Nutrizione e supplementazione
e nell’atleta infortunato
Nutraceutici in medicina dello sport

Processo di guarigione delle lesioni

Fase Infiammatoria
Fase Proliferativa
Fase di Rimodellamento

Modulare la risposta infiammatoria
- L’inattività è uno stato infiammatorio low-grade
- La risposta infiammatoria è necessaria nel processo di guarigione

Evitare una risposta infiammatoria eccessiva
Evitare uno stato infiammatorio prolungato

Bosutti A et al. *Calorie restriction modulates inactivity-induced changes in the inflammatory markers C-reactive protein and pentraxin-3.* J Clin Endocrinol Metab 2008; 93:3226-3229.
Tipton KD. *Nutrition for Acute Exercise-Induced Injuries.* Ann Nutr Metab 2010;57 (Suppl. 2):43-53
Characterization of inflammatory responses to eccentric exercise in humans

Running title: Inflammation and eccentric exercise

Jonathan Peake, Kazunori Nosaka, Katsuhiko Suzuki

During exercise
- mechanical damage to muscle tissue

After exercise
- leukocyte infiltration
- inflammation

Recovery
- proliferation of satellite cells
- acquisition of protective effect

Figure 1. Exercise-induced muscle damage and subsequent muscle inflammation and regeneration process (PMN, polymorphonuclear leucocyte; Mb, myoglobin; CK, creatine kinase; ROS, reactive oxygen species)
level of ATP could decrease to concentrations sufficiently low to induce muscle damage, particularly in the presence of severe glycogen depletion.

the activation of number of Ca2+ dependant proteolytic and phospholipolytic pathways, which degrade structural and contractile myofibre proteins as well as the myofibre membrane.

Phagocytic phase during which the inflammatory response allows the removal of damaged tissue, and the regenerative phase, during which the damaged muscle fibres repair.

Metabolic Stress Model

Metabolic consequences of exercise-induced muscle damage. Tee JC, Bosch AN, Lambert MI.
Oxidant stress and inflammation

Representation of the interaction between oxidant stress and inflammation. IκB, inhibitory subunit of NF-κB; IL, interleukin; NF-κB, nuclear factor κB; PG, prostaglandin; TNF, tumor necrosis factor.
Various dietary components including long chain ω-3 fatty acids, antioxidant vitamins, plant flavonoids, prebiotics and probiotics have the potential to modulate predisposition to chronic inflammatory conditions and may have a role in their therapy.

Concept of how nutrients might act in an anti-inflammatory manner.
Supplementation with long-chain n-3 polyunsaturated fatty acids (PUFA) consistently demonstrates an improvement in symptoms and a reduction in NSAID usage. Evidence relating to other fatty acids, antioxidants, zinc, iron, folate, other B vitamins, calcium, vitamin D and fluoride are also considered. The present evidence suggests that RA patients should consume a balanced diet rich in long-chain n-3 PUFA and antioxidants.
Foods containing compounds with anti-inflammatory and analgesic properties, that may help ease the symptoms of osteoarthritis as well as improve the overall health of patients.
alterations in gut microbiota, increased intestinal permeability, and metabolic endotoxemia likely play a role in the development of a chronic low-grade inflammatory state in the host that contributes to the development of obesity and associated chronic metabolic diseases.
Major Points where Dietary or Bacterial Metabolites Intersect with the Immune System
Muscle remodeling involves myogenesis, reinnervation, and revascularization and is regulated by multiple biochemical pathways, including those initiated by inflammatory cytokines, growth factors. Muscle repair coincides with injury-induced inflammation, and some inflammatory cytokines, such as IL-4, LIF, TGF-β, IL-6, and TNF-α regulate myogenic potential (Tidball, 2005). Damaged muscle produces monocyte and macrophage chemoattractants, and blockade of inflammatory cell infiltration impairs muscle regeneration (Chazaud et al., 2003; Jejurikar and Kuzon, 2003; Lescaudron et al., 1999), possibly due to a reduction in macrophage-secreted factors inducing myoblast proliferation (Bondesen et al., 2004; Robertson et al., 1993).
can be considered to have two main stages, either of which may be influenced by nutrition.

Stage 1: Tissue Repair, Immobilization and Atrophy

Stage 2: Rehabilitation and Hypertrophy
Immediately following a severe injury, an inflammatory response is initiated. The inflammatory response is necessary for proper healing.

