Sjögren's: what research means for your treatment and gland function

Mechanisms, biomarkers, personalized treatment and the evidence for regeneration

Olga Goodman, MD

Editorial review: November 21, 2026.

Original article: https://dr.rheumaview.com/sjogren/research-regeneration-en/

What can this chapter help me understand?

Research on Sjögren's is trying to answer several different questions: why the illness develops, why people experience it differently, which measurements can guide care, and whether damaged glands can recover. A discovery can be important before it is ready to guide a prescription. This chapter explains where the evidence stands and what to ask about a new test or treatment.

The central distinction is between changing a laboratory result, helping a person feel or function better, and rebuilding working tissue. These outcomes can overlap, but one does not prove the others. It is an educational review, not an individual treatment plan. [1, 31]

What happens inside the glands?

The glands contain cells that make fluid, ducts that carry it out, supporting tissue, blood vessels and nerves. Immune cells and gland cells communicate through chemical signals. Sjögren's can disturb this whole system; gland cells are participants in inflammation as well as its targets. Researchers now study both the individual cells and their positions within the tissue. [8, 9]

This helps explain why a single test cannot describe everything. The amount of inflammation, the remaining ability to release saliva or tears, and the effect on daily life are different pieces of information. A useful care plan can address several pieces at once. Symptom care still matters while research works toward treatments that change the underlying disease.

Do genes or infections explain why I developed Sjögren's?

Genetic studies identify many small contributions to susceptibility rather than one gene that determines the illness. A risk finding does not tell an individual which medicine will work. