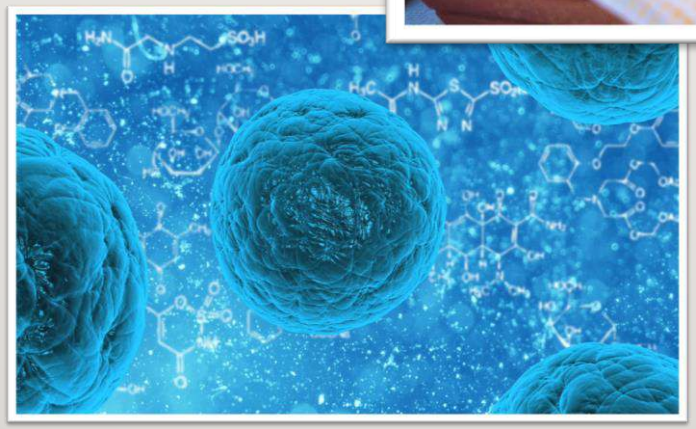
Supplements, Nutrition, and Lifestyle Medicine to Support Stem Cell Therapy

Tal Cohen, DAOM, LAc



R3 STEM CELL™

- REPAIR
- REGENERATE
- RESTORE

Why use supplements?

Patients are looking for faster results!

(e.g. less pain and swelling, improved mobility)

Certain herbs and supplements can stimulate and promote the activity of stem cells and might increase the effectiveness of the treatment.

Udalamaththa VL, Jayasinghe CD, Udagama PV. Potential role of herbal remedies in stem cell therapy: proliferation and differentiation of human mesenchymal stromal cells. Stem Cell Research & Therapy. 2016;7(1). doi:10.1186/s13287-016-0366-4.

Patient feels better = more referrals to you!

How many American adults are taking supplements?

A. Unknown
B. 25 percent of population
C. 52 percent of population
D. Only seniors, hypochondriacs, and naturopaths take vitamins

52% of US adults report use of supplements in 2011–2012

JAMA The Journal of the American Medical Association

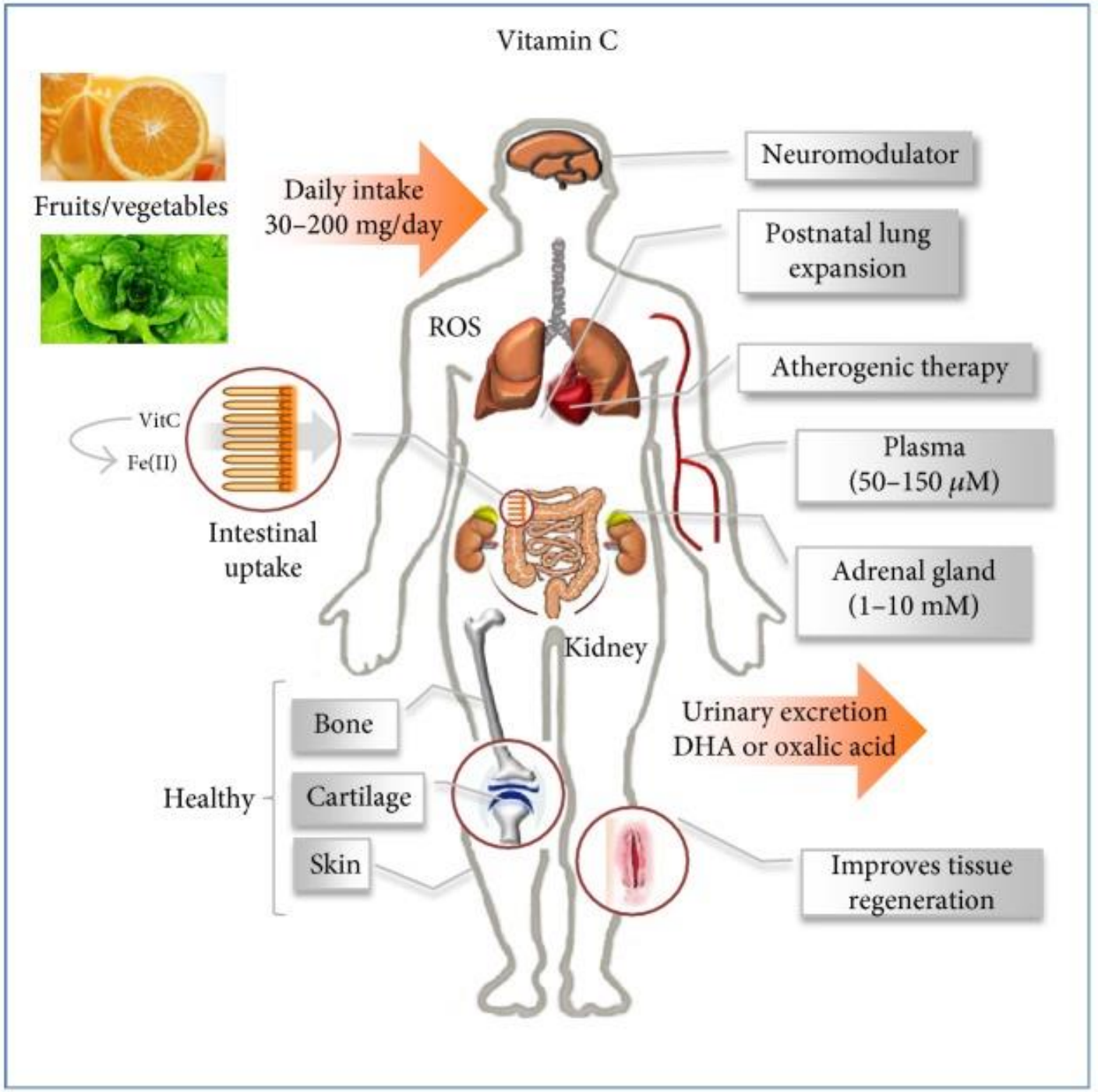
Kantor, E. D., Rehm, C. D., Du, M., White, E., & Giovannucci, E. L. (2016). Trends in Dietary Supplement Use among US Adults From 1999–2012. *JAMA*, *316*(14), 1464–1474. http://doi.org/10.1001/jama.2016.14403

Supplements provide additional revenue for many clinics.

Nutritional Supplements & Herbs to support stem cells function.

Vitamin C is required for healthy function, regeneration of tissue, and can promote the function of Stem Cells.

D'Aniello C, Cermola F, Patriarca EJ, Minchiotti G. Vitamin C in Stem Cell Biology: Impact on Extracellular Matrix Homeostasis and Epigenetics. Stem Cells Int. 2017;2017:8936156. doi: 10.1155/2017/8936156. Epub 2017 Apr 20.



Effect of Vit C activity appears to be dose dependent within a physiological concentration range.

A dosage that is too low or too high can damage the function of Stem Cells.

D'Aniello C, Cermola F, Patriarca EJ, Minchiotti G. Vitamin C in Stem Cell Biology: Impact on Extracellular Matrix Homeostasis and Epigenetics. Stem Cells Int. 2017;2017:8936156. doi: 10.1155/2017/8936156. Epub 2017 Apr 20.

Vitamin C 250 to 500mg Twice Daily

All berries, kale, Brussels Sprouts, broccoli

USE POWDER WITH ORGANIC GREENS

Provides a variety of nutrients and antioxidants in an easy and simple way.

Vitamin D may protect normal stem cells that play an important role in development and tissue/organ regeneration. It also has an anticancer effect.

- ✓ Eat food high in vitamin D: Fatty fish, like mackerel, and salmon.
- ✓ 3oz or one cup of mushrooms
- ✓ Supplementation of 5,000IU of Vitamin D3 (cholecalciferol)

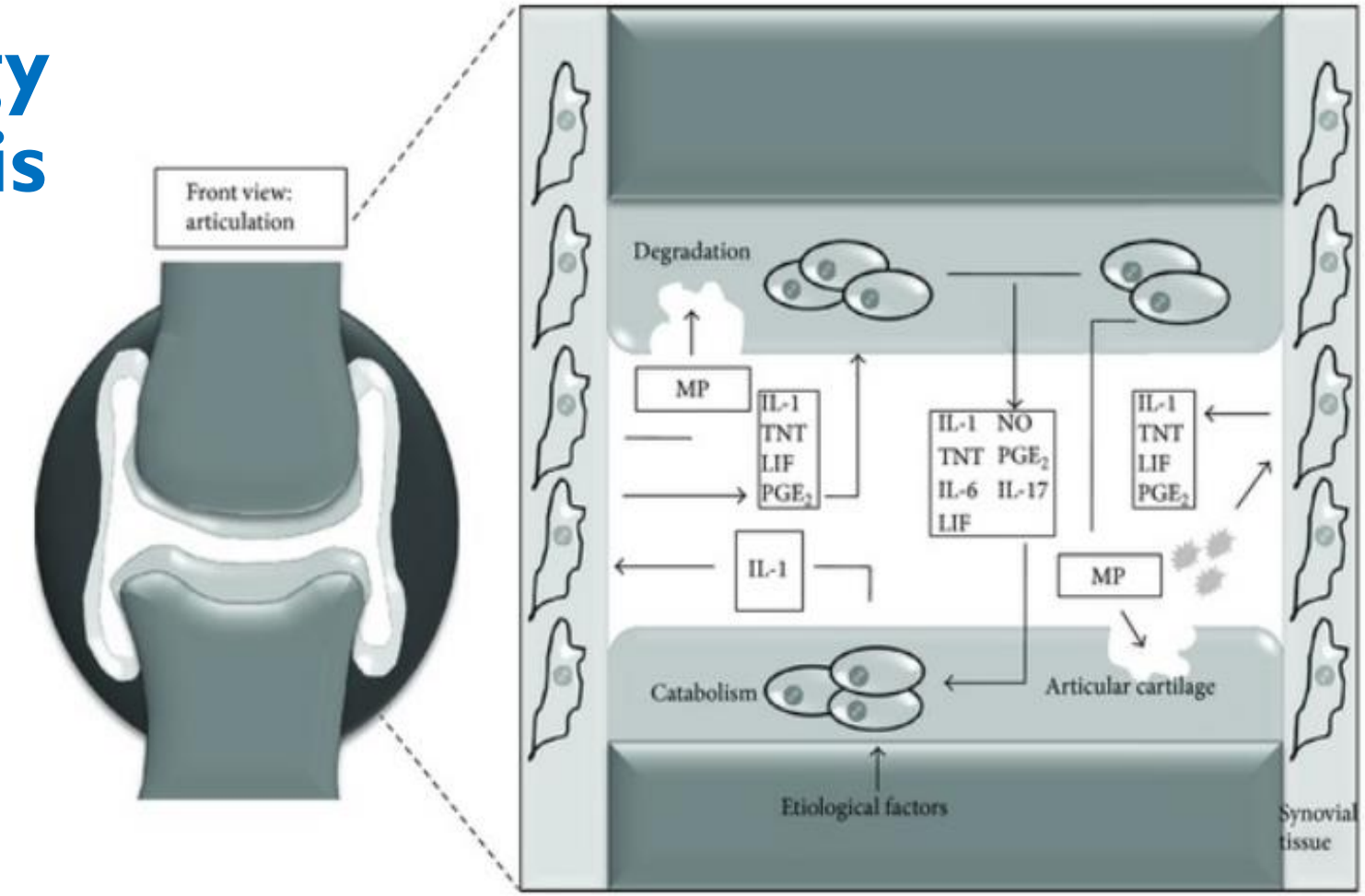
Abdelbaset-Ismail, A., Pedziwiatr, D., Suszyńska, E., Sluczanowska-Glabowska, S., Schneider, G., Kakar, S. S., & Ratajczak, M. Z. (2016). Vitamin D3 stimulates embryonic stem cells but inhibits migration and growth of ovarian cancer and teratocarcinoma cell lines. Journal of Ovarian Research, 9, 26. http://doi.org/10.1186/s13048-016-0235-x

"Recent studies revealed that bioactive compounds, naturally occurring in seaweeds, herbs, fruits and vegetables, possess the ability to modulate self-renewal and differentiation potential of adult stem cells, ***targeting a broad range of intracellular signal transduction pathways****."*

Kornicka, K., Kocherova, I., & Marycz, K. (2017). The effects of chosen plant extracts and compounds on mesenchymal stem cells-a bridge between molecular nutrition and regenerative medicine- concise review. Phytotherapy Research, 31(7), 947-958. doi:10.1002/ptr.5812

Physiopathology of osteoarthritis

Catabolism process is triggered by numerous proinflammatory and proteolytic molecules which generate a local vicious circle.



IL: interleukin; TNF: tumoral necrosis factor; NO: nitric oxide; PG: prostaglandins; MP: metalloproteases; LIF: leukemia inhibitory factor.

Salazar, J., Bello, L., Chávez, M., Añez, R., Rojas, J., & Bermúdez, V. (2014). Glucosamine for osteoarthritis: biological effects, clinical efficacy, and safety on glucose metabolism. Arthritis, 2014, 432463.

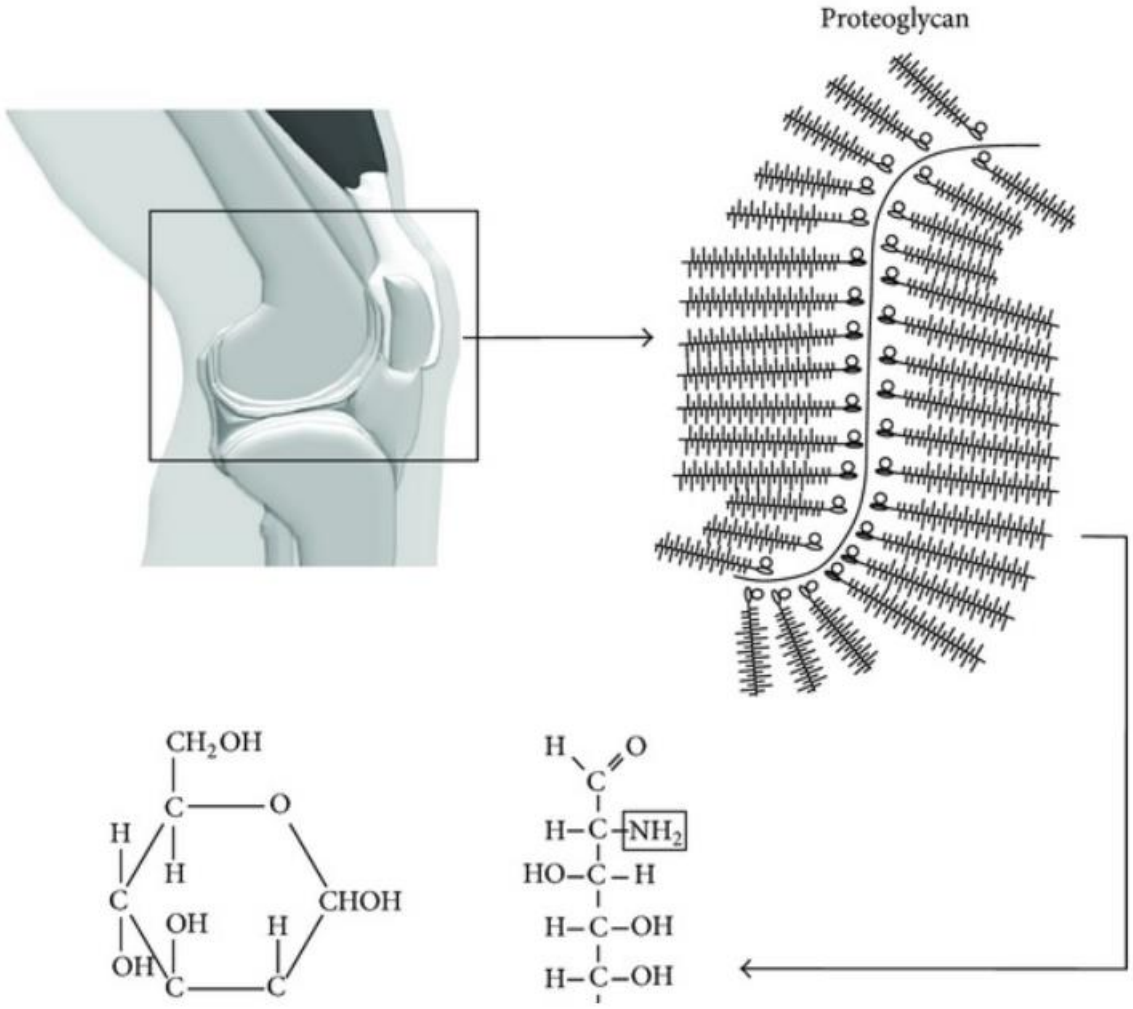
"Deeply investigated, herbal extract which increases tissue regeneration and promotes stem cell growth may be successfully applied in the field of biomaterials. Promoting the endogenous stem cell multipotency and their differentiation ***potential may additionally support the regenerative processes after MSCs transplantation.*** *"*

Kornicka, K., Kocherova, I., & Marycz, K. (2017). The effects of chosen plant extracts and compounds on mesenchymal stem cells-a bridge between molecular nutrition and regenerative medicine- concise review. Phytotherapy Research, 31(7), 947-958. doi:10.1002/ptr.5812

Management (treatment) of OA

1. Risk factor management and nonpharmacologic measures.
   - Education
   - Walking aids
   - Joint protection
   - Postural hygiene
   - Physical activity
   - Weight control
2. Rapid-acting drugs
   - Paracetamol
   - NSAIDs
   - Opioids
   - Intra-articular corticosteroids
3. Slow-acting drugs (SYSADOA)
   - Glucosamine
   - Chondroitin
   - Hyaluronic acid
   - Diacerein
4. Invasive methods
   - Articular lavage and infiltration
   - Surgical treatment

Salazar, J., Bello, L., Chávez, M., Añez, R., Rojas, J., & Bermúdez, V. (2014). Glucosamine for osteoarthritis: biological effects, clinical efficacy, and safety on glucose metabolism. Arthritis, 2014, 432463.



What is Glucosamine?

An amino-monosaccharideessential and a noncellular component of connective tissue, cartilage, ligaments, and other structures. (1)

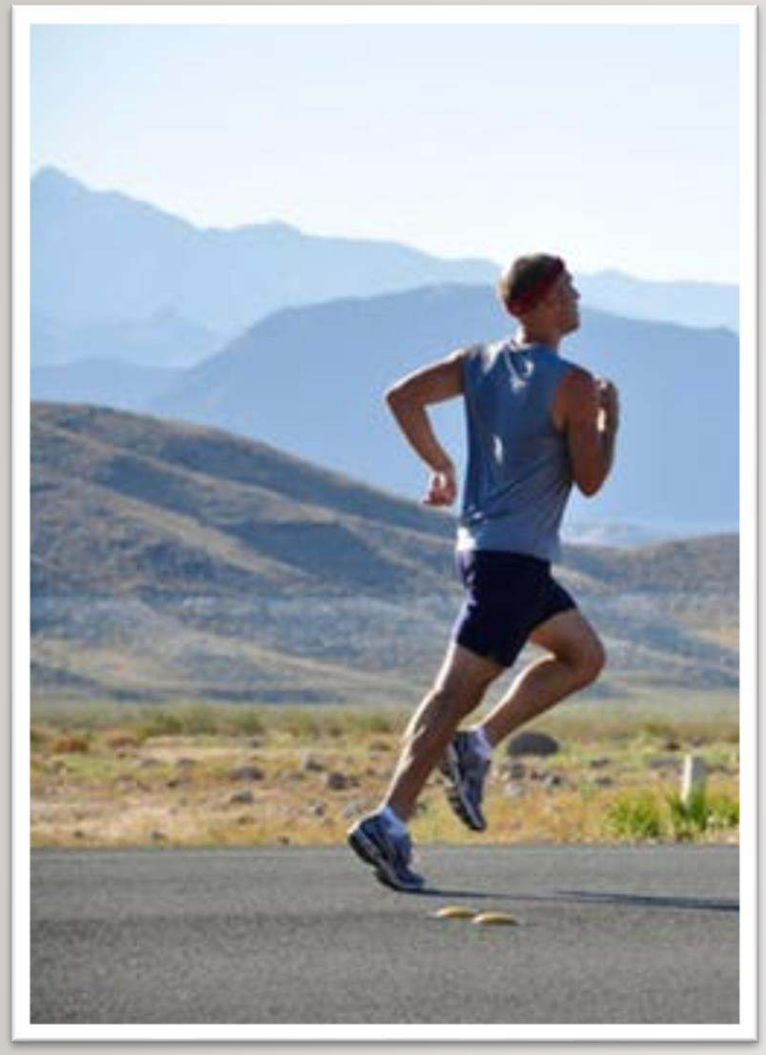
The main compounds:
glucosamine hydrochloride,
glucosamine sulfate,
N-acetylglucosamine. (2)

1. Anderson, JW., Nicolosi, RJ., Borzelleca, JF. (2005) Glucosamine effects in humans: a review of effects on glucose metabolism, side effects, safety considerations and efficacy. Food Chem Toxicol. 43(2), 187-201.
2. Salazar, J., Bello, L., Chávez, M., Añez, R., Rojas, J., & Bermúdez, V. (2014). Glucosamine for osteoarthritis: biological effects, clinical efficacy, and safety on glucose metabolism. Arthritis, 432463.

Systemic review: Clinical effectiveness of glucosamine and chondroitin in OA

- "Inconsistent conclusions with only modest effects on reported pain and function."
- "A reduction in joint space narrowing was more consistently observed."
- "The biological mechanism of glucosamine sulphate and chondroitin remains uncertain."

Black, C., Clar, C., Henderson, R., Maceachern, C., Mcnamee, P., Quayyum, Z., . . . Thomas, S. (2009). The clinical effectiveness of glucosamine and chondroitin supplements in slowing or arresting progression of osteoarthritis of the knee: A systematic review and economic evaluation. Health Technology Assessment, 13(52). doi:10.3310/hta13520



Studies demonstrate that glucosamine has many favorable effects on cartilage:

- ✓ **Anabolic stimulating effect on cartilage synthesis.**
- ✓ **Inhibits by means of several anti-inflammatory**
- ✓ **Antioxidant activity**
- ✓ **Improves function/mobility of the joint**

In most trials, dosages of 1500 mg/day were used; the dose was as safe as placebo and was tolerated better than NSAIDs.

(2011). Effects of Glucosamine and Chondroitin Sulfate on Cartilage Metabolism in OA: Outlook on Other Nutrient Partners Especially Omega-3 Fatty Acids. International journal of rheumatology, 2011, 969012.

eular

fighting rheumatic & musculoskeletal diseases together

"In the European League Against Rheumatism (EULAR) recommendation concerning knee OA, they gave CS both the highest evidence grade and the highest recommendation strength, 1A and A, respectively."

ULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT).
Jordan KM, Arden NK, Doherty M, Bannwarth B, Bijlsma JW, Dieppe P, Gunther K, Hauselmann H, Herrero-Beaumont G, Kaklamanis P, Lohmander S, Leeb B, Lequesne M, Mazieres B, Martin-Mola E, Pavelka K, Pendleton A, Punzi L, Serni U, Swoboda B, Verbruggen G, Zimmerman-Gorska I, Dougados M, Standing Committee for International Clinical Studies Including Therapeutic Trials ESCISIT.
Ann Rheum Dis. 2003 Dec; 62(12):1145-55.

Curcumin is derived from the rhizomes (underground stems) of the plant Curcuma longa.

Curcumin has powerful antioxidant and anti-inflammatory properties, and is the most active constituent of turmeric.

Curcumin: Clinical Dosage

Meta-analysis of randomized clinical trials (RCTs) provides evidence that supports the efficacy of turmeric extract (about 1000 mg/day of curcumin) in the treatment of arthritis

Daily, J. W., Yang, M., & Park, S. (2016). Efficacy of Turmeric Extracts and Curcumin for Alleviating the Symptoms of Joint Arthritis: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. Journal of Medicinal Food, 19(8), 717–729. http://doi.org/10.1089/jmf.2016.3705

367 primary knee osteoarthritis patients with a pain score of 5 or higher were randomized to receive **ibuprofen 1,200** mg/day or **Curcumin extract 1,500** mg/day for 4 weeks

The capsules were identical in appearance and the patients were asked to take only these pills in three dosages

Clinical Interventions in Aging

Kuptniratsaikul, V., Dajpratham, P., Taechaarpornkul, W., Buntragulpoontawee, M., Lukkanapichonchut, P., Chootip, C., … Laongpech, S. (2014). Efficacy and safety of Curcuma domestica extracts compared with ibuprofen in patients with knee osteoarthritis: a multicenter study. Clinical Interventions in Aging, 9, 451–458. http://doi.org/10.2147/CIA.S58535

After 4 weeks the study concluded that:

Curcumin extracts are as effective as ibuprofen for the treatment of knee osteoarthritis.

Number of events of abdominal pain/discomfort was significantly higher in the ibuprofen group

Clinical Interventions in Aging

Kuptniratsaikul, V., Dajpratham, P., Taechaarpornkul, W., Buntragulpoontawee, M., Lukkanapichonchut, P., Chootip, C., … Laongpech, S. (2014). Efficacy and safety of Curcuma domestica extracts compared with ibuprofen in patients with knee osteoarthritis: a multicenter study. Clinical Interventions in Aging, 9, 451–458. http://doi.org/10.2147/CIA.S58535

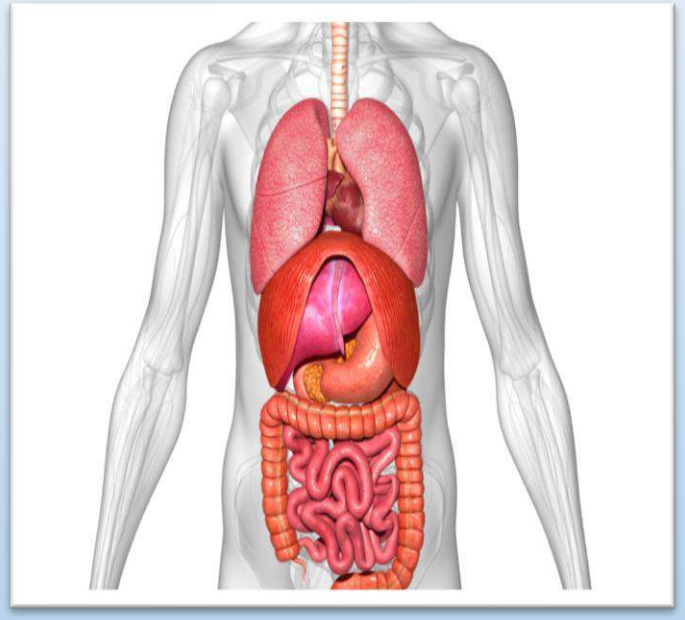
Animal studies show that **Curcumin stimulated neural stem cells proliferation**, and in combination with stem cell therapy, **induced profound recovery from severe spinal cord** injury as evidenced by improved functional locomotor recovery, increased body weight, and soleus muscle mass

Ormond, D. R., Shannon, C., Oppenheim, J., Zeman, R., Das, K., Murali, R., & Jhanwar-Uniyal, M. (2014). Stem cell therapy and curcumin synergistically enhance recovery from spinal cord injury. *PloS one*, *9*(2), e88916. doi:10.1371/journal.pone.0088916

Findings demonstrate that curcumin in conjunction with stem cell therapy synergistically improves recovery from severe spinal cord injury.

Ormond, D. R., Shannon, C., Oppenheim, J., Zeman, R., Das, K., Murali, R., & Jhanwar-Uniyal, M. (2014). Stem cell therapy and curcumin synergistically enhance recovery from spinal cord injury. *PloS one*, *9*(2), e88916. doi:10.1371/journal.pone.0088916

Curcumin Bioavailability



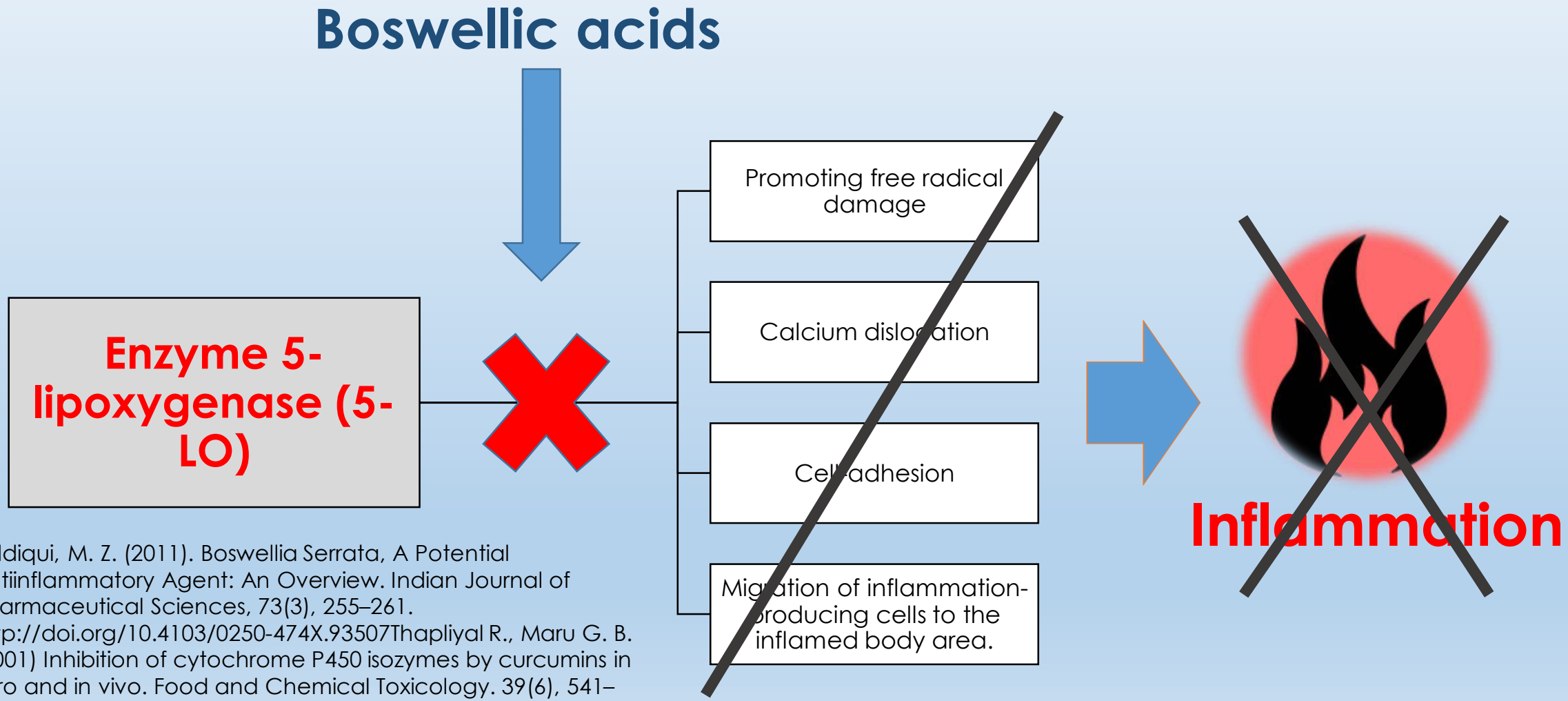
- Low bioavailability for local GI inflammatory diseases
- Higher bioavailability for systemic inflammation (e.g. joints)
- Adding piperine, the major active component of black pepper, to curcumin has been shown to increase bioavailability by 2000%

Hewlings, S. J., & Kalman, D. S. (2017). Curcumin: A Review of Its' Effects on Human Health. Foods, 6(10), 92. http://doi.org/10.3390/foods6100092

Boswellia Serrata

A natural and affordable agent that can reduce the inflammatory process

Boswellia Serrata



Siddiqui, M. Z. (2011). Boswellia Serrata, A Potential Antiinflammatory Agent: An Overview. Indian Journal of Pharmaceutical Sciences, 73(3), 255–261. http://doi.org/10.4103/0250-474X.93507Thapliyal R., Maru G. B. (2001) Inhibition of cytochrome P450 isozymes by curcumins in vitro and in vivo. Food and Chemical Toxicology. 39(6), 541–547, doi: 10.1016/S0278-6915(00)00165-4.