Muscle loss is a decrease in the rate of muscle protein, particularly myofibrillar protein synthesis. Interestingly – perhaps unexpectedly to many – protein breakdown also decreases, at least in humans.
Metabolic consequences of exercise-induced muscle damage.

Tee JC, Bosch AN, Lambert MI.

Carbohydrate ingestion during early recovery from exercise-induced muscle injury may promote proinflammatory reactions within skeletal muscle.


Fig. 1. Muscle damage characteristics as determined by stress profile.

Tee JC, Bosch AN, Lambert MI.
delay in the restoration of muscle glycogen is likely due to a decrease in insulin sensitivity. Eccentric exercise causes damage to the sarcolemma and it is likely that this alteration in membrane integrity decreases the rate of insulin-stimulated glucose transport.

High dietary carbohydrate for 3 days after eccentric exercise did increase intramuscular carbohydrate storage.

carbohydrate administration has little or no effect in attenuating signs and symptoms of muscle damage.

muscle requires a prolonged period of time to recover from damage and that athletes should be cautious about competing too soon after an event that may have caused damage.
The anti-inflammatory effects of caloric restriction or ketogenic diets may be mechanistically linked to BHB-mediated inhibition of the NLRP3 inflammasome, and point to the potential use of interventions that elevate circulating BHB against NLRP3-mediated proinflammatory diseases.
Increased synthesis of myofibrillar proteins in response to resistance exercise will lead to hypertrophy of atrophied muscles. Moreover, tendon collagen synthesis is increased during rehabilitation from immobilization. Since, the energy cost of muscle protein synthesis is high, energy requirements will increase. The primary nutritional goal will be to support muscle growth and increased strength with rehabilitation and training.

**Fig. 3.** Flow diagram of the metabolic and functional changes in muscle and tendon when activity is restored following immobilization due to injury. Exercise and amino acids stimulate muscle and exercise stimulates tendon synthesis, thus restoring muscle size and function. Note that the time course of the return of muscle mass and strength is often much slower than the loss during immobilization.

The notion that dramatically increasing protein intake results in a proportional increase in muscle size and function is not supportable.


occurs with much less dietary protein than many believe necessary (e.g. approx. 1.4 g/kg/day)


The high-quality protein dose that appears to maximally stimulate muscle protein synthesis is close to 20–25 g; above this point protein synthesis is not additionally stimulated.
Table 2. Mechanisms of mTORC1 activation by Western diet

<table>
<thead>
<tr>
<th>Compound of Western diet</th>
<th>Mechanisms of mTORC1 activation</th>
</tr>
</thead>
<tbody>
<tr>
<td>High total calories (− high energy)</td>
<td>Reduced activity of AMPK</td>
</tr>
<tr>
<td>High glycemic load (− high energy)</td>
<td>Reduced activity of AMPK</td>
</tr>
<tr>
<td></td>
<td>Increased insulin signaling</td>
</tr>
<tr>
<td>High fat intake (− high energy)</td>
<td>Reduced activity of AMPK</td>
</tr>
<tr>
<td>High alcohol intake (− high energy)</td>
<td>Reduced activity of AMPK</td>
</tr>
<tr>
<td>High dairy protein intake (− high leucine)</td>
<td>Increased insulin/IGF-1 signaling and leucine-mediated mTORC1 activation</td>
</tr>
<tr>
<td>High meat intake (− high leucine)</td>
<td>Leucine- and IGF-1-mediated mTORC1 activation</td>
</tr>
</tbody>
</table>
Evaluation of protein undernourishment on the condylar process of the Wistar rat mandible correlation with insulin receptor expression.
Cavalli MA1, Gonçalves A1, Pereira JN1, Silva JB1, Boldrini Sde C2, Liberti EA2.

**Protein Undernourishment**

*our results suggest vitamin K is implicated in progression of several distinct pathologies of OA affected joint tissues.*

Increased protein intake may support increased protein turnover, but the amount necessary may not be as high as many believe ... A recent study suggested that increased protein intake enhances recovery from immobilization but other results are somewhat equivocal.

within total energy requirements and does not restrict the amount of carbohydrate or essential fat intake, then elevating protein intake may not be a problem. There seems little reason to increase protein intake with the goal of increasing tendon collagen synthesis. Neither muscle nor tendon collagen synthesis responds to provision of amino acids.

