

WELCOME TO YOUR JOINT CARE DNA™ REPORT

Congratulations on making the decision to take the Joint Care DNA™ test. Today's DNA technology provides an unprecedented look at how our bodies are constructed and what the future holds. Joint Care DNA™ looks at a number of different genetic markers in your body responsible for the production of Collagen, the material which prevents the bones in your joints from coming into direct contact with each other. With this data, you can better understand your own joint health and the role your genes may play.

Important: How to Read Your Results

When you receive your DNA results, we recommend reviewing them with your doctor to understand what kind, if any, lifestyle changes you can make to optimize your joint health. This is not a diagnostic test, meaning it will not diagnose a specific injury or cause of joint discomfort. This test can supplement your knowledge of your body to help you maintain optimal joint health.

The genetic results are denoted by the letters A, T, C and G that represent the building blocks of DNA. At a specific location, we inherit two copies of DNA; one from each parent. If both copies are the same the same letters are indicated, i.e. T, T. If the two copies are different then different letters are shown, i.e. T, C. These differences are known as SNPs and represent spelling difference in our DNA that are commonly used as genetic markers.

Genetic results have been coded into Green and Red colors. A Green result means that your body does not have a genetic variant for the gene we tested or if present, one copy of the variant. A Red result means that you have two copies of the variant. Third-party research has identified this variant and suggests that it may influence the quality of collagen produced by the body. We recommend that you read the published research available in your Results report and review with your doctor. Your results can help you make better lifestyle choices which may improve your overall joint health.




Disclaimer: No action should be taken solely on its content; regardless of the perceived scientific merit, instead readers should consult health care professionals on any matter related to their health. The information obtained from referenced materials are believed to be accurate, as presented by their respective authors, but DNA Diagnostics Center assumes no liability for any personal interpretation. Readers, previous and future customers who fail to consult their Physicians prior to the purchase and subsequent use of any product, assume the risk of any adverse effects.

PERSONAL INFO	
Name	Jane Doe
Reference #	888412255
Date of Testing	5/2/2016



YOUR RESULTS

Below are your individual results among the genetic markers tested by our laboratory. For help interpreting these results, see the **Personal Information** section. To learn more about these different genes, please visit the links provided in our **Published Research** section.

<p>Gene Tested: COL1A1</p> <p>This gene controls the body's ability to produce a primary component of type 1 collagen. Type 1 collagen is the most abundant type of collagen in the body, and it helps strengthen and support ligaments, tendons, cartilage, bone, and other connective tissues.</p>	
<p>Gene Tested: TNC</p> <p>This gene regulates the production of a glycoprotein called tenascin C. Tenascin C plays a role in the inflammatory response in joints.</p>	
<p>Gene Tested: Col5a1</p> <p>This gene controls the body's ability to create one of the components that make up type 5 collagen. Type 5 collagen molecules bundle themselves into long, thin strands, or "fibrils," with type 1 collagen strands. Type 5 collagen regulates the overall diameter of those fibrils.</p>	

KEY



A Green result means that your body does not have a genetic variant for the gene we tested.



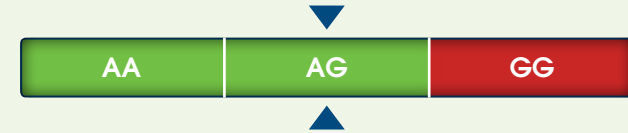
A Red result is indicative of a genetic variant at a specific genetic marker. This means that this gene may be affecting your body in a specific way, for example influencing your quality of collagen. If you receive this result, we encourage you to learn more about this gene in our published research section and review your results with a doctor to understand what lifestyle changes you can make to maximize your joint health.



The Blue arrows indicate what result you received.

Gene Tested: MMP3

This gene regulates an enzyme that is involved in the breakdown of the collagen matrix inside connective tissues.

**Gene Tested: COL11a1**

This gene controls the body's ability to produce one of the two main building blocks that make up type 11 collagen, which is found in cartilage and inside the discs separating the spinal vertebrae. Type 11 collagen helps maintain the spacing and diameter of type 2 collagen in cartilage. The arrangement and size of type 2 collagen fibrils is essential for the normal structure of these tissues.