Boswellia Serrata

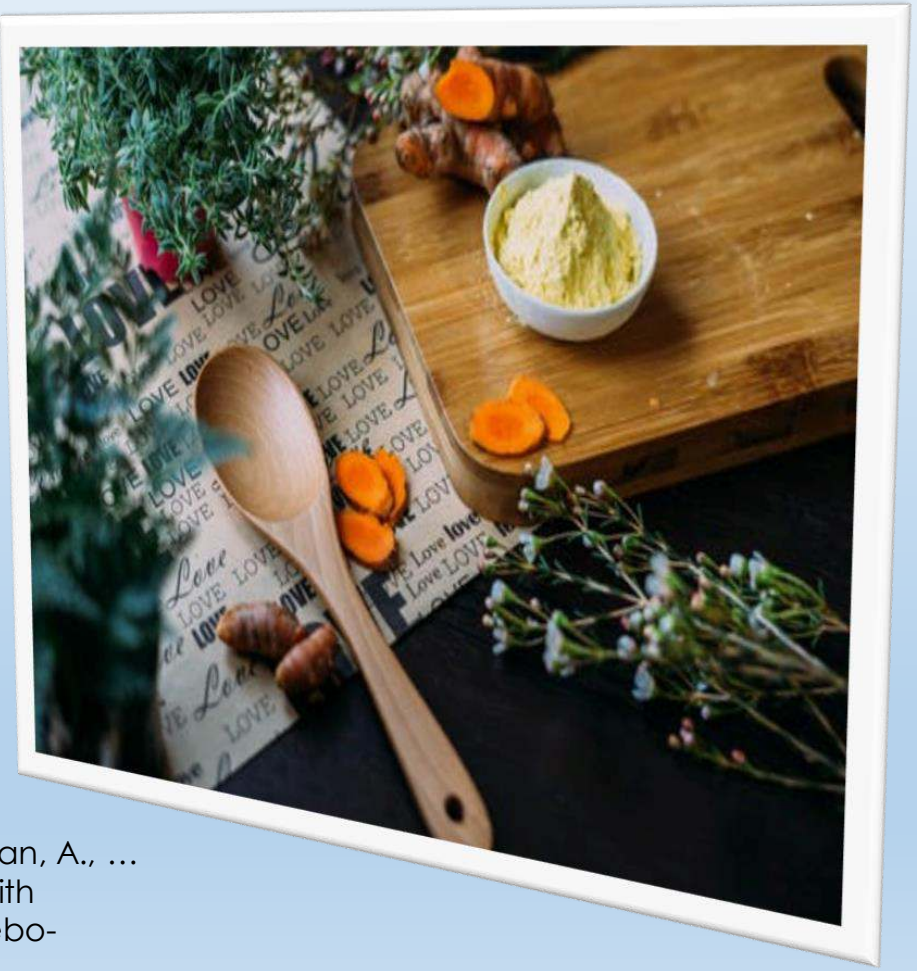
Curcumin combined with boswellic acid extract led to improvement in physical performance and reduction in joint pain and morning stiffness. The use of Boswellia and curcumin supplements was well tolerated and safe. (1)

1. Haroyan, A., Mukuchyan, V., Mkrtchyan, N., Minasyan, N., Gasparyan, S., Sargsyan, A., … Hovhannisyan, A. (2018). Efficacy and safety of curcumin and its combination with boswellic acid in osteoarthritis: a comparative, randomized, double-blind, placebo-controlled study. BMC Complementary and Alternative Medicine, 18, 7. http://doi.org/10.1186/s12906-017-2062-z

Boswellia Serrata

Recommended dosage of Boswellia is 500 to 1,000mg twice a day.

The use of Boswellia and curcumin supplements was well tolerated and safe. (1)



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Omega-3 fatty acids are long-chain polyunsaturated essential fatty acids (PUFAs)

Omega-3 fatty acids

A randomized, double blind trial, of 12 weeks of treatment with six n-3 PUFA capsules (**3.6 g per day**)

Significant improvement of morning stiffness and joint tenderness with consumption of omega-3 supplement

Nielsen GL, Faarvang KL, Thomsen BS, Teglbjaerg KL, Jensen LT, Hansen TM, Lervang HH, Schmidt EB, Dyerberg J, Ernst E. (1992) The effects of dietary supplementation with n-3 polyunsaturated fatty acids in patients with rheumatoid arthritis: a randomized, double blind trial. Eur J Clin Invest, 22(10), 687-91.

Anti-Inflammatory Effect of Fish Oil: Omega 3

Animal studies show that fish oil could serve as promising source of chondroprotective agents.

"Our results showed that DHA and EPA as well as omega-3 sources could suppress matrix degradation in cytokine-induced cartilage"

Myers, S. P., & Oliver, C. (2017). Effects of different omega-3 sources, fish oil, krill oil, and green-lipped mussel against cytokine-mediated canine cartilage degradation. In Vitro Cell Dev Biol Anim. 2017 doi: 10.1007/s11626-016-0125-y. In Vitro Cellular & Developmental Biology - Animal, 53(9), 775-775. doi:10.1007/s11626-017-0188-4

Fish oil in knee osteoarthritis: a randomised clinical trial of low dose versus high dose

Catherine L Hill,[1,2] Lynette M March,[3] Dawn Aitken,[4] Susan E Lester,[1] Ruth Battersby,[1] Kristin Hynes,[3] Tanya Fedorova,[3] Susanna M Proudman,[5] Michael James,[5] Leslie G Cleland,[5] Graeme Jones[3]

Handling editor Tore K Kvien

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/annrheumdis-2014-207169).

[1]Rheumatology Unit, The Queen Elizabeth Hospital, Woodville, South Australia
[2]University of Adelaide, The Health Observatory, Adelaide,

ABSTRACT

Objectives To determine whether high-dose fish oil is superior to low-dose supplementation for symptomatic and structural outcomes in knee osteoarthritis (OA).

Methods A randomised, double-blind, multicentre trial enrolled 202 patients with knee OA and regular knee pain. They were randomised 1:1 to high-dose fish oil (4.5 g omega-3 fatty acids) 15 mL/day or (2) low-dose fish oil (blend of fish oil and sunola oil; ratio of 1:9, 0.45 g omega-3 fatty acids) 15 mL/day. The primary

Since synovitis and cartilage degradation are common to both RA and OA, it is possible that fish oil may be useful in OA.

Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), the main omega-3 fatty acids in fish oil, decrease synthesis of the cyclooxygenase omega-6 fatty acid metabolite, prostaglandin E2 also a target of NSAID action. EPA and DHA are also precursors of the E-resolvins and D-resolvins that suppress inflammatory cytokine production

No change in serum C reactive protein. Low-dose fish oil resulted in better pain and function scores at 18 and 24 months compared with high-dose fish oil.

Received 17 December 2014
Revised 17 August 2015
Accepted 19 August 2015

Conclusions In people with symptomatic knee OA, there was no additional benefit of a high-dose fish oil compared with low-dose fish oil. The combination

spread. An Australian study of 260 000 people reported 32.6% had taken omega-3 supplements within the past four weeks with presence of OA

A total of 302 participants:

High-dose fish oil supplying 4.5 g EPA+DHA per day vs low dosage of 0.45 g EPA+DHA per day, (equivalent to 1.5 standard 1 g fish oil capsule daily)

Hill CL, March LM, Aitken D. (2016) Fish oil in knee osteoarthritis: a randomised clinical trial of low dose versus high dose Annals of the Rheumatic Diseases. 75, 23-29.

If you increase consumption of omega-6 and reduce the consumption of omega-3, you increase the risk of chronic diseases and inflammation

Simopoulos AP. Omega-3 fatty acids in inflammation and autoimmune diseases. J Am Coll Nutr. 2002 Dec;21(6):495-505.

Anti-Inflammatory Effect of Fish Oil: Omega 3

- ✓ **Altered cell membrane phospholipid fatty acid composition**
- ✓ **Balance excess in n-6 linoleic acid which is typically consumed in 5 to 20-fold greater amounts than α-linolenic acid**
- ✓ **Inhibition of activation of the pro-inflammatory transcription factor nuclear factor kappa B**
- ✓ **Reducing expression of inflammatory genes, activation of the anti-inflammatory transcription factor NR1C3.**

Calder P.C. (2013). Omega-3 polyunsaturated fatty acids and inflammatory processes: nutrition or pharmacology?. British journal of clinical pharmacology, 75(3), 645-62.

Combining Glucosamine Chondroid and Omega 3

"…the treatment with chondroprotectives, such as glucosamine sulfate, chondroitin sulfate, hyaluronic acid, collagen hydrolysate, or nutrients, such as antioxidants and omega-3 fatty acids is a promising therapeutic approach."

Jerosch J. (2011). Effects of Glucosamine and Chondroitin Sulfate on Cartilage Metabolism in OA: Outlook on Other Nutrient Partners Especially Omega-3 Fatty Acids. International journal of rheumatology, 2011, 969012.

International Journal of Rheumatology

Resveratrol

Resveratrol is a natural polyphenol that is found in the skin of red grapes, cranberries, peanuts and root extracts of the weed Polygonum Cuspidatum

Camins, A., Junyent, F., Verdaguer, E., Beas-Zarate, C., Rojas-Mayorquín, A. E., Ortuño-Sahagún, D., & Pallàs, M. (2009). Resveratrol: An Antiaging Drug with Potential Therapeutic Applications in Treating Diseases. Pharmaceuticals (Basel, Switzerland), 2(3), 194-205.

Resveratrol

Resveratrol showed **antioxidant and immunomodulatory** effects for some autoimmune diseases, such as **rheumatoid arthritis, systemic lupus** erythematosus, **psoriasis**, **inflammatory bowel diseases**, and **type 1 diabetes** mellitus.

JBC JOURNAL OF BIOLOGICAL CHEMISTRY

nutrients

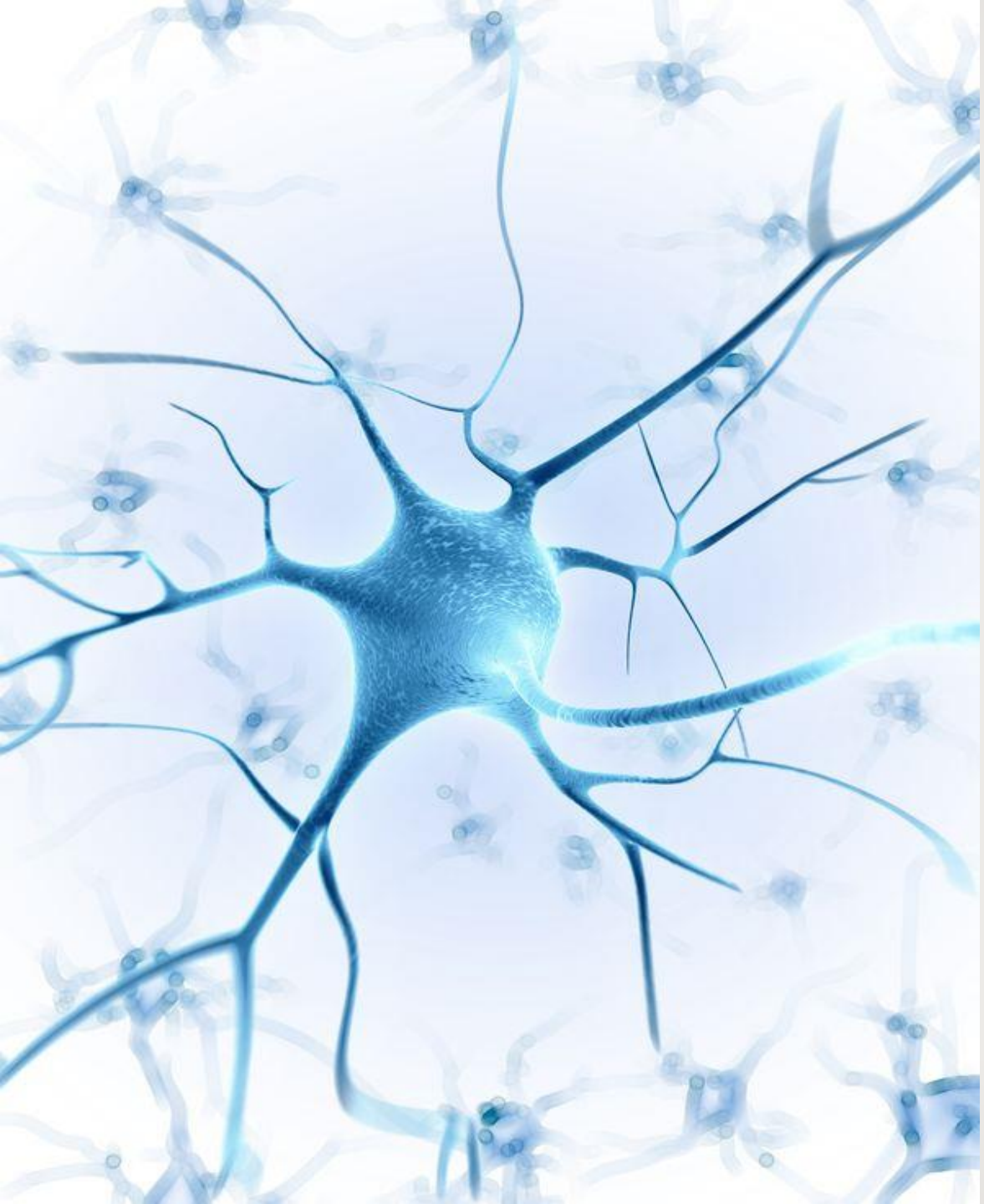
Resveratrol reduces the inflammatory process by inhibiting proinflammatory cytokines and T-cell differentiation.