Sintesi proteica e rigenerazione muscolare

- Riduzione cellule satelliti
- Inflamazione cronica silente
- Danneggiamento ossidativo delle proteine e del DNA mitocondriale

Compromissione della capacità di riparare e rigenerare le fibre muscolari danneggiate

Perdita di massa, forza, prestazione muscolare

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**Benefits of antioxidant supplements for knee osteoarthritis: rationale and reality**

Ashok Kumar Grover and Sue E. Samson

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**Oxidative stress**

- ↑IL1-β, TNF-α
- ↑iNOS, ↓SOD, ↓Catalase
- ↑NO, ↑Superoxide, ↑H₂O₂
- ↓Prolidase, ↑Lipid peroxidation
- ↑Peroxy nitrite
- ↑Telomere erosion
- ↓Collagen II synthesis
- ↓Collagen breakdown
- ↑Metalloproteases
- ↑4-hydroxynonenal
- ↓Proline
- ↓Proline erosion

Cartilage damage
NO reduces Ca\(^{2+}\) cycling and rallenta “cross-bridge cycling kinetics”

sarcoplasmic reticulum Ca\(^{2+}\)-ATPase (SERCA) as the plausible site downstream of dietary nitrate
NUTRITIONAL SUPPORT

- Vitamin C
- Vitamin A
- Vitamin D
- Zinc
- Vitamin K
- Calcium
- antiossidanti

Diagram:
- Injury → Immobilization
  - ↓ Basal muscle protein synthesis
  - ↔ Resistance to anabolic stimulus, e.g. amino acids
  - ↓ Myofibrillar protein synthesis
  - ↓ Sarcoplasmic protein synthesis
  - ↓ Mitochondrial protein synthesis
  - ↓ Collagen (muscle and tendon) synthesis
  - ↓ Muscle size
  - ↓ Muscle oxidative capacity
  - ↓ Muscle connective tissue
  - Impaired tendon structure
  - ↓ Muscle strength
  - ↓ Muscle function
  - ↓ Athletic performance
  - ↓ Activity
  - ↑ Risk of metabolic disease

Omega-3 FA?
Leucine?
Nutraceutical Support

Glucosamine - Chondroitin  Methyl-Sulfonyl-Methane

Omega 3  Arginine

Boswellia Serrata  Superox Dismutase

Curcumin
Results suggest that curcumin may be a potentially useful drug to prevent loss of muscle mass, only if it is easily assimilated.

Previous observations provide strong evidence that NF-kB is involved in muscle wasting during different catabolic conditions and that NF-kB inhibitors may be efficacious in the management of muscle-wasting conditions. Of note, inhibition of NF-kB activity is an important mechanism by which curcumin may exert beneficial effects.

Curcumin (diferuloylmethane), a component of the spice turmeric (Curcuma longa) and responsible for the yellow color of curry, is a potential drug.
A growing body of evidence clearly indicates that dietary supplementation or intravenous administration of Arg is beneficial in improving reproductive, cardiovascular, pulmonary, renal, gastrointestinal, liver and immune functions, as well as facilitating wound healing, enhancing insulin sensitivity, and maintaining tissue integrity.

Arginine degradation occurs via multiple pathways that are initiated by arginase, nitric-oxide synthase, Arg:glycine amidinotransferase, and Arg decarboxylase. These pathways produce nitric oxide, polyamines, proline, glutamate, creatine, and agmatine with each having enormous biological importance.
Superoxide dismutases (SODs) are the major antioxidant defense systems against \( \text{O}_2^- \), which consist of three isoforms of SOD in mammals: the cytoplasmic Cu/ZnSOD (SOD1), the mitochondrial MnSOD (SOD2), and the extracellular Cu/ZnSOD (SOD3), all of which require catalytic metal (Cu or Mn) for their activation.

In addition, SODs play a critical role in inhibiting oxidative inactivation of nitric oxide, thereby preventing peroxynitrite formation and endothelial and mitochondrial dysfunction.

Enzymatic activity of SOD1 depends on the presence of the Cu and Zinc.

SOD is commercially obtained from marine phytoplankton, bovine liver, horseradish, cantaloupe and by fermenting certain bacteria, though it is found in most living forms at diverse concentrations.

