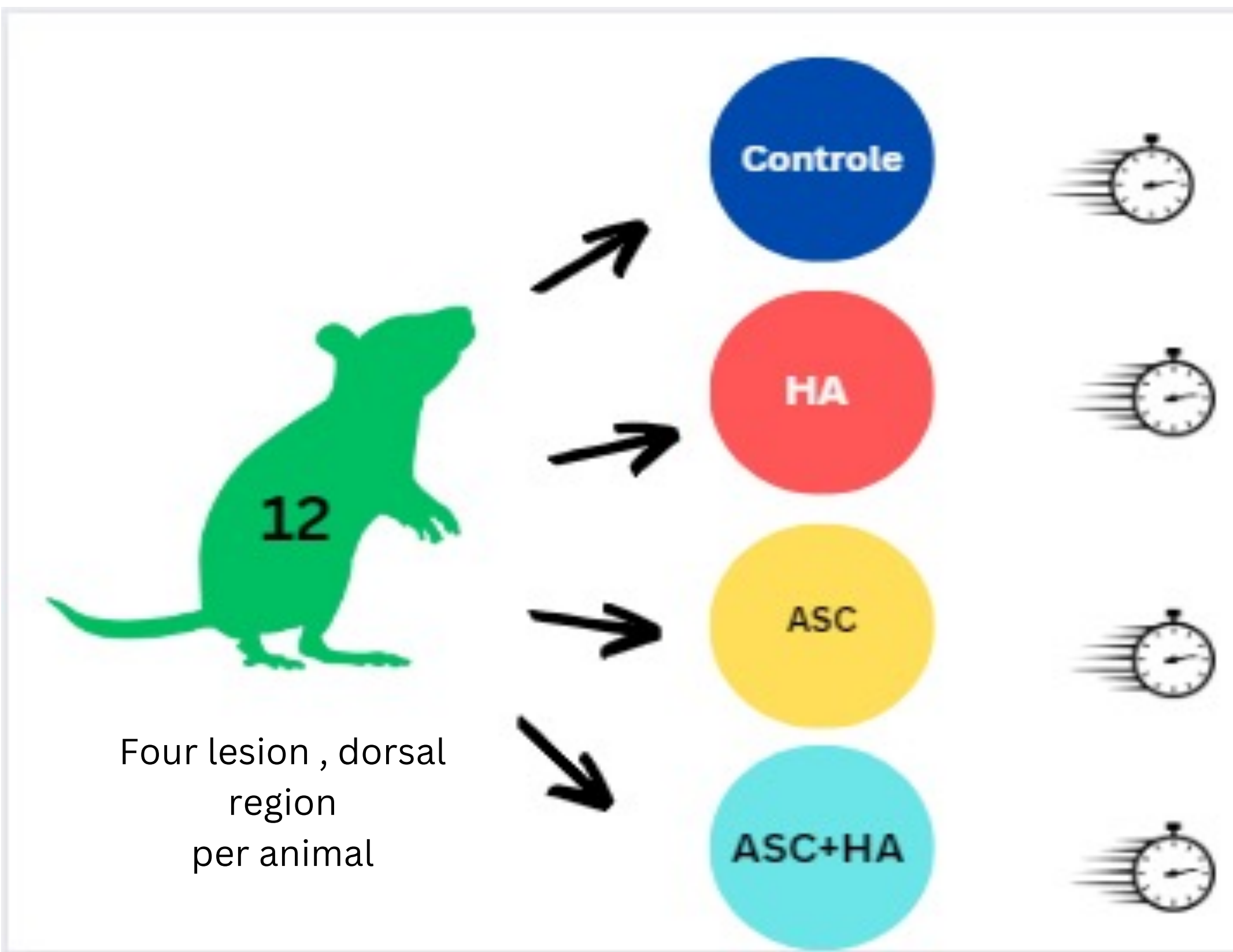


Introduction

1-2% of the world's population will develop a chronic skin wound in their time
In the USA, more than 25 billion per year
Regenerative medicine is an alternative. The association of stem cells and scaffolds could improve the wound-healing process.

Research question: Is Comercial hyaluronic acid associated with ADSC improve wound healing?