**Gene Tested: BGN (Location 1)**

This gene regulates the production of the protein biglycan. Biglycan is an important component of articular cartilage, and also provides structural and biochemical support to the collagen matrix surrounding it.

**KEY**

A Green result means that your body does not have a genetic variant for the gene we tested.



A Red result is indicative of a genetic variant at a specific genetic marker. This means that this gene may be affecting your body in a specific way, for example influencing your quality of collagen. If you receive this result, we encourage you to learn more about this gene in our published research section and review your results with a doctor to understand what lifestyle changes you can make to maximize your joint health.



The Blue arrows indicate what result you received.

Gene Tested: COL12a1

This gene directs the body's production of type 12 collagen. Type 12 collagen influences how type 1 collagen interacts with the collagen matrix.

**Gene Tested: COL5a1-DPN**

A variant of COL5a1.

**Gene Tested: COL27a1**

This gene controls a protein that plays a crucial role in tissue growth and repair, and provides structure in the collagen matrix. It is also active during the transition of cartilage to bone, as in infants and young children.

**KEY**

A Green result means that your body does not have a genetic variant for the gene we tested.



A Red result is indicative of a genetic variant at a specific genetic marker. This means that this gene may be affecting your body in a specific way, for example influencing your quality of collagen. If you receive this result, we encourage you to learn more about this gene in our published research section and review your results with a doctor to understand what lifestyle changes you can make to maximize your joint health.



The Blue arrows indicate what result you received.

EDUCATION

Joints are complex parts of our anatomy that we rarely notice until a few unfamiliar cracks and pops grab our attention, or we wake up stiff and achy. We wonder, “What’s happening to me? Moving is supposed to be easy!”

As you learn more about your own joint health genetic profile, it’s important also to learn how joints are structured and how they work. This information will provide a foundation for understanding how different therapies, exercise, and lifestyle choices help support and maintain joint function. Let’s get started with looking at some frequently asked questions about joints.

What are joints?

Joints are the connections between bones that allow us to bend, twist, and flex our bodies. Each joint enables a specific kind of movement. The knee, for example, works like a hinge. Joints in the neck pivot from side to side, and the shoulders and hips allow multi-directional motion. (The shoulder, for example, rotates almost 360 degrees.) If you’ve ever wrestled open a rusty gate, you can guess where this comparison is going. Initially the hinges are stiff and resistant but once the gate gets moving, it swings freely. Joints work the same way. The more they move, the better they function. For optimum mobility, aim for at least 30 minutes of exercise daily, and include activities that move all joints.

What are the parts of the joint?

In addition to bones, joints contain five other important parts:

- **Cartilage.** Perhaps the most well-known part of a joint, cartilage covers the ends of each bone where they come together. The material is a sort of cushion, or “shock absorber,” that reduces friction in a joint.
- **Ligaments.** These fibrous connective tissues attach bones together and help keep joints stable.
- **Synovium.** Each joint is encapsulated in a fluid-filled sack. The synovium is the inner layer of that sack, and it secretes synovial fluid.
- **Synovial fluid.** This fluid, which is similar to egg whites in its consistency, surrounds each joint. In addition to acting as a lubricant and providing additional shock absorption, it nourishes the cartilage and ligaments.
- **Tendons.** Like ligaments, tendons are fibrous connective tissues; rather than connecting bones to bones, tendons connect muscles to bones. Their job is to enable movement.

What is collagen, and why is it important for joint health?

Collagen is a protein and a key building block for connective tissue found throughout the body. It is especially concentrated in joint cartilage and ligaments.

Its long, thin protein strands form a matrix that gives connective tissue its strength. Healthy collagen synthesis is necessary for connective tissues to maintain their structural integrity, which in turn keeps joint motion stable and smooth.

How should problem joints be exercised?

Although exercising a stiff or sore joint may be challenging, it is actually one of the best ways to help improve the joint’s strength and range of motion. The key is to push the joint enough to stimulate improvement, but not so far as to cause injury.

Depending on your fitness level and your specific joint issue, this may mean working up a serious sweat, or it may mean simply rotating the troublesome joint through its full range of motion a few times.

If you’re not sure how hard you should be working a joint, consult a physical therapist or trainer. They will be able to help you learn the difference between the discomfort that builds strength and the discomfort that can lead to injury. Listen to your body, and modify exercises as appropriate.

Is running bad for your knees?

Research increasingly shows that running isn't as risky as previously thought and that runners are no more likely to suffer from joint problems than non-runners. However, a daily run may not be the best exercise choice if your joints are weak, you are overweight, or you have had previous joint injuries.

Mixing an occasional run with lower impact aerobic activities like swimming, cycling, or inline skating will build endurance and strength but without as much long-term repetitive impact on the spine and weight-bearing joints (i.e., hips, knees, and ankles). This helps minimize the chance connective tissue could become strained.

How can you tell if a joint is injured or just aging?

The only way to know for sure is to see a doctor, preferably an orthopedist. These specialists are uniquely trained to evaluate joint structure and movement, and to prescribe the most appropriate treatments. If you're experiencing joint issues, never assume that you're "just getting old." Always get it checked out. Age may be a contributing factor, but other issues may exist as well.

How much can losing weight improve joint health?

Probably more than you think. Research shows that weight losing just one pound can reduce the load on your knees by four pounds. If you lose five pounds, the benefit is 20 pounds of reduced load; 10 pounds, and the benefit is 40 pounds. It's easy to see how quickly this can add up. An additional benefit of losing weight is that it makes exercise in general easier and the more of that you do, the more you're supporting your joint health.

What are the most common treatments for joint health?

As is the case with many health concerns, joint discomfort can be treated using a wide range of options, from simple RICE therapy (rest, ice, compression, elevation) to full joint replacement. Other potential treatments include OTC and prescription medications, physical therapy, chiropractic manipulation, steroid injections, and acupuncture. Some people also benefit from taking nutritional supplements formulated for joint health.



NUTRITIONAL SUPPLEMENTS

An increasingly popular way to promote and maintain healthy joints is by taking nutritional supplements that nourish bones and connective tissues.

How Supplements Help

Supplements are helpful tools for making sure your body has enough nutrients to carry out the natural, daily maintenance routines that keep joints working smoothly. These tasks include replacing old bone with new bone, repairing muscle, and reconstructing the collagen matrix, to name just a few.

Ideally, essential joint-health nutrients are consumed in the foods we eat. However, this can vary greatly depending on your diet making supplements a convenient way to reinforce nutrient stores and to support the integrity of bones, muscles, ligaments, and tendons.

Buying and Using Joint Supplements

The most common and well-known supplements for joint health are glucosamine and chondroitin sulfate. Both have been available for years, but now are just two of many options on the market. The table [at right/below] will help you learn more about other popular and supportive ingredients.

As you shop, you'll notice that many companies offer supplements formulated with blends of multiple ingredients. Selecting the one that's right for you will involve a bit of trial and error. Not everyone responds to supplements in the same way so if you don't realize your desired results with your first product, try another. Just be sure to take each one according to its label recommendation, and long enough for the product to have an effect (30 days is a good rule of thumb).

One other bit of shopping advice: Be wary of products that claim they can rebuild joints. No supplement or medication, for that matter has been proven to effectively repair joint damage. Once a joint has deteriorated, it will remain that way unless it is replaced. If a supplement claims to have this miracle ability, save your money. It's probably too good to be true.

Always Talk to Your Doctor

Finally, be sure to tell your doctor if you decide to try a supplement. This is extremely important, as supplements can and sometimes do interact with prescription and over-the-counter drugs. Sharing your intention with your physician will help prevent any adverse effects.



TOP 15 SUPPLEMENT OPTIONS AND THEIR ROLE IN JOINT HEALTH

Glucosamine: A building block of cartilage, also present in a joint's synovial fluid

Chondroitin sulfate: A structural component of cartilage

Hyaluronic acid: A chief component of the shock-absorbing synovial fluid inside joints

Methylsulfonylmethane (MSM): A rich source of sulfur that is involved in building and repairing connective tissue, as well as hair, skin, and nails

Boswellia serrata: Also known as the herb frankincense, supports collagen maintenance and a healthy inflammatory response

Vitamin C: Necessary for collagen synthesis

Undenatured type II collagen (UC-II): Supports collagen maintenance and a healthy inflammatory response

S-adenosyl-L-methionine (SAM-e): Supports a healthy inflammatory response

Univestin: Supports a healthy inflammatory response

Omega-3 fatty acids: Supports a healthy inflammatory response

Turmeric (curcumin): Supports a healthy inflammatory response

Vitamin D: Supports bone growth

Calcium: Supports bone growth

Magnesium: Necessary for more than 300 biochemical reactions in the body, including bone growth and maintenance of muscle tissue

Whey Protein: Rich in amino acids necessary to build proteins found in muscle and connective tissue

LIFESTYLE & EXERCISE

Your day-to-day habits have a significant impact on your ability to maintain flexibility and strength throughout life. The better your choices, obviously, the better your results.

Following are eight suggestions for maximizing the health and longevity of your joints. Whether you adopt them one at a time or all together, you can expect to feel their positive effects both now and in the future.

8 Tips for Supporting Long-Term Joint Health

1. Use it, or lose it. Though it may seem somewhat counterintuitive to subject stiff and achy joints to daily exercise, movement is the surest way to keep joints loose and well lubricated and to avoid “rusty gate syndrome.” If you’ve ever wrestled open a rusty gate, you can guess where this comparison is going. Initially the hinges are stiff and resistant but once the gate gets moving, it swings freely. Joints work the same way. The more they move, the better they function. For optimum mobility, aim for at least 30 minutes of exercise daily, and include activities that move all joints.

2. Rotate each joint through its full range of motion, daily. In addition to keeping joints limber, exercise has the added benefit of nourishing the shock-absorbing tissue between bones known as cartilage especially when joints are put through their full range of motion. Cartilage is somewhat unique in joint anatomy. Whereas muscles, and ligaments all receive vital nutrients from blood flow, cartilage does not. Instead, it takes in nourishment from the synovial fluid around it, as the bones rotate. It’s helpful to picture cartilage as a kind of sponge that contracts and expands based on where rotational pressure is applied. When it contracts, waste is squeezed out. When it expands, fresh nutrients are absorbed. So, rotating each joint through its full range of motion each day means that its cartilage is receiving as much nutritional support as possible.

3. Maintain a healthy weight. According to Harvard University Medical School, the weight exerted on your knees when walking across level ground is equal to 1.5 times your body weight. So if, for example, you weigh 200 pounds which is just over the average weight of a U.S. male each step puts 300 pounds of pressure on your knee. If you walk 5,000 steps a day, that’s 30 tons of load your knees have to carry! (More if you go up or down stairs, or squat to pick something up off the floor.) Given this, it’s easy to see how a small, sustained weight loss of 10–15 pounds could have a major impact on the long-term health of weight-bearing joints. In fact, one study found that for every one pound of weight lost by obese patients, the impact on knees was reduced by four pounds. If you are overweight, set a goal to lose 5–10 pounds. Then target another 5–10 pounds, if appropriate, until you reach a weight that is comfortable and sustainable.

4. Reduce the overall impact and/or frequency of repetitive exercise. Although there’s been some recent debate about whether running has a positive or negative influence on long-term joint health, it’s still a good idea to vary your exercise routine in ways that reduce the kind of repetitive impact that can break down tendons and ligaments. For example, rather than running every day, run just two or three days, and add days when you swim, bike, or walk. At the gym, choose the rowing machine or elliptical trainer instead of the stair-climber or treadmill. These changes will allow you to continue exercising your joints, with less cumulative strain plus, you’ll be conditioning muscle groups in new ways, improving your overall strength.



5. Build muscle strength. The stronger your muscles, the more effective they are at helping maintain balance and stability. This is important for joint health because muscles, tendons, and ligaments all share the workload when a joint moves. When your muscles can't perform, it puts extra strain on the other parts of the joint, and increases the risk that connective tissues will become loose or injured further compromising strength and movement. You can reduce this risk by adding resistance training to your exercise regimen. Many people equate this type of exercise with weight lifting. Certainly, that's one way to go if you're up for joining a gym. But you can also build muscle through body weight exercises such as squats and lunges for the lower body, and push-ups and pull-ups for the upper body. Resistance bands are another great work-out-at-home option. Look online for guidance on specific exercises. Yet another alternative for building muscle strength is yoga. This practice works all muscle groups in addition to improving flexibility, which can also help support and maintain joint health.

6. Stay hydrated. Drinking more water supports joint health by ensuring that the body can produce adequate amounts of synovial fluid. This fluid surrounds joint and plays three important roles: (1) it acts as a lubricant, (2) it serves as a vehicle for delivering nutrients to cartilage, and (3) it provides some additional shock absorbency. When production of synovial fluid is low, joints can feel stiff and less cushiony, and are prone to higher levels of wear and tear as a result. Aim to stay in step with the well-known hydration recommendation of drinking at least eight eight-ounce glasses of water a day.

7. Adopt a non-inflammatory diet. Can what you eat really influence joint health? Yes! Because maintaining a healthy inflammatory response can influence joint comfort, the same non-inflammatory diet recommended for heart health can also benefit joints. That means avoiding foods high in sugar and omega-6 fats, as well as all processed foods and alcohol. Many people also find that their joints are affected by foods from the "nightshade" family, including red and green peppers, tomatoes, potatoes, and eggplant, and steer clear of those foods as well. What should you eat? More foods rich in sulfur, which is a building block of collagen. Those foods include egg yolks, onions, garlic, horseradish, and cruciferous vegetables (Brussels sprouts, broccoli, cauliflower, cabbage, kale, radishes, turnips, kohlrabi, and mustard).

8. Improve your posture. Finally, sit up straight! Posture can influence the health of all weight-bearing joints, but is particularly relevant to the neck and back. After all, each of the 33 vertebrae in your spine is a joint. Keeping your head up, shoulders pulled in, and neck, shoulders, and pelvis in a straight line helps maintain your ability to twist and bend as needed, and keeps your weight evenly balanced so one part of your body doesn't bear more than another.



General

Collins M and Raleigh SM. Genetic risk factors for musculoskeletal soft tissue injuries. *Med Sport Sci*. 2009;54:136-49.

Fujii K et al. Biochemical properties of collagen from ligaments and periarticular tendons of the human knee. *Knee Surg Sports Traumatol Arthrosc*. 1994;2(4):229-33.

Gabrielle T et al. The dawning age of genetic testing for sports injuries. *Clin J Sport Med*. 2015 Jan; 25(1):1-5.

Maffulli N et al. The genetics of sports injuries and athletic performance *Muscles Ligaments Tendons J*. 2013 Jul-Sep; 3(3):173-189.

O'Brien M. Structure and metabolism of tendons. *Scand J Med Sci Sports*. 1997 Apr;7(2):55-61.

GDF5

Buxton P et al. Growth/differentiation factor-5 (GDF-5) and skeletal development. *J Bone Joint Surg Am*. 2001;83-A Suppl 1(Pt 1):S23-30.

Capellini TD et al. When evolution hurts: height, arthritis risk, and the regulatory architecture of GDF5 function. *The FASEB Journal* . April 2012;26(1): Supplement 457.1.

Egli RJ et al. Functional analysis of the osteoarthritis susceptibility-associated GDF5 regulatory polymorphism. *Arthritis Rheum*. 2009 Jul;60(7):2055-64.

Evangelou E et al. Large-scale analysis of association between GDF5 and FRZB variants and osteoarthritis of the hip, knee, and hand. *Arthritis Rheum*. 2009 Jun;60(6):1710-21.

Huétink K et al. Genetic contribution to the development of radiographic knee osteoarthritis in a population presenting with nonacute knee symptoms a decade earlier. *Clin Med Insights Arthritis Musculoskelet Disord*. 2016 Apr 28;9:57-63.

Liu J et al. Rs143383 in the growth differentiation factor 5 (GDF5) gene significantly associated with osteoarthritis (OA)—A comprehensive meta-analysis. *Int J Med Sci*. 2013;10(3):312-319.

Martínez A et al. GDF5 polymorphism associated with osteoarthritis: risk for rheumatoid arthritis. *Ann Rheum Dis*. 2008 Sep;67(9):1352-3.

Rouault K et al. Evidence of association between GDF5 polymorphisms and congenital dislocation of the hip in a Caucasian population. *Osteoarthr Cartilage*. 2010 Sep;18(9):1144-49.

Vaes RB et al. Genetic variation in the GDF5 region is associated with osteoarthritis, height, hip axis length and fracture risk: the Rotterdam study. *Ann Rheum Dis*. 2009 Nov;68(11):1754-60.

Williams FM et al. GDF5 single-nucleotide polymorphism rs143383 is associated with lumbar

disc degeneration in Northern European women. *Arthritis Rheum*. 2011 Mar;63(3):708-12. doi: 10.1002/art.30169.

Zhang R et al. A comprehensive meta-analysis of association between genetic variants of GDF5 and osteoarthritis of the knee, hip and hand. *Inflamm Res*. 2015 Jun;64(6):405-14.

MMP3

Chen JJ et al. Expression and significance of MMP3 in synovium of knee joint at different stage in osteoarthritis patients. *Asian Pac J Trop Med*. 2014 Apr;7(4):297-300.

Green MJ et al. Serum MMP-3 and MMP-1 and progression of joint damage in early rheumatoid arthritis. *Rheumatology (Oxford)*. 2003 Jan;42(1):83-8.

Houseman M et al. Baseline serum MMP-3 levels in patients with rheumatoid arthritis are still independently predictive of radiographic progression in a longitudinal observational cohort at 8 years follow up. *Arthritis Res Ther*. 2012 Feb 7;14(1):R30.

Raleigh SM et al. Variants within the MMP3 gene are associated with Achilles tendinopathy: possible interaction with the COL5A1 gene. *Br J Sports Med*. 2009 Jul;43(7):514-20.

Shi J et al. Explore the variation of MMP3, JNK, p38 MAPKs, and autophagy at the early stage of osteoarthritis. *IUBMB Life*. 2016 Apr;68(4):293-302.
 Sun S et al. The active form of MMP-3 is a marker of synovial inflammation and cartilage turnover in inflammatory joint diseases. *BMC Musculoskelet Disord*. 2014 Mar 19;15:93.

Yoshihara Y et al. Matrix metalloproteinases and tissue inhibitors of metalloproteinases in synovial fluids from patients with rheumatoid arthritis or osteoarthritis. *Ann Rheum Dis*. 2000 Jun;59(6):455-61.

COL5A1

Kevin O'Connell, et al. Interactions between collagen gene variants and risk of anterior cruciate ligament rupture. *Eur J Sport Sci*. 2015;15(4):341-350.

Lim ST et al. The COL5A1 genotype is associated with range of motion. *J Exerc Nutrition Biochem*. 2015 Jun;19(2):49-53.

Posthumus M et al. The COL5A1 gene is associated with increased risk of anterior cruciate ligament ruptures in female participants. *Am J Sports Med*. 2009 Nov;37(11):2234-40.

COL1A1

Belangero PS et al. Gene expression analysis in patients with traumatic anterior shoulder instability suggests deregulation of collagen genes. *J Orthop Res*. 2014 Oct;32(10):1311-6.

Ficek K et al. Gene variants within the COL1A1 gene

are associated with reduced anterior cruciate ligament injury in professional soccer players. *J Sci Med Sport*. 2013 Sep;16(5):396-400.

Flynn RK et al. The familial predisposition toward tearing the anterior cruciate ligament: a case control study. *Am J Sports Med*. 2005 Jan;33(1):23-8.

Keen RW et al. Association of polymorphism at the type I collagen (COL1A1) locus with reduced bone mineral density, increased fracture risk, and increased collagen turnover. *Arthritis Rheum*. 1999 Feb;42(2):285-90.

Khoschnau S et al. Type I collagen alpha1 Sp1 polymorphism and the risk of cruciate ligament ruptures or shoulder dislocations. *Am J Sports Med*. 2008 Dec;36(12):2432-6.

Mann V et al. A COL1A1 Sp1 binding site polymorphism predisposes to osteoporotic fracture by affecting bone density and quality. *J Clin Invest*. 2001 Apr;107(7):899-907.