Methylsulfonylmethane (MSM) is an organosulfur compound with the formula $\text{(CH}_3\text{)}_2\text{SO}_2$. It is also known by several other names including DMSO$_2$, methyl sulfone, and dimethyl sulfone. This colorless solid features the sulfonyl functional group and is considered relatively inert chemically. It occurs naturally in some primitive plants, is present in small amounts in many foods and beverages, and is marketed as a dietary supplement.

Oxidative stress and inflammation[edit]
Multiple human and animal trials indicate MSM may reduce oxidative stress and inflammation, although it is not a direct antioxidant. In human studies, MSM has been shown to protect muscles from damage by reducing the amount of oxidative stress damage incurred through exercise. The total antioxidant capacity was significantly increased after taking MSM. Studies in animals indicate a hepatoprotective effect of MSM against several toxins including acetaminophen, paraquat, and carbon tetrachloride. Animal models of experimental colitis and pulmonary hypertension indicate a protective effect as well.

DOSING: Typical doses adult dosages range from 500 to 8,000 mg daily with or after meals.
Msm

Citoprotezione
_in particolare del DNA_

Neutralizzazione
_Degli autoanticorpi in corso di riparazione tissutale_

Sintesi dei proteoglicani
_Macromolecole responsabili della capacità di resistere a forze di compressione_

Collagene V
_Regola l’assortimento e la disposizione tridimensionale dei collagene tendinei_

Distribuzione del Cl e del Na
_Mantenimento delle caratteristiche bioelettriche del tendine_
Physically active men were supplemented with either placebo or MSM (3 grams per day) for 28 days before performing 100 repetitions of eccentric knee extension exercise.

*MSM appears to dampen the release of inflammatory molecules in response to exercise*, resulting in a less incendiary environment, allowing cells to still have the capacity to mount an appropriate response to an additional stimulus after exercise.

Before and after the 28 day intervention period, subjects performed 18 sets of knee extension exercise in an attempt to induce muscle damage (and to be used partly as a measure of exercise performance). Sets 1-15 were performed at a predetermined weight for 10 repetitions each, while sets 16-18 were performed to muscular failure. Muscle soreness (using a 5-point Likert scale), fatigue (using the fatigue-inertia subset of the Profile of

MSM, especially when provided at *3.0 grams per day*, may favorably influence selected markers of exercise recovery...
Indian Frankincense

[Frankincense, Boswellia, Boswellin, Salai Guggal] Boswellia serrata

Origin: Gum resin from the bark of the Boswellia tree found in India.
Claims: Reduces inflammation and treats rheumatoid arthritis (RA), osteoarthritis (OA) and bursitis symptoms. It may also be used to treat symptoms of ulcerative colitis and Crohn’s disease.

What we know: Boswellic acids – the active components – may have strong anti-inflammatory and analgesic properties. They may also help prevent cartilage loss and inhibit the autoimmune process, making Indian frankincense/boswellia a potential therapy for RA in addition to OA.

Studies: In a 2004 study, Indian frankincense/boswellia was tested as a treatment for knee OA. Researchers recruited 30 people with knee OA and gave half the group a daily supplement containing 333 mg of Indian frankincense/boswellia; others got placebo. People who took Indian frankincense/boswellia reported less knee pain, better mobility and an ability to walk longer distances than those taking placebo.

A 2008 study in India, where Indian frankincense/boswellia is a traditional remedy, found that a supplement called 5-Loxin significantly improved OA pain and function within seven days and slowed cartilage damage after 3 months.

A 2008 British review found Indian frankincense/boswellia safe and effective for both OA and RA, though results of RA trials have been mixed.

Dosage: Capsule or tablet; typically 300 mg to 400 mg three times per day. Look for products with 60-percent boswellic acids, the active ingredient.
Meccanismi di protezione dei PUFA
The ω-3 FA DHA has been shown to address several of the hallmark pathologic features of this injury, such as excitotoxicity, oxidative stress, antinflammation.
**Table 1. Overview of principal nutraceuticals and their properties**

<table>
<thead>
<tr>
<th>Nutraceutical</th>
<th>Biological effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucosamine and chondroitin sulphate (GlcN-CS)</td>
<td>Increase collagen synthesis, ameliorate mechanical properties, organization of collagen bundles and resistance to fatigue, helpful in the management of pain.</td>
</tr>
<tr>
<td>Vitamin C (Vit C)</td>
<td>Stimulate hydroxyproline synthesis of procollagen, enhance angiogenesis and maturation of Col III to Col I fibers, anti-inflammatory and antioxidant effect.</td>
</tr>
<tr>
<td>Collagen I (Col I)</td>
<td>Increase mechanical properties, beneficial effects on collagen-rich tissues.</td>
</tr>
<tr>
<td>L-arginine-α-keto-glutarate</td>
<td>Substrate of NOS, increase NO levels and collagen synthesis.</td>
</tr>
<tr>
<td>Curcumin</td>
<td>Neoangiogenesis and apoptosis inhibitor, antioxidant effect, stimulate tenocytes survival.</td>
</tr>
<tr>
<td>Boswellic acid</td>
<td>Elastase and 5-LO activity inhibition, reduce TNFα, IL-1, IL-2, IL-4, IL-6 e INFγ levels.</td>
</tr>
<tr>
<td>Methilsulfonilmethane (MSM)</td>
<td>Analgesic, anti-inflammatory and antioxidant effects, reduce MDA and GSSG levels.</td>
</tr>
<tr>
<td>Bromelain</td>
<td>Decrease lymphocytes rolling, anti edema, antioxidant and immunosuppressive effects, reduce MDA levels.</td>
</tr>
</tbody>
</table>
Il **solfato di condroitina** è un glicosaminoglicano (GAG) solfato, composto da una catena alternata di zuccheri (N-acetilgalattosamina e acido glucuronico). Si trova normalmente associata a proteine, a formare un proteoglicano. Una catena di condroitina può avere oltre 100 zuccheri, ognuno dei quali può legare ioni solfato in posizione e quantità variabili. Il solfato di condroitina è un importante componente strutturale della cartilagine, dandogli la quasi totalità della resistenza alla compressione.

La **glucosammina** è un amminomonosaccaride (o glicosammina) e uno dei principali precursori della sintesi delle proteine glicosilate e dei lipidi. È uno dei maggior componenti del guscio dei crostacei e di altri artropodi, nei funghi e molti organismi superiori. È uno dei componenti del lipopolisaccaride dei batteri Gram-negativi. Non è un monosaccaride in senso stretto del termine, in quanto la sua formula molecolare non corrisponde alla formula generale Cn(H₂O)n.
OSTEOARTHRITIS: CHONDROITIN SULFATE LONG TERM UTILIZATION REDUCES CONSUMPTION OF COXIBS, NSAIDS & ANALGESICS

GLUCOSAMINE SULPHATE INDUCES CARTILAGE QUALITATIVE MORPHOLGICAL CHANGES IN OSTEOARTHRITIS: AN ULTRASONOGRAPHIC AND MRI EVIDENCE

**Origin:** Chondroitin is a component of human connective tissues found in cartilage and bone. In supplements, chondroitin sulfate usually comes from animal cartilage.

**Claims:** Reduces pain and inflammation, improves joint function and slows progression of osteoarthritis (OA).

**What we know:** Believed to enhance the shock-absorbing properties of collagen and block enzymes that break down cartilage. Helps cartilage retain water and may reverse cartilage loss when used with glucosamine.

**Studies:** The largest study to date, the 2006 Glucosamine/chondroitin Arthritis Intervention Trial (GAIT) looked at 1,600 people with knee OA. The first phase found that a small subset of patients with moderate-to-severe arthritis experienced significant pain relief from combined glucosamine and chondroitin. The 2008 phase found that glucosamine and chondroitin, together or alone, did not slow joint damage. And in the two-year-long 2010 phase, glucosamine and chondroitin were found as effective for knee OA as celecoxib (Celebrex).

But a 2010 meta-analysis of 10 trials involving more than 3,000 patients published in BMJ found no benefit from chondroitin, glucosamine or both.

A separate 2011 study showed a significant improvement in pain and function in patients with hand OA using chondroitin alone. Benefits of chondroitin and glucosamine remain controversial, but the supplements appear extremely safe.
Use of glucosamine and chondroitin supplements is associated with lower concentrations of hsCRP and PGE-M. This study offers an important piece of evidence to suggest that these supplements might have anti-inflammatory potential.
This is the first study investigating the effect of glucosamine supplementation on rehabilitation outcomes in athletes who underwent ACL reconstruction. It was found that glucosamine-sulfate (1000 mg/day, for 8 weeks) did not positively affect the rehabilitation outcomes.
Randomised, Double-Blind, Parallel, Placebo-Controlled Study of Oral
Glucosamine, Methylsulfonylmethane and their Combination in
Osteoarthritis.

Usha PR, Naidu MU.

Clin Drug Investig. 2004;24(6):353-63

The efficacy and safety of a combination of glucosamine hydrochloride, chondroitin
sulfate and bio-curcumin with exercise in the
treatment of knee osteoarthritis: a randomized,
double-blind, placebo-controlled study
Glucosamine and chondroitin supplementation may lower systemic inflammation
<table>
<thead>
<tr>
<th>Gene</th>
<th>Function</th>
<th>Effect size</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEACAM1</td>
<td>Cell-cell adhesion</td>
<td>-2.45</td>
<td>8.7x10^{-15}</td>
</tr>
<tr>
<td>SUZ12</td>
<td>Proliferation and histone methyltransferase activity [50, 51]</td>
<td>1.09</td>
<td>1.7x10^{-14}</td>
</tr>
<tr>
<td>THBS4</td>
<td>Cell-to-cell and cell-to-matrix interactions, extracellular mitogen</td>
<td>-1.88</td>
<td>2.1x10^{-14}</td>
</tr>
<tr>
<td>GADD45A</td>
<td>Induced in response to DNA damage</td>
<td>-1.37</td>
<td>2.8x10^{-14}</td>
</tr>
<tr>
<td>ITGA5</td>
<td>Adhesion and cell-surface mediated signaling</td>
<td>-1.54</td>
<td>9.7x10^{-14}</td>
</tr>
<tr>
<td>ITGB4</td>
<td>Adhesion and cell-surface mediated signaling</td>
<td>-1.89</td>
<td>1.2x10^{-13}</td>
</tr>
<tr>
<td>CSF3(GCSF)</td>
<td>Cytokine involved in hematopoiesis and induction of granulocytes</td>
<td>-3.06</td>
<td>2.1x10^{-13}</td>
</tr>
<tr>
<td>PKNOX1</td>
<td>RNA polymerase II distal enhancer</td>
<td>1.43</td>
<td>2.8x10^{-13}</td>
</tr>
<tr>
<td>IL13</td>
<td>Immuno regulatory cytokine involved in inhibition of allergic reaction, particularly in the airways</td>
<td>-6.29</td>
<td>3.5x10^{-13}</td>
</tr>
<tr>
<td>C1orf58</td>
<td>Mediates macrophage inflammatory response</td>
<td>3.67</td>
<td>4.6x10^{-13}</td>
</tr>
<tr>
<td>SON</td>
<td>Splicing co-factor for cell-cycle progression and DNA-repair, involved in differentiation of hematopoietic cells</td>
<td>1.02</td>
<td>6.4x10^{-13}</td>
</tr>
<tr>
<td>MUC3B</td>
<td>Provides protective barrier against infectious agents at mucosal surfaces</td>
<td>3.83</td>
<td>1.3x10^{-12}</td>
</tr>
<tr>
<td>RUNX1</td>
<td>Subunit of transcription factor that binds to many enhancers and promoters, involved in development of normal hematopoiesis</td>
<td>3.93</td>
<td>1.4x10^{-12}</td>
</tr>
<tr>
<td>IL17D</td>
<td>Cytokine involved in the stimulation of other cytokines, e.g., IL6, IL8, and CSF</td>
<td>-2.27</td>
<td>1.6x10^{-12}</td>
</tr>
<tr>
<td>BCAS2</td>
<td>Component of pre-mRNA spliceosome complex</td>
<td>1.72</td>
<td>2.3x10^{-12}</td>
</tr>
<tr>
<td>KCNE3</td>
<td>Modulates gating kinetics of potassium voltage channel complexes</td>
<td>1.75</td>
<td>3.2x10^{-12}</td>
</tr>
<tr>
<td>CD44</td>
<td>Cell adhesion and migration, receptor for hyaluronic acid</td>
<td>1.50</td>
<td>3.3x10^{-12}</td>
</tr>
<tr>
<td>VEPH1</td>
<td>Function unknown</td>
<td>1.80</td>
<td>3.7x10^{-12}</td>
</tr>
<tr>
<td>HB-EGF</td>
<td>Normal heart function, smooth muscle cell proliferation, may be involved in macrophage mediated proliferation</td>
<td>-1.47</td>
<td>5.2x10^{-12}</td>
</tr>
<tr>
<td>VCP</td>
<td>Putative ATP-binding protein in vesicle transport and fusion, 26S proteasome function and assembly of peroxisomes</td>
<td>-2.10</td>
<td>6.8x10^{-12}</td>
</tr>
<tr>
<td>COMP</td>
<td>Structural integrity of cartilage, potent suppressor of apoptosis in chondrocytes</td>
<td>-2.08</td>
<td>7.4x10^{-12}</td>
</tr>
<tr>
<td>IL6</td>
<td>Chemokine, chemoattractant and potent angiogenic factor</td>
<td>-2.35</td>
<td>9.9x10^{-12}</td>
</tr>
<tr>
<td>CAPN5 (NCL1)</td>
<td>Intracellular protease, binds to titin</td>
<td>-2.09</td>
<td>1.0x10^{-11}</td>
</tr>
<tr>
<td>GCM2</td>
<td>Transcription factor regulating parathyroid development</td>
<td>1.23</td>
<td>1.0x10^{-11}</td>
</tr>
<tr>
<td>PKC</td>
<td>Regulation of cell growth and immune responses</td>
<td>-0.89</td>
<td>1.3x10^{-11}</td>
</tr>
<tr>
<td>LASP1</td>
<td>Regulation of actin-based cytoskeletal activities</td>
<td>-1.42</td>
<td>1.4x10^{-11}</td>
</tr>
<tr>
<td>SPP1</td>
<td>Attachment of osteoclasts to the mineralized bone matrix; also a cytokine that upregulates expression of interferon-gamma and interleukin-12</td>
<td>-6.45</td>
<td>1.7x10^{-11}</td>
</tr>
<tr>
<td>EFNB3</td>
<td>Ligand for Eph receptors involved in migration, repulsion and adhesion during neural, vascular and epithelial development</td>
<td>-3.24</td>
<td>1.9x10^{-11}</td>
</tr>
<tr>
<td>HOXA4</td>
<td>Transcription factor that may regulate gene expression, morphogenesis and differentiation</td>
<td>1.88</td>
<td>2.3x10^{-11}</td>
</tr>
<tr>
<td>IL1β</td>
<td>Cytokine involved in inflammatory response</td>
<td>-2.65</td>
<td>2.3x10^{-11}</td>
</tr>
<tr>
<td>EGFR</td>
<td>Cell proliferation</td>
<td>1.80</td>
<td>3.1x10^{-11}</td>
</tr>
<tr>
<td>PRKQ</td>
<td>Kinase involved in diverse cellular signaling pathways including T-cell activation, proliferation,</td>
<td>-1.68</td>
<td>3.1x10^{-11}</td>
</tr>
</tbody>
</table>
The mechanisms of action of neither CS nor GlcN in cartilage and subchondral bone tissues affected with osteoarthritis still not fully determined