Method



Endpoints

Percentage of wound healing

Flowmeter

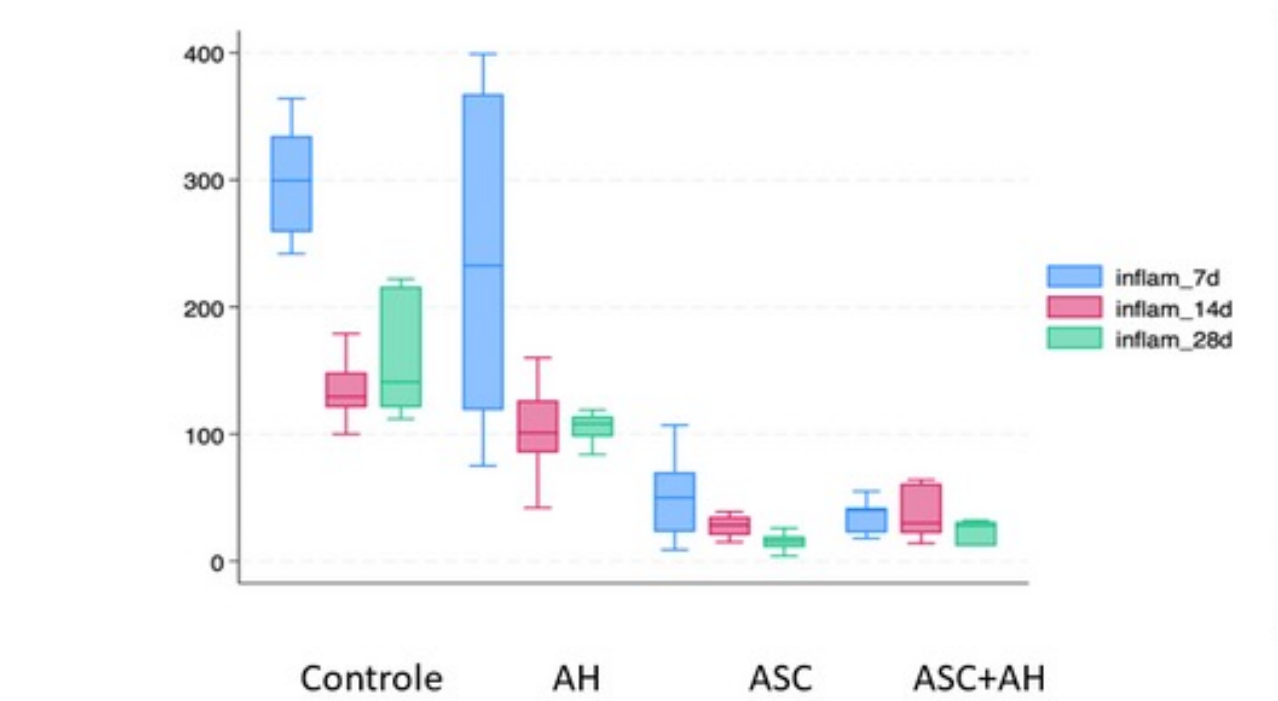
Histologic analysis-HE- inflammatory cells counting, neoangiogenesis,

PCR (IL-1f-10. TNF, CD-68, MMP-3, MMP-9_)

Table 1. Percentage of wound healing by group and time

Time (days)	Control (n=8)	AH (n=8)	ASC (n=8)	ASC+AH (n=8)
7	0% (0/8)	0% (0/8)	0% (0/8)	0% (0/8)
14	12.5% (1/8)	37.5% (3/8)	37.5% (3/8)	37.5% (3/8)
28	37.5% (3/8)	75% (6/8)	87.5% (7/8)	75% (6/8)