1. Oliveira, A. L. de B., Monteiro, V. V. S., Navegantes-Lima, K. C., Reis, J. F., Gomes, R. de S., Rodrigues, D. V. S., … Monteiro, M. C. (2017). Resveratrol Role in Autoimmune Disease—A Mini-Review. Nutrients, 9(12), 1306. http://doi.org/10.3390/nu9121306
2. Mobasheri, A., Shayan, P., Lueders, C., Stahlmann, R., & Shakibaei, M. (2012). Resveratrol Modulates Interleukin-1β-induced Phosphatidylinositol 3-Kinase and Nuclear Factor κB Signaling Pathways in Human Tenocytes. Journal of Biological Chemistry, 287(45), 38050-38063. doi:10.1074/jbc.m112.377028 Retrieved from http://www.jbc.org/content/287/45/38050.full.html

Resveratrol Dosage

No standard dosage was found

My recommendation:
500mg Japanese Knotweed (Polygonum cuspidatum) Root Extract (standardized for 50% Trans-Resveratrol, **yielding 250 mg**) TD



Nutritional & Supplements Protocol for Nerve Regeneration

"Resveratrol treatment significantly increased the mRNA and protein expression levels of neuronal markers"

"The ratio of neuron-like cells was about 5% (Figure 1). However, with resveratrol (30.0 mg/L) treatment of hUC-MSCs for 1 h, the ratio of neuron-like cells reached 50%."

Guo, L., Wang, L., Wang, L., Yun-Peng, S., Zhou, J. J., Zhao, Z., & Li, D. P. (2017). Resveratrol Induces Differentiation of Human Umbilical Cord Mesenchymal Stem Cells into Neuron-Like Cells. Stem cells international, 2017, 1651325.

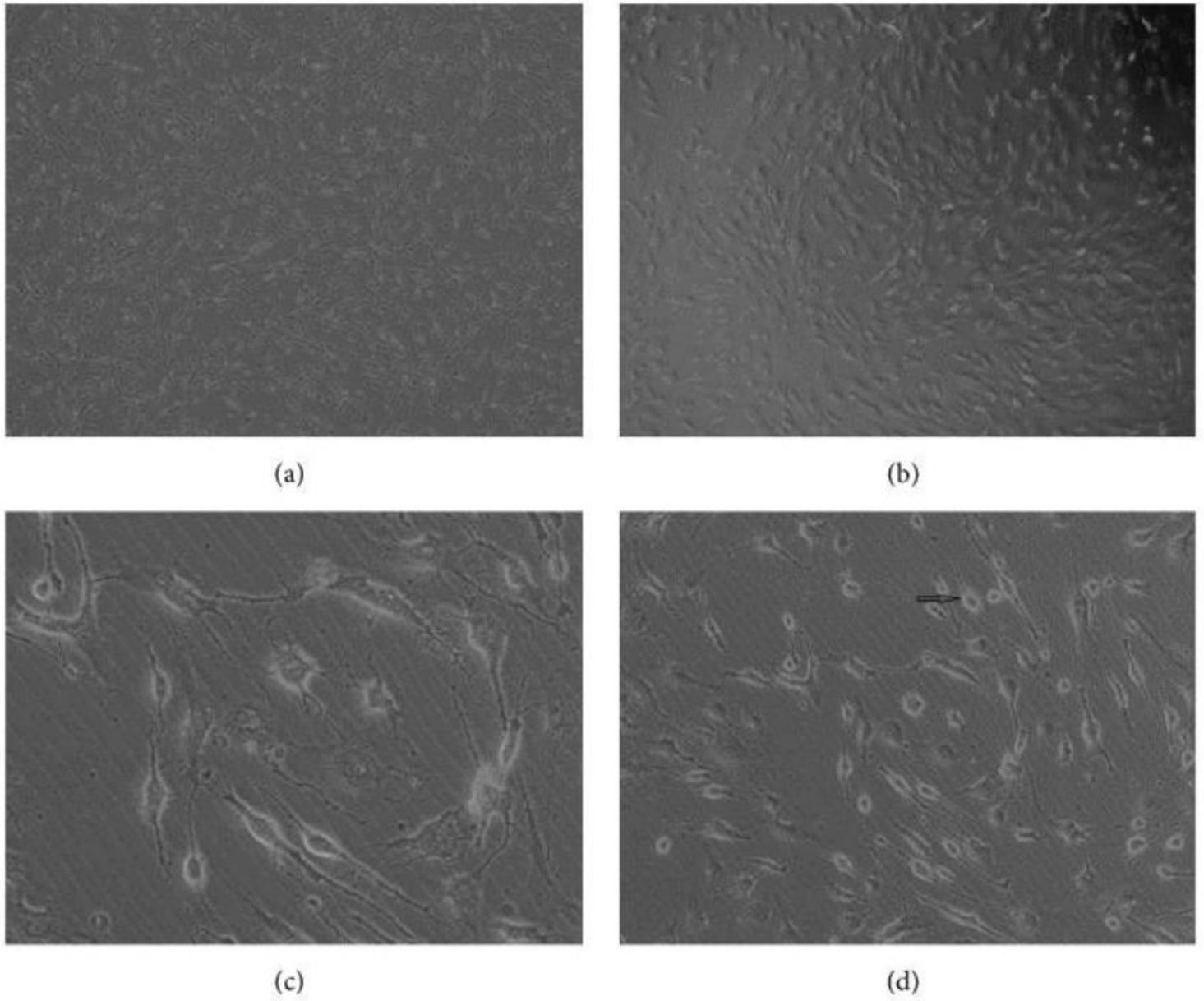
INTERNATIONAL JOURNAL OF STEM CELLS

"Furthermore, the cells appeared connected into a net-like pattern. After 6 h treatment with resveratrol (30 mg/L), 85%~90% of the hUC-MSCs displayed neuron-like shape"

INTERNATIONAL JOURNAL OF STEM CELLS

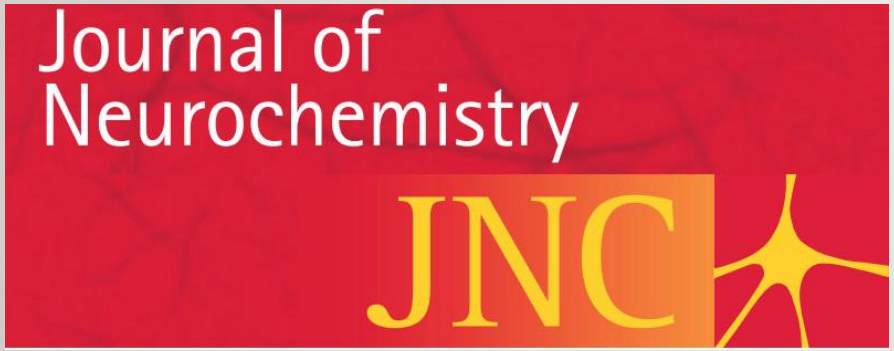
Guo, L., Wang, L., Wang, L., Yun-Peng, S., Zhou, J. J., Zhao, Z., & Li, D. P. (2017). Resveratrol Induces Differentiation of Human Umbilical Cord Mesenchymal Stem Cells into Neuron-Like Cells. Stem cells international, 2017, 1651325.

Images showing that different concentrations of resveratrol (0.0 mg/L (a), 7.5 mg/L (b), 15.0 mg/L (c), and 30.0 mg/L (d)) induce differentiation of hUC-MSCs into neuron-like cells.



Guo, L., Wang, L., Wang, L., Yun-Peng, S., Zhou, J. J., Zhao, Z., & Li, D. P. (2017). Resveratrol Induces Differentiation of Human Umbilical Cord Mesenchymal Stem Cells into Neuron-Like Cells. Stem cells international, 2017, 1651325.

Zinc deficiency impairs the renewal of neural stem cells in the hippocampus.



Han J, Zhao J, Jiang J, Ma X, Liu X, Wang C, Jiang S, Wan C. Zinc deficiency impairs the renewal of hippocampal neural stem cells in adult rats: involvement of FoxO3a activation and downstream p27(kip1) expression. J Neurochem. 2015 Sep;134(5):879-91. doi: 10.1111/jnc.13199. Epub 2015 Jul 7.

Zinc deficiency impairs the renewal of neural stem cells in the hippocampus.

Eat food high in zinc:
beef, lamb, spinach, pumpkin seeds, squash seeds, nuts, dark chocolate, chicken, beans, and mushrooms

Han J, Zhao J, Jiang J, Ma X, Liu X, Wang C, Jiang S, Wan C. Zinc deficiency impairs the renewal of hippocampal neural stem cells in adult rats: involvement of FoxO3a activation and downstream p27(kip1) expression. J Neurochem. 2015 Sep;134(5):879-91. doi: 10.1111/jnc.13199. Epub 2015 Jul 7.

Astragalus Membranaceus *was found to have antioxidant, anti-inflammatory, immunoregulatory, anticancer, hypolipidemic, antihyperglycemic, and hepatoprotective properties.(1)*

It enhances the survival of bone-marrow-derived mesenchymal stem cells.(2)

1. Liu, P., Zhao, H., & Luo, Y. (2017). Anti-Aging Implications of Astragalus Membranaceus (Huangqi): A Well-Known Chinese Tonic. Aging and disease, 8(6), 868-886. doi:10.14336/AD.2017.0816
2. Zhu XL, Zhu BD. Mechanisms by which Astragalus membranaceus injection regulates hematopoiesis in myelosuppressed mice. Phytother Res. 2007 Jul; 21(7):663-7.

A&D Aging and Disease
About Editorial Board Submission Archives

Ginkgo Biloba *enhances proliferation of neural stem cells in the subventricular zone and dentate gyrus, and significantly improves learning and memory in rats with vascular dementia.*

Neural Regeneration Research

Wang, J., Chen, W., & Wang, Y. (2013). A ginkgo biloba extract promotes proliferation of endogenous neural stem cells in vascular dementia rats. Neural regeneration research, 8(18), 1655-62.

