regenerative effect of exosomes derived from bone marrow mesenchymal stem cells in type 1 diabetes. Stem Cells Translational Medicine. 2019;8: 593-605.
- 14. Narbute K, Pilipenko V, Pupure J, et al. Intranasal administration of extracellular vesicles derived from human teeth stem cells improves motor symptoms and normalizes tyrosine hydroxylase expression in the substantia nigra and striatum of the 6-hydroxydopamine-treated rats. Stem Cells Translational Medicine. 2019;8:490-499.
- Baek G, Choi H, Kim Y, Lee HC, Choi C. Mesenchymal stem cellderived extracellular vesicles as therapeutics and as a drug delivery platform. Stem Cells Translational Medicine. 2019;8:880-886.
- Mastrolia I, Foppiani EM, Murgia A, et al. Challenges in clinical development of mesenchymal stromal/stem cells: concise review. Stem Cells Translational Medicine. 2019;8:1135-1148.
- Hoogduijn MJ, Lombardo E. Mesenchymal stromal ells anno 2019: dawn of the therapeutic era? Concise review. Stem Cells Translational Medicine. 2019;8:1126-1134.
- Zarbin M, Sugino I, Townes-Anderson E. Concise review: update on retinal pigment epithelium transplantation for age-related macular degeneration. Stem Cells Translational Medicine. 2019;8: 466-477.
- Borlongan CV. Concise review: stem cell therapy for stroke patients: are we there yet? Stem Cells Translational Medicine. 2019;8:983-988.
- Xu S, Liu C, Ji HL. Concise review: therapeutic potential of the mesenchymal stem cell derived secretome and extracellular vesicles for radiation-induced lung injury: progress and hypotheses. Stem Cells Translational Medicine. 2019;8:344-354.