Histologic analysis



Gene expression analysis

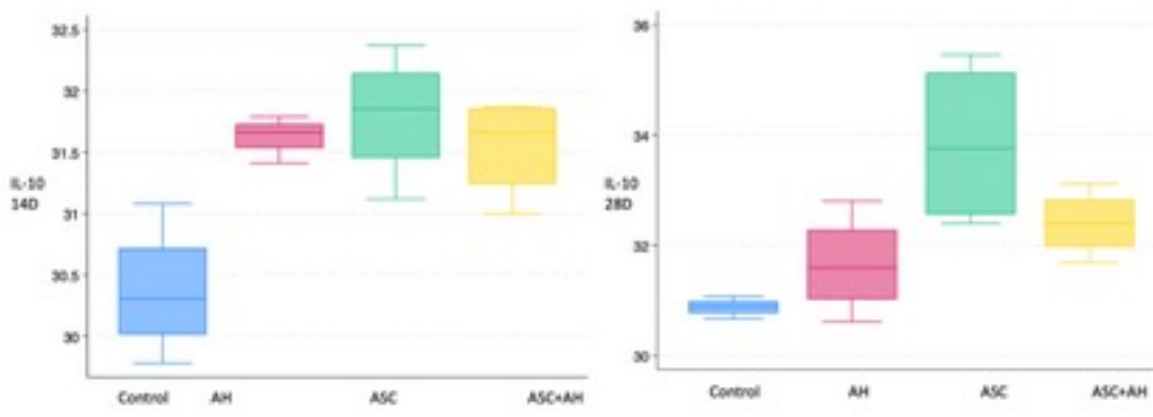


Figura 6. Análise no 14º e 28º dia pós-operatório da