Posthumus M et al. Genetic risk factors for anterior cruciate ligament ruptures: COL1A1 gene variant. *Br J Sports Med*. 2009 May;43(5):352-6.

Smith H et al. Risk factors for anterior cruciate ligament injury: A review of the literature—Part 2: Hormonal, genetic, cognitive function, previous injury, and extrinsic risk factors. *Sports Health*. 2012 Mar; 4(2): 155-161.

COL12A1

Bell RD et al. Collagen gene variants previously

associated with anterior cruciate ligament injury risk are also associated with joint laxity. *Sports Health*. 2012 Jul; 4(4): 312-318.

O'Connell K et al. Interactions between collagen gene variants and risk of anterior cruciate ligament rupture. *Eur J Sport Sci*. 2011;15(4):341-50.

Posthumus M et al. The association between the COL12A1 gene and anterior cruciate ligament ruptures. *Br J Sports Med*. 2010 Dec;44(16):1160-5.

COL11A1

Li Y et al. A fibrillar collagen gene, Col11a1, is essential for skeletal morphogenesis. *Cell*. 1995 Feb 10;80(3):423-30.

Raine EV et al. Allelic expression analysis of the osteoarthritis susceptibility gene COL11A1 in human joint tissues. *BMC Musculoskelet Disord*. 2013 Mar 8;14:85.

COL27A1

Jenkins E et al. The new collagen gene COL27A1 contains SOX9-responsive enhancer elements. *Matrix Biol*. 2005 May;24(3):177-84.

Pace JM et al. Identification, characterization and expression analysis of a new fibrillar collagen gene, COL27A1. *Matrix Biol*. 2003 Mar;22(1):3-14.

BGN

Berendsen AD et al. Biglycan modulates angiogenesis and bone formation during fracture healing. *Matrix Biol.* 2014 Apr;35:223-31.

Chen XD et al. The small leucine-rich proteoglycan biglycan modulates BMP-4-induced osteoblast differentiation. *FASEB J.* 2004 Jun;18(9):948-58.

TNC

Ikemura S et al. Effect of tenascin-C on the repair of full-thickness osteochondral defects of articular cartilage in rabbits. *J Orthop Res.* 2015 Apr;33(4):563-71.

Lerman RH et al. Nutritional approach for relief of joint discomfort: A 12-week, open-case series and illustrative case report. *Integr Med (Encinitas).* 2015 Oct;14(5):52-61.

Lugo JP et al. Efficacy and tolerability of an undenatured type II collagen supplement in modulating knee osteoarthritis symptoms: a multicenter randomized, double-blind, placebo-controlled study. *Nutr J.* 2016 Jan 29;15:14.

Saunders CJ et al. Investigation of variants within the COL27A1 and TNC genes and Achilles tendinopathy in two populations. *J Orthop Res.* 2013 Apr;31(4):632-7.

Education

<http://www.webmd.com/arthritis/caring-your-joints>

<http://www.health.harvard.edu/pain/simple-tips-to-protect-your-joints>

<https://health.clevelandclinic.org/2016/05/snap-crackle-pop-need-know-joint-noises/>

<https://health.clevelandclinic.org/2016/06/ok-push-pain-exercise/>

<https://health.clevelandclinic.org/2015/10/5-ways-youre-making-knee-pain-worse/>

<https://health.clevelandclinic.org/2015/12/how-to-keep-your-joints-healthy-with-the-right-exercise/>

Supplements

<http://www.nutritionexpress.com/article+index/buyers+guides/best+joint+products/showarticle.aspx?id=1682>

http://newhope.com/health/top-10-ingredients-joint-and-bone-health#slide-1-field_images-244341

<http://www.nutraingredients-usa.com/Markets/Bone-Joint-health-The-big-ingredients-for-a-booming-market>

<http://www.nutraingredients.com/Research/Science-The-emerging-ingredients-for-joint-health>

Lifestyle & Exercise

<http://www.cdc.gov/nchs/fastats/body-measurements.htm> Accessed June 29, 2016

<http://www.health.harvard.edu/pain/why-weight-matters-when-it-comes-to-joint-pain> Accessed June 29, 2016

<http://www.ncbi.nlm.nih.gov/pubmed/15986358>