A 24-week randomized controlled trial with 404 outpatients ≥ 50 years diagnosed with mild to moderate dementia, Alzheimer's disease, or vascular dementia, with neuropsychiatric features.
240 mg once-daily preparation of Ginkgo biloba extract.

Pharmacopsychiatry

Ihl R, Tribanek M, Bachinskaya N, GOTADAY Study Group. Efficacy and tolerability of a once daily formulation of Ginkgo biloba extract EGb 761® in Alzheimer's disease and vascular dementia: results from a randomised controlled trial.
Pharmacopsychiatry. 2012 Mar; 45(2):41-6.

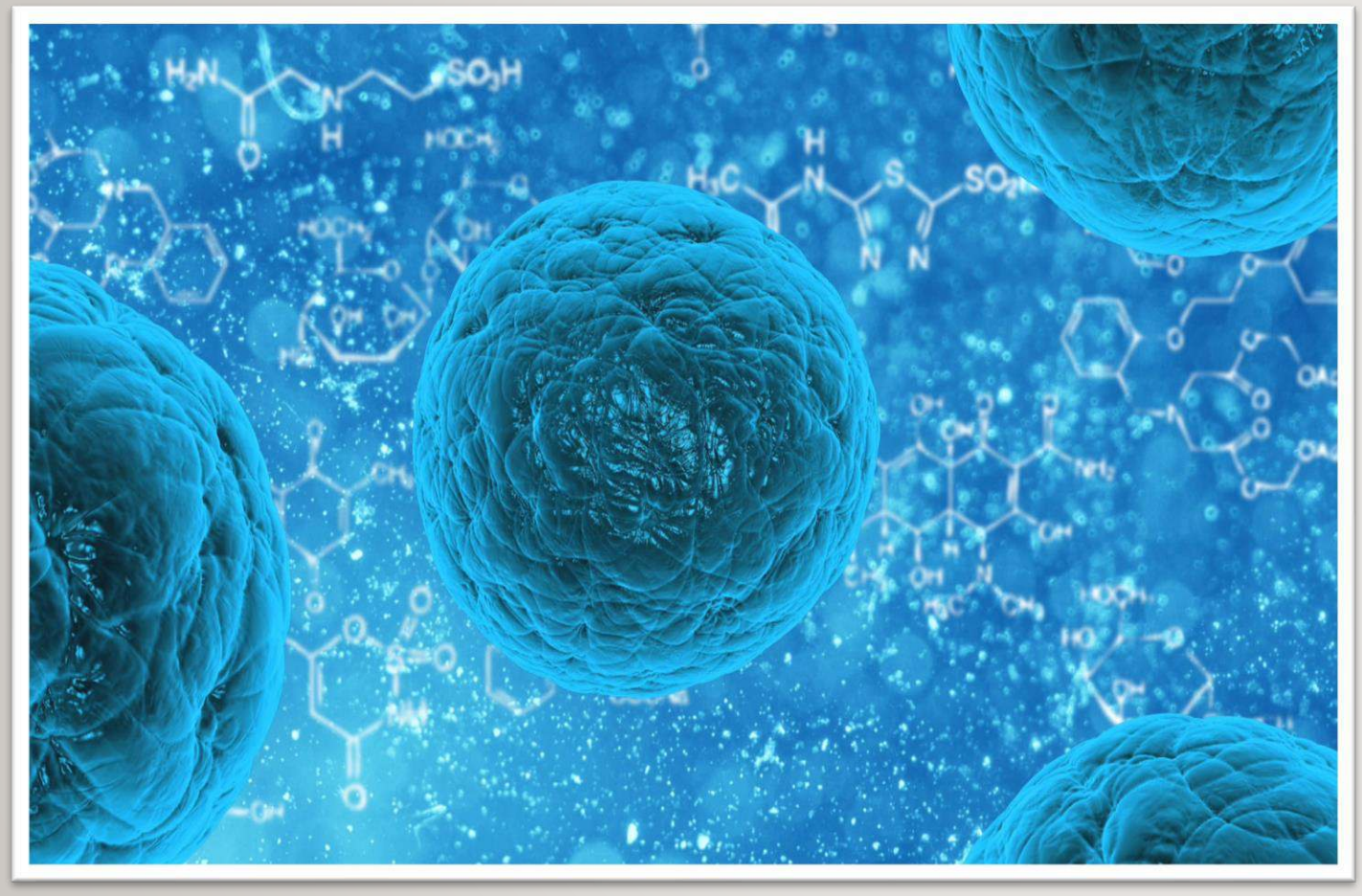
240 mg of Ginkgo Biloba once-daily improved cognitive functioning, neuropsychiatric symptoms and functional abilities in both types of dementia

Pharmacopsychiatry

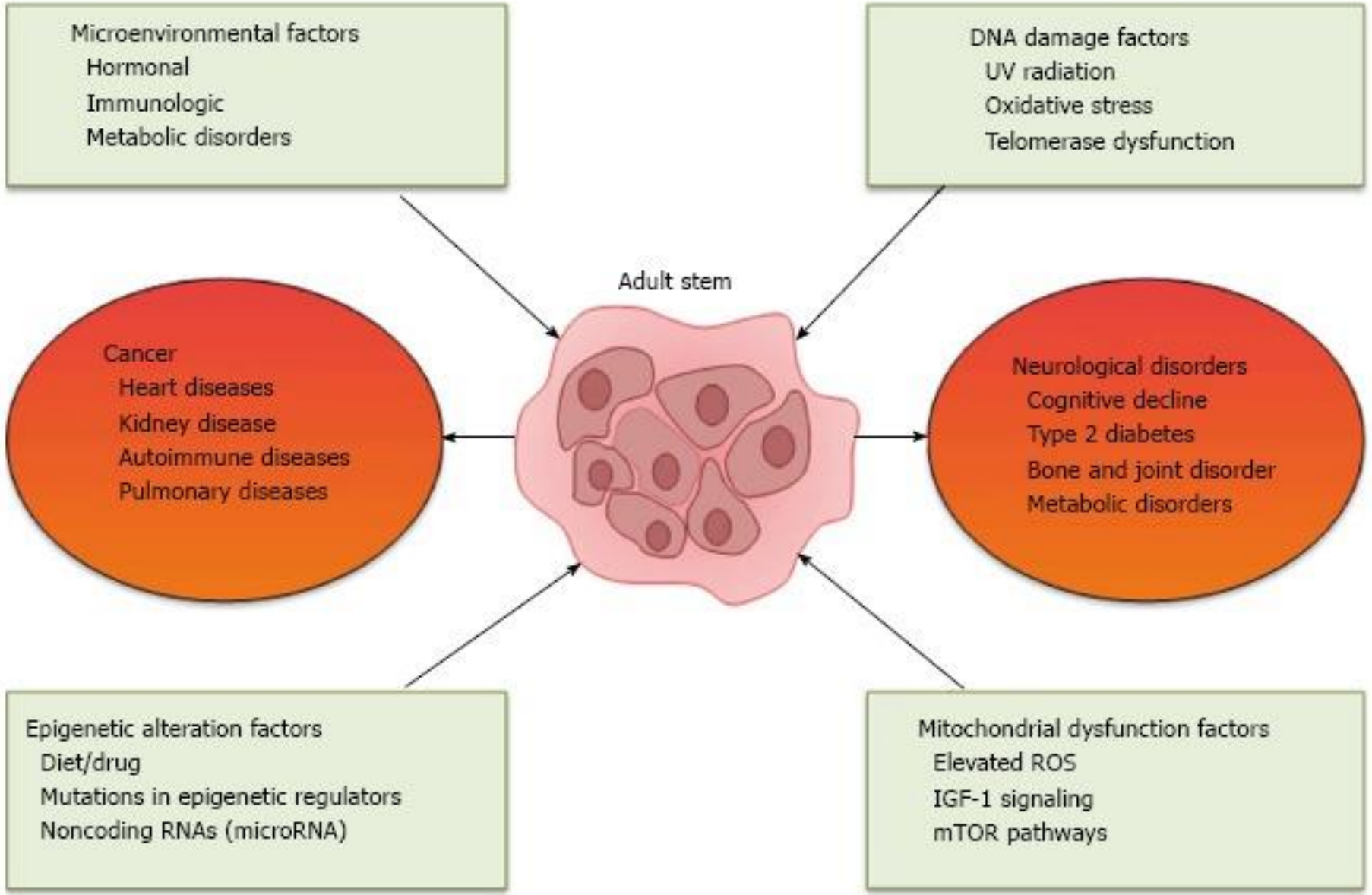
Ihl R, Tribanek M, Bachinskaya N, GOTADAY Study Group. Efficacy and tolerability of a once daily formulation of Ginkgo biloba extract EGb 761® in Alzheimer's disease and vascular dementia: results from a randomised controlled trial.

Pharmacopsychiatry. 2012 Mar; 45(2):41-6.

Protect Stem Cells From Damage



What can inhibit stem cells or reduce their ability to regenerate new tissue?



Ahmed, A. S. I., Sheng, M. H., Wasnik, S., Baylink, D. J., & Lau, K.-H. W. (2017). Effect of aging on stem cells. World Journal of Experimental Medicine, 7(1), 1–10. http://doi.org/10.5493/wjem.v7.i1.1

What damage our stem cells?

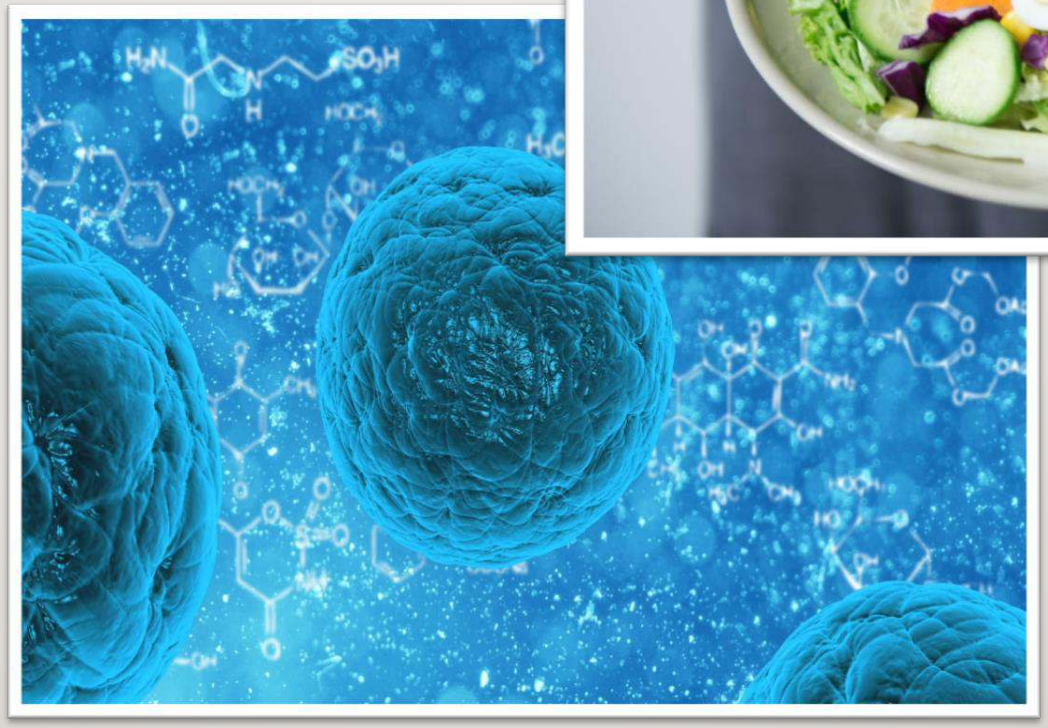
Drugs or Medications

Environmental toxins

UV Radiation and Free Radicles

Ahmed, A. S. I., Sheng, M. H., Wasnik, S., Baylink, D. J., & Lau, K.-H. W. (2017). Effect of aging on stem cells. World Journal of Experimental Medicine, 7(1), 1–10. http://doi.org/10.5493/wjem.v7.i1.1

Dietary Changes to Support Stem Cells Therapy



Reduce Exposure to Environmental Toxins

Organophosphates (insecticides and herbicides)

They are used heavily by farmers, and are found in non-organic vegetables, fruits, and animal products.