Nevertheless, it is a challenging task to understand how a carbohydrate-based compound with high molecular weight like CS (20–50 kDa) could be absorbed after oral administration and then remain sufficiently undegraded.

necessity of a precise and detailed determination of the chemical structures of the CS and GlcN present in these pharmaceutical preparations to support clinical and preclinical studies
Nutraceutici in medicina dello sport

• Epidemiologically, vit D is linked to **decr risk of cancer, multiple sclerosis, flu, hypertension, diabetes, & mood disorders.**
• **Most human diets contain little vit D, unless wild-caught fatty fish is eaten.**
• Age, **latitude**, time of day, **season of the year, use of sunblock, and pigmentation** can dramatically affect the production of vit D in the skin.
• If vit D affects athletic performance, then measurements of physical performance should peak in the late summer, start to decline in early autumn, and reach their nadir in late winter. **Guess what...?**

Main Benefits:
• Strengthens bones
• Helps prevent/treat cold & flu
• Inhibits tumor proliferation
• Protects against CVD
• Enhances NM function

Google: Vitamin D Council, Vitamin D Society
How to use gelatin to promote collagen synthesis

To treat injuries

Consuming 15 grams of gelatin one hour before 6 minutes of jump rope resulted in a 2-fold greater increase in collagen synthesis than intermittent exercise for 6 minutes on its own.

Gelatin: a food source with similar amino acids found in collagen.

Ingest gelatin 1 hour before 5-6 minute protective session
At least 6 hours before or after other training

Jumping rope for 6 min with gelatin resulted in 2-fold greater increase in collagen synthesis than jumping only.
Grazie per la vostra Cortese Attenzione