expressão gênica de IL-10

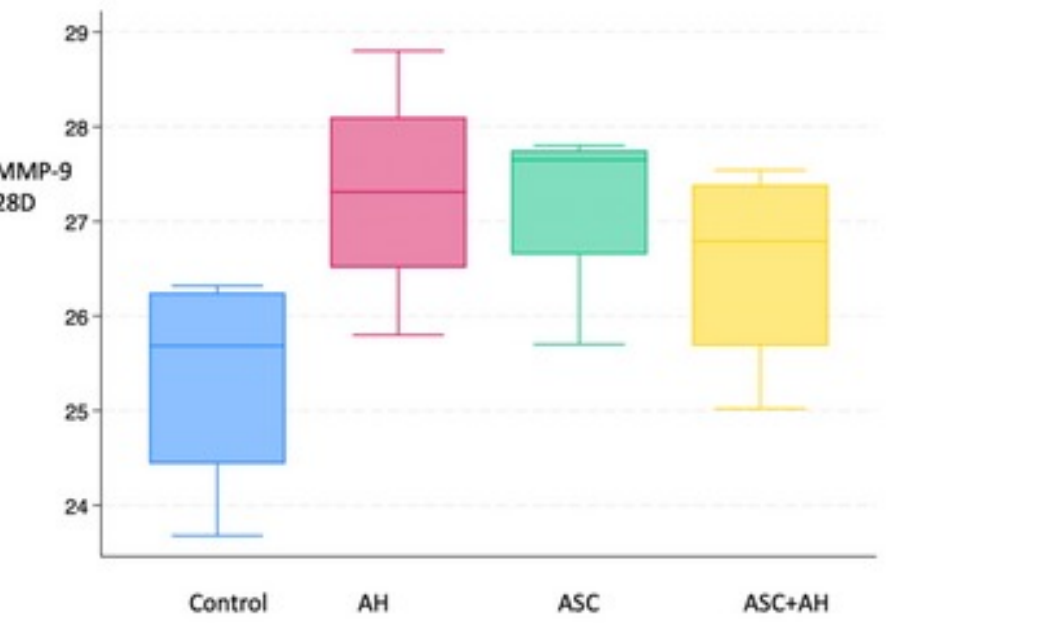
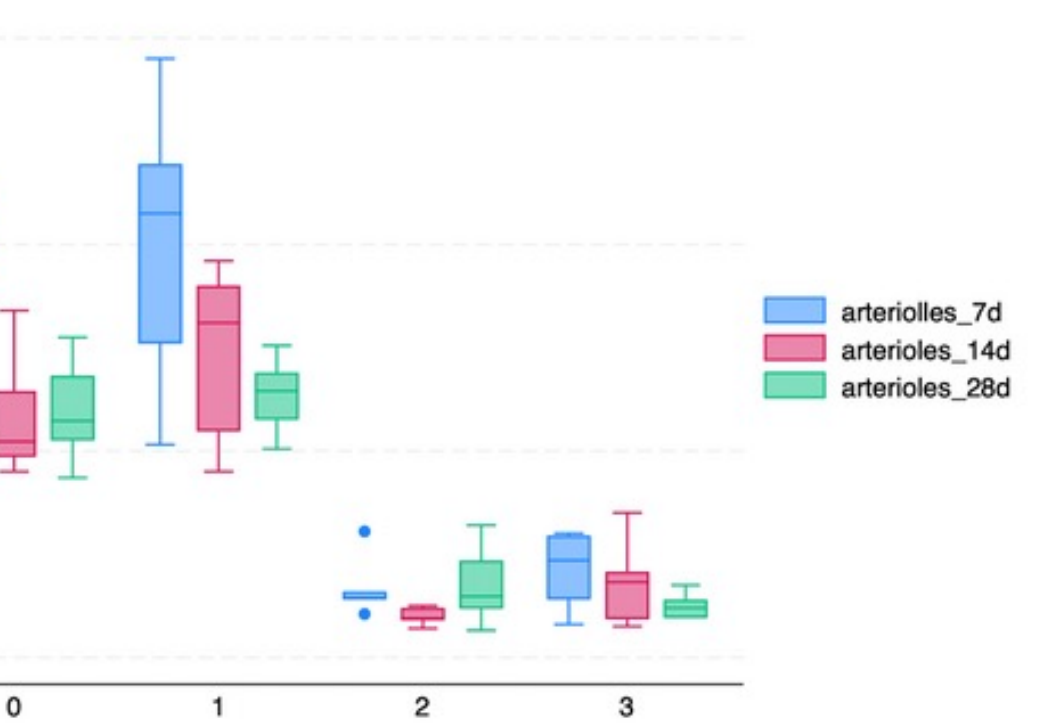
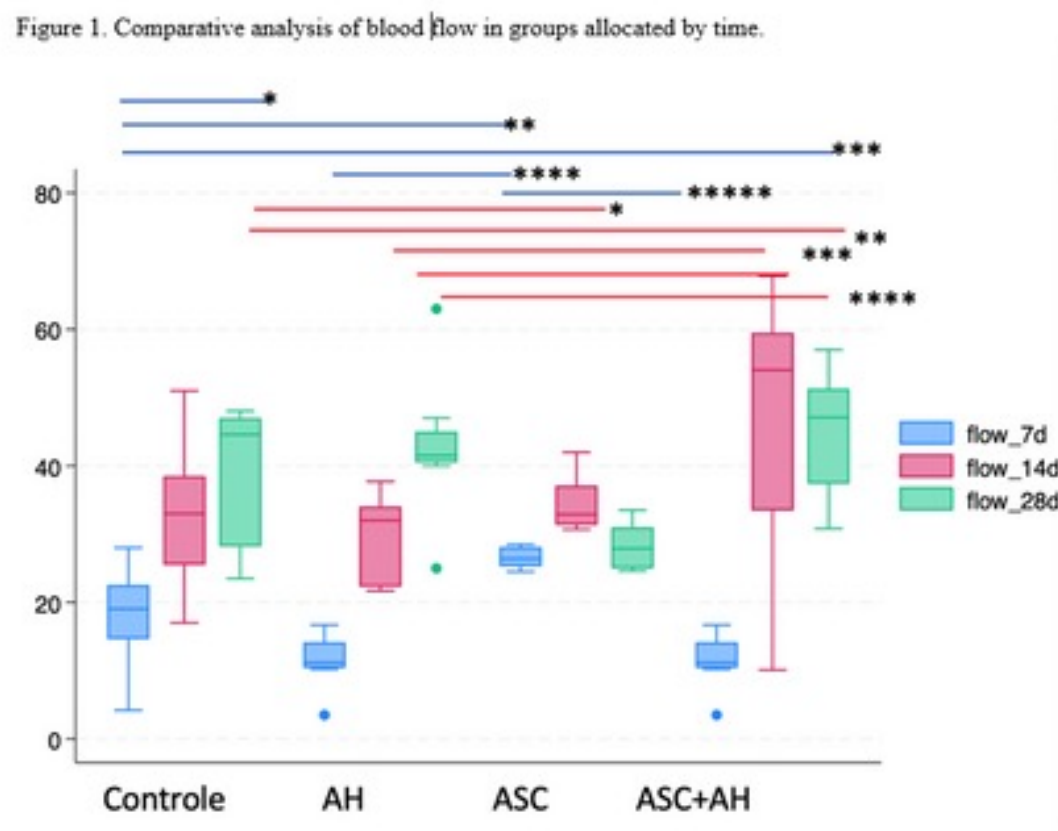


Figura 7. Análise no 28º dia pós-operatório da expressão gênica MMP-9

References

- Gartwiler, E. A., & Hom, D. B. (2011). Skin Histology and Physiology of Wound Healing. *Facial Plastic Surgery Clinics of North America*, 19(3), 441-453. doi:10.1016/j.fsc.2011.06.009
- Sun, B. K., Spradshel, Z., & Khavari, P. A. (2014). Advances in skin grafting and treatment of cutaneous wounds. *Science*, 346(6212), 942-945. doi:10.1126/science.1253836
- Kazani, G. S. (1984). Definitions and Guidelines for Assessment of Wounds and Evaluation of Healing. *Archives of Dermatology*, 120(4), 489. doi:10.1001/archderm.120.4.489
- Pozay, N., Yaghoobi, R., Raffet, E., Mehraban, A., & Fely, A. (2014). Skin Wound Healing and Phytomedicine: A Review. *Skin Pharmacology and Physiology*, 27(6), 303-310. doi:10.1159/00036747
- Gong, H., Tikani, D. J., Hager, S., Hayer, J., & Mirzazadeh, U. (2017). Skin wound healing: an update on the current knowledge and concepts. *European Surgical Research*, 56(2-3), 81-94.
- Ramamoorthy, S. S. (2005). Acute Wounds. *Clinics in Plastic Surgery*, 32(2), 195-208. doi:10.1016/j.cps.2004.12.001
- Santos, I. C. R. V., Souza, M. A. D. O., Andrade, L. N. V. D., Lopes, M. P., Silva, M. F. A. D. B., & Santiago, R. T. (2014). Caracterização do atendimento de pacientes com feridas na Atenção Primária.
- Murphree, R. W. (2017). Impairments in Skin Integrity. *Nursing Clinics of North America*, 52(3), 405-417. doi:10.1016/j.cnur.2017.04.008
- Tateno MTOL, Vicente YAMVA, Moriya T. Wound biology and healing. *Medicina (Rio de Janeiro)* 2018;41(1): 259-64.
- Jablonik K, Ni G, Sonnergen H, Schmittchen A, Pang C, Bagel R, Cai J. Prevalence and incidence of chronic wounds and related complications: a protocol for a systematic review. *Syst Rev*. 2016 Sep 8;5(1):152. doi: 10.1186/s13643-016-0329-y. PMID: 27609108; PMCID: PMC501042.
- de Oliveira, B. G. B., de Alencar Castro, J. B., & Graeppler, J. M. (2013). Panorama epidemiológico e clínico de pacientes com feridas crônicas tratados em ambulatório (Epidemiologic and clinical overview of patients with chronic wounds treated at ambulatory). *Revista Enfermagem UFPA*, 21(1), 612-617.
- Vieira, C. P. D. B., & Araújo, T. M. E. D. (2018). Prevalência e fatores associados a feridas crônicas em idosos na atenção básica. *Revista da Escola de Enfermagem da USP*, 52.
- Instituto Brasileiro de Geografia e Estatística. *Projeção da população do Brasil e das Unidades da Federação*. Disponível em: https://www.ibge.gov.br/apps/populacao/projecao/index.html?utm_source=portal&utm_medium=popclock. Acesso em 27/03/2020 às 17:36
- Lindholm C, Searle R. Wound management for the 21st century: combining effectiveness and efficiency. *Int Wound J*. 2016;13 Suppl 2:5-18. doi:10.1111/iwj.12623
- da Rosa Silva, C. F., Santana, R. F., de Oliveira, B. G., & do Carmo, T. G. (2017). High prevalence of skin and wound care of hospitalized elderly in Brazil: a prospective observational study. *BMC research notes*, 10(1), 11. <https://doi.org/10.1186/s13104-017-2410-0>
- Han, G., & Cella, R. (2017). Chronic Wound Healing: A Review of Current Management and Treatments. *Advances in Therapy*, 34(3), 389-410. <https://doi.org/10.1007/s12325-017-0481-y>
- Vinard, G. M., de Marcon, L., & Vinard, V. M. (2018). Skin Wound Healing: Refractory Wounds and Novel Solutions. *Methods in Molecular Biology*. doi:10.1007/978-1-4939-9115-0_161
- Terziol, A., Pimentel, M. A., Gomes, G. J., & Harper, C. M., Jr (2015). Regenerative Medicine Build-Out: Stem cells translational medicine. *ADT*, 1375-1379. https://doi.org/10.1007/978-1-4939-9115-0_161
- Trothelot, D., & Rouleau, M. G. (2017). Mesenchymal Stem/Stromal Cells in Regenerative Medicine: Past, Present, and Future. *Cellular Reprogramming*, 19(4), 217-224. doi:10.1089/cell.2016.0042
- Han, S., Sun, H., Huang, K. C., & Kim, S. W. (2010). Adipose-derived stromal vascular fraction cells: update on clinical utility and efficacy. *Critical Reviews™ in Eukaryotic Gene Expression*, 25(2).
- Castella, L., Planat-Benard, V., Laharrague, P., & Cousin, B. (2011). Adipose-derived stromal cells: their identity and uses in clinical trials, an update. *World Journal of Stem Cells*, 3(4), 25.
- Hu, C., Yang, D., Xu, J., Li, Z., Jin, X., & Zhang, J. (2011). Locally administered adipose-derived stem cells accelerate wound healing through differentiation and vasculogenesis. *Cell transplantation*, 20(2), 205-216.
- Godwin, M., Abushou, A. I., Ghannem, E., Hamad, A. M., Said, A. M., & Abou-Dain, M. M. (2018). Adipose-derived stem cells: Effectiveness and advances in delivery in diabetic wound healing. *Biomedicine & Pharmacotherapy*, 107, 625-633.
- Zografou, A., Papadopoulos, O., Tsiglis, C., Kavantzas, N., Michalopoulos, E., Chatsimantou, T., ... & Perrea, D. (2013). Autologous transplantation of adipose-derived stem cells enhances skin graft survival and wound healing in diabetic rats. *Annals of plastic surgery*, 71(2), 205-210.
- Kern, N. Q., Beane, J. L., Yuan, T., George, M., Stofner, C. M., Keller, B. B., ... & LeBlanc, A. J. (2018). Adipose-derived cells improve left ventricular diastolic function and increase microvascular perfusion in advanced age. *PLoS one*, 13(8).
- Dong Y, Cui M, Qu J, Wang X, Kwon SH, Barreira J, Elavasseri N, Gurtner GC. Conformable hyaluronic acid hydrogel delivers adipose-derived stem cells and promotes regeneration of burn injury. *Acta Biomater*. 2020 May;108:56-66. doi: 10.1016/j.actbio.2020.03.040. Epub 2020 Apr 3. PMID: 32051786.
- Alameddini E, Oryan A, Mohammadi AA. Hyaluronic acid hydrogel loaded by adipose stem cells enhances wound healing by modulating IL-1β, TGF-β1, and bFGF in burn wound model in rat. *J Biomed Mater Res B Appl Biomater*. 2020 Feb;108(2):555-567. doi: 10.1002/jbm.b.34411. Epub 2019 May 13. PMID: 31081894. Copy
- Hu, M. S., Hong, W., Seneath-Yapa, K., Zimmermann, A. S., Chung, M. T., Enquist, M., ... & Lorenz, H. P. (2014). Adipose-derived stem cells promote engraftment of autologous skin grafts in diabetic mouse models. *Journal of Surgical Research*, 186(2), 478-479.
- Maharic, M. K., Bagheri, M., Sifjov, Z., Jakhani, B. M., Akrami, M., Rohani, L., ... & Omrani, G. R. (2018). Adipose tissue-derived mesenchymal stem cell (AD-MSC) promotes skin wound healing in diabetic rats. *Diabetes research and clinical practice*, 192(1), 228-234.
- Falacora A, Baldini E, Manfredini S, Vetrari S. Hyaluronic Acid in the Third Millennium. *Polymers*. 2018; 10(7):1017. <https://doi.org/10.3390/polym10071017>
- Lwakura, M., Kreyer, A., Speyer, M. S., Gault, A. R., & Grzela, T. (2016). Hyaluronic Acid in Inflammation and Tissue Regeneration: Wounds - a compendium of clinical research and practice, 28(3), 78-88.