Are these dangerous?

"Studies suggest that pesticides may be related to various diseases, including **cancers**, as well as having **neurological, mental and reproductive effects**."

Cohen M. Environmental toxins and health--the health impact of pesticides. Australian Family Physician [serial online]. December 2007;36(12):1002-1004. Available from: MEDLINE Complete, Ipswich, MA. Accessed October 30, 2017.

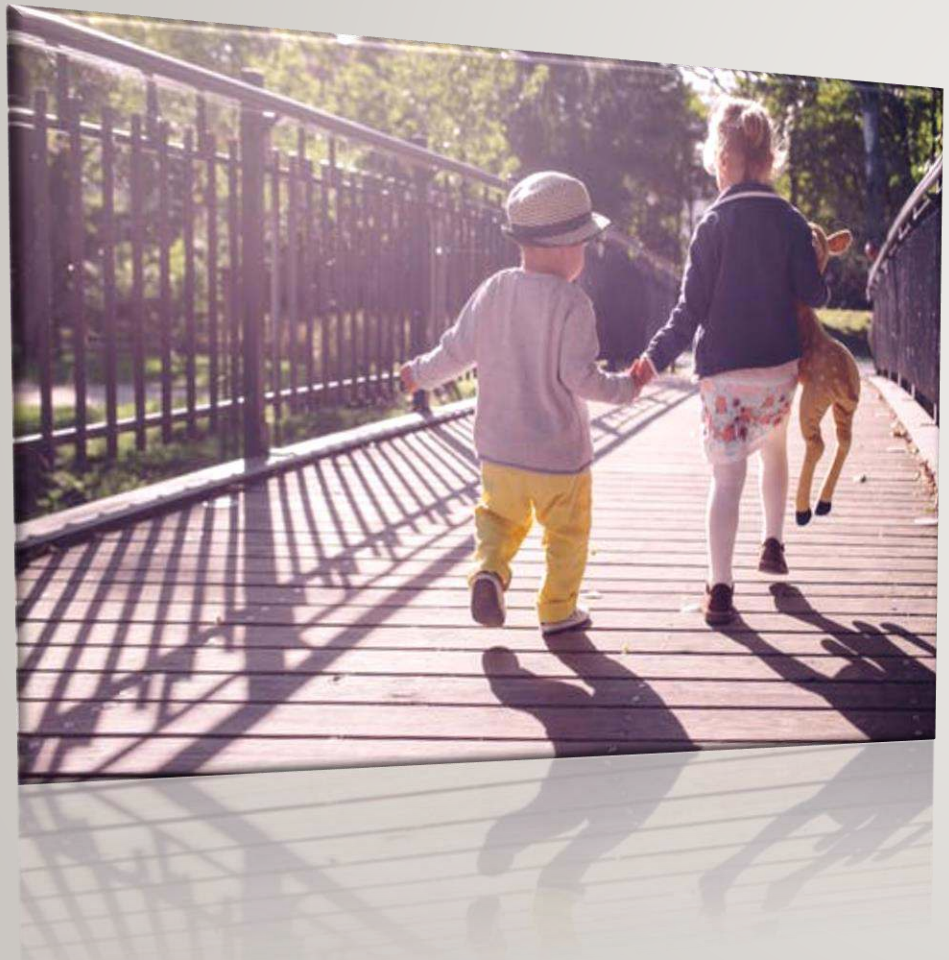
Organophosphates (insecticides and herbicides)

A study conducted in Seattle, Washington.

Measured dietary organophosphorus pesticide exposure in a group of 23 elementary school-age children through urinary biomonitoring twice a day.

They substituted most of children's conventional diets with organic food items for 5 consecutive days.

Organophosphates (insecticides and herbicides)



After five days on organic diet,

levels of pesticides <u>decreased</u> to the non-detected levels.

It also stayed ‘nondetectable’ until the conventional diets were reintroduced.

"In conclusion, we were able to demonstrate that an organic diet provides a dramatic and immediate protective effect against exposures to organophosphorus pesticides that are commonly used in agricultural production."

Lu C, Toepel K, Irish R, Fenske RA, Barr DB, Bravo R. Organic Diets Significantly Lower Children's Dietary Exposure to Organophosphorus Pesticides. *Environmental Health Perspectives*. 2006;114(2):260-263. doi:10.1289/ehp.8418.

Cruciferous Vegetables & Inflammation

Indole-3-Carbinol (I3C)enzyme, found in Cruciferous vegetables, inhibits expression of proinflammatory cytokines, such as interleukin-6 (IL-6).

Cruciferous vegetables, including broccoli, cauliflower, cabbage, brussels sprouts, rutabaga/swede, turnip, and watercress.

Chang, H.-P., Wang, M.-L., Hsu, C.-Y., Liu, M.-E., Chan, M.-H., & Chen, Y.-H. (2011). Suppression of inflammation-associated factors by indole-3-carbinol in mice fed high-fat diets and in isolated, co-cultured macrophages and adipocytes. International Journal of Obesity (2005), 35(12), 1530–1538. http://doi.org/10.1038/ijo.2011.12

Remove Foods that Increase Inflammation:

1. Sugar
2. Gluten (wheat)
3. Processed or fast food

"Sugar Sweetened Beverages may also increase T2DM and cardiovascular risk independent of obesity, as a potential contributor to a high dietary glycemic load and ***increased fructose metabolism leading to inflammation,*** *insulin resistance, impaired beta-cell function, and high blood pressure."*

Malik, V. S., Popkin, B. M., Bray, G. A., Després, J. P., & Hu, F. B. (2010). Sugar-sweetened beverages, obesity, type 2 diabetes mellitus, and cardiovascular disease risk. Circulation, 121(11), 1356-64.

Regular consumption of sugar-sweetened soda, but not diet soda, is **associated with increased risk of seropositive RA** in women, independent of other dietary and lifestyle factors.

Hu, Y., Costenbader, K. H., Gao, X., Al-Daabil, M., Sparks, J. A., Solomon, D. H., Hu, F. B., Karlson, E. W., … Lu, B. (2014). Sugar-sweetened soda consumption and risk of developing rheumatoid arthritis in women. The American journal of clinical nutrition, 100(3), 959-67.

"Gluten-containing diet increased the level of potent pro-inflammatory (IL-17, IFN-γ) cytokines, as well as of IL-2 and IL-4."

Immunology

British Society for immunology

Antvorskov, J. C., Fundova, P., Buschard, K., & Funda, D. P. (2012). Dietary gluten alters the balance of pro-inflammatory and anti-inflammatory cytokines in T cells of BALB/c mice. Immunology, 138(1), 23-33.

Evidence from *in vitro*, *in vivo* and human intervention studies that describe how the consumption of wheat, but also other cereal grains, can contribute to the manifestation of chronic inflammation and autoimmune diseases by increasing intestinal permeability and initiating a pro-inflammatory immune response.

de Punder, K., & Pruimboom, L. (2013). The dietary intake of wheat and other cereal grains and their role in inflammation. Nutrients, 5(3), 771-87. doi:10.3390/nu5030771

Healthy Fats: (up your intake, it fuels your brain and reduce inflammation)

- Avocado
- Coconut oil
- Olive oil
- Butter or Ghee from Grass Fed Cows
- Omega 3 from fish, seafood, or seaweed.

Healthy Protein (without hormones or antibiotics).

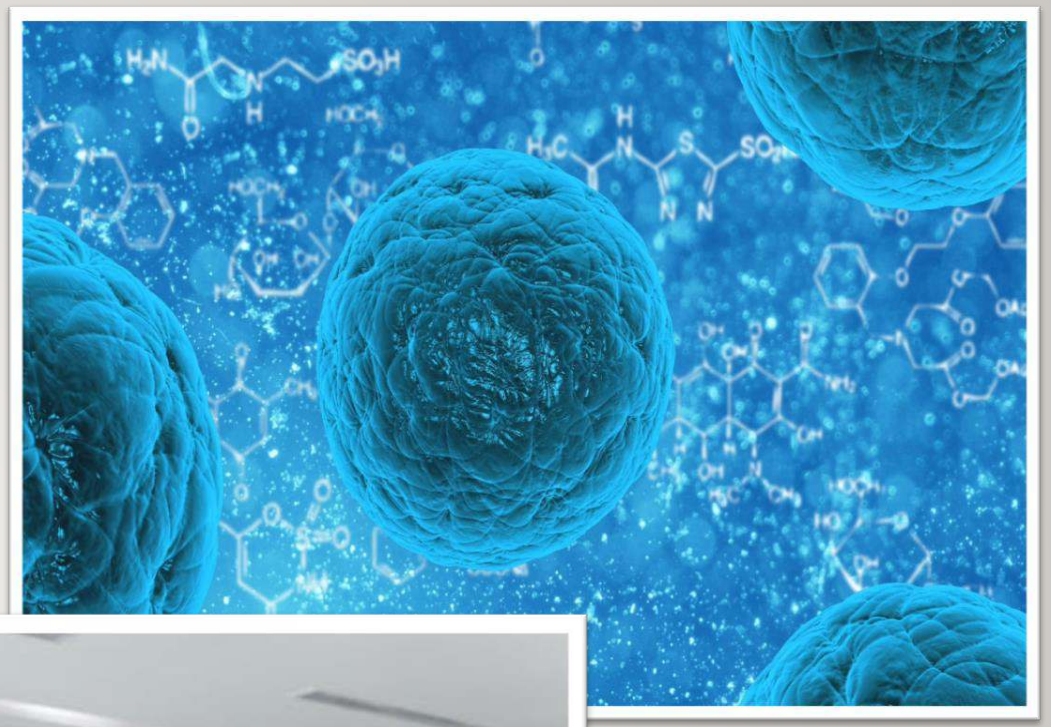
- Grass-fed Beef or Bison
- Pastured Eggs (organic/free range)
- Sockeye Salmon (wild caught)
- Chicken (organic, free range, anti-biotic free)

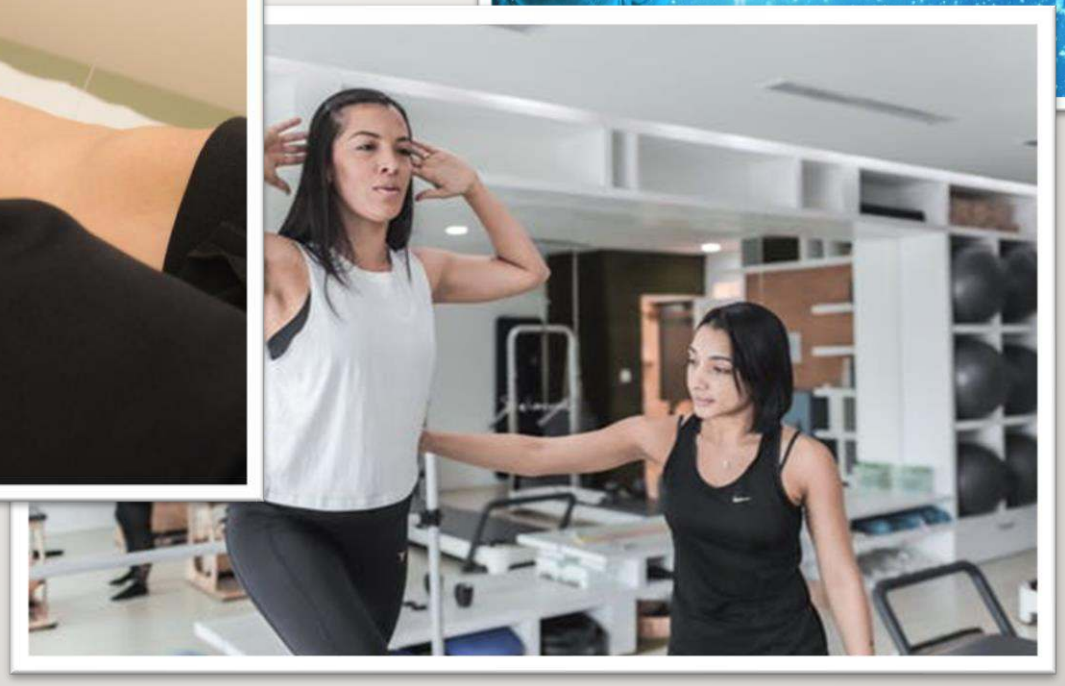
Avoid tuna fish or canned food!

Healthy carbs: (up your intake, it fuels your brain and reduce inflammation)

- Quinoa
- Organic brown rice
- Lintel noodles/pasta (gluten free)
- Yams and other root vegetables
- Legumes: Hummus, beans

Supporting Treatments





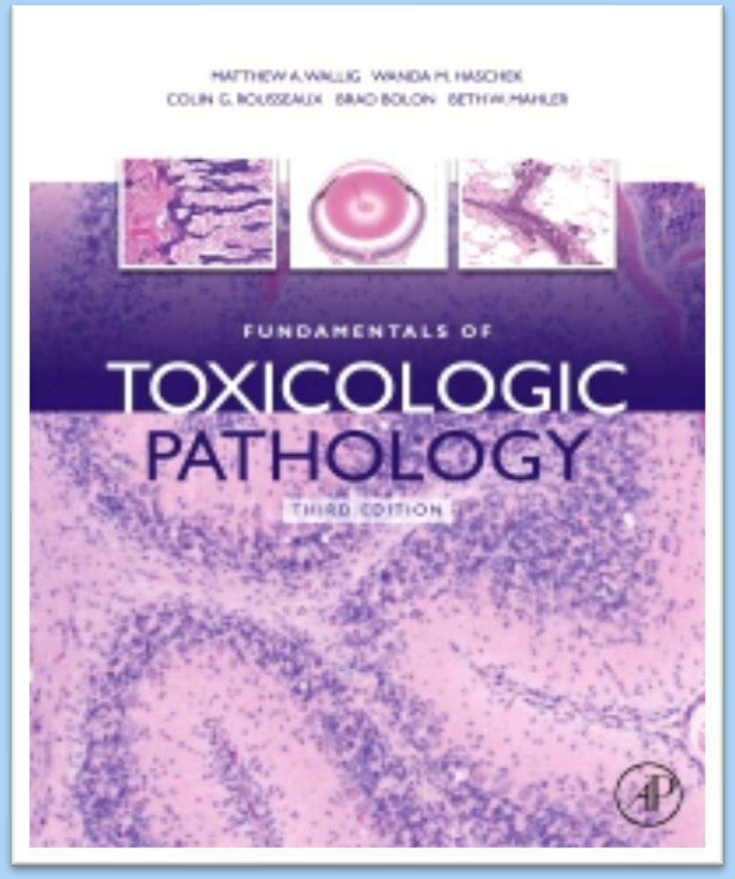
Why Our Therapies Work So Well

Acupuncture in certain points promotes the activity of stem cells and regeneration.

Jiang, S., Chen, W., Zhang, Y., Zhang, Y., Chen, A., Dai, Q., … Lin, H. (2016). Acupuncture Induces the Proliferation and Differentiation of Endogenous Neural Stem Cells in Rats with Traumatic Brain Injury. Evidence-Based Complementary and Alternative Medicine : eCAM, 2016, 2047412. http://doi.org/10.1155/2016/2047412

Why Our Therapies Work So Well

Stimulation with Electro-acupuncture can promote the activity of stem cells and regeneration.



Yan Q, Ruan J-W, Ding Y, Li W-J, Li Y, Zeng Y-S. Electro-acupuncture promotes differentiation of mesenchymal stem cells, regeneration of nerve fibers and partial functional recovery after spinal cord injury. Experimental and Toxicologic Pathology. 2011;63(1-2):151-156. doi:10.1016/j.etp.2009.11.002.

Role of Physical Therapy in OA Patients

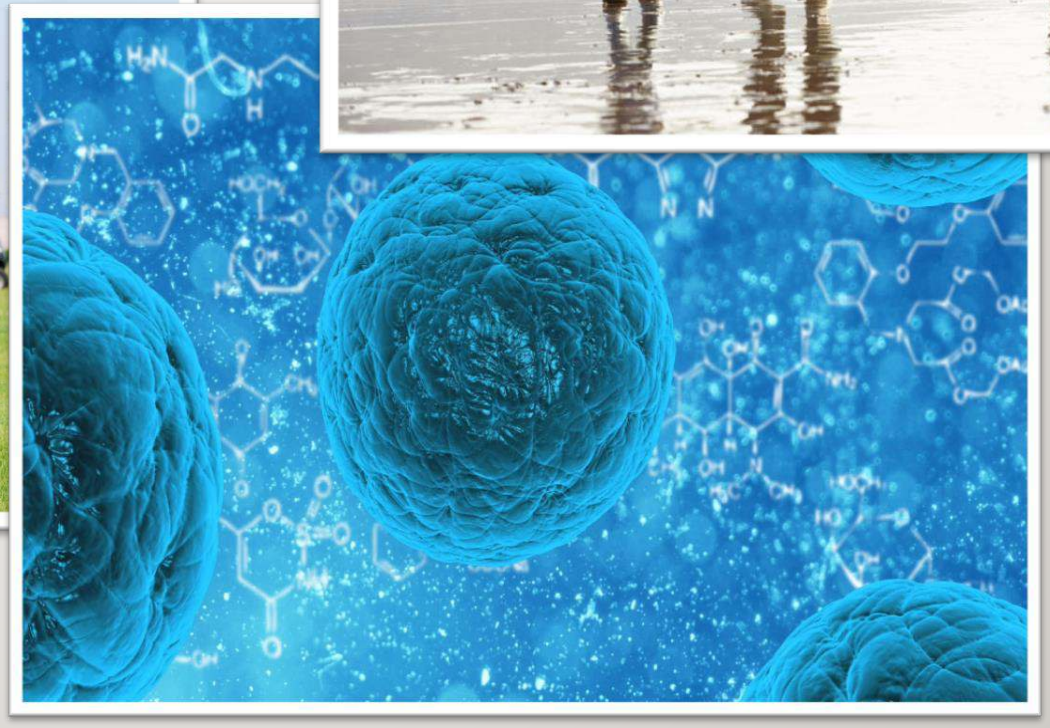
56 patients with knee OA were assigned into 2 random groups. Treatment group (NSAIDs and 10 sessions acupuncture)without exercise and treatment group with exercise for knee muscles.

Role of Physical Therapy in OA Patients

Patients with knee OA in exercise group had significant improvement in pain, disability, walking, stair climbing, and sit up speed after 1 and 3 months, as well as 1 year follow-up.

Nejati, P., Farzinmehr, A., & Moradi-Lakeh, M. (2015). The effect of exercise therapy on knee osteoarthritis: a randomized clinical trial. Medical journal of the Islamic Republic of Iran, 29, 186.

Guidelines After Stem Cell Therapy



Guideline: Stay active, but do not over use.

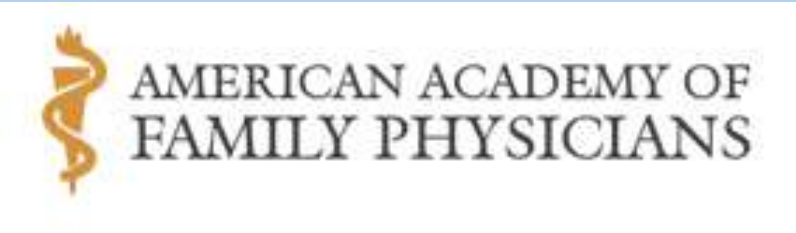
After joint injection:

- Ankle, knees, hips, or lower back injection avoid running or weights training for at least 30 days.
- Shoulders or back do not lift heavy for 2 months.
- Fingers or thumbs – avoid texting.

Considerations in treatment of patients with supplements

Herbs & Supplements: Interaction with Medication

- Curcumin (in high dosages) and blood thinners (e.g. Coumadin)
- Fish oil is safe to consume (my experience: 2g daily)
- Ginkgo no interaction with warfarin or aspirin directly
- Ginkgo demonstrated antiplatelet activity when combined with NSAID drugs, especially aspirin, might cause severe bleeding, including intracranial bleeding
- Resveratrol might interact with some medications. Use low amount (250mg/day)
- Do not recommend consumption of green vegetables with anti-coagulant drugs



American Academy of Family Physicians. (2018) Herbal and Dietary Supplement–Drug Interactions in Patients with Chronic Illnesses. Retrieved from https://pdfs.semanticscholar.org/0685/6ae00b3ca62eb770e4a7684d3a6299656fc2.pdf

Disadvantages for Use of Supplements in Stem Cell Therapy

- Supplements cost money
- Requires setup and inventory management
- Patients on anticoagulation medication are not a good fit for curcumin or resveratrol.

Advantages for Use of Supplements in Stem Cell Therapy

- ✓ **Improve results (reduction in inflammation, pain, etc.)**
- ✓ Charge for a **Stem Cell Program** instead of Stem Cell Injection.
- ✓ 50% of patients continue with supplements after 6 weeks (extra revenue: 10 patients x $150 = $1500/month)
- ✓ Patient actively participate in treatment process.

Supplements, Nutrition, and Lifestyle Medicine to Support Stem Cell Therapy

Thank you!

Tal Cohen, DAOM, Lac.

www.ANewWay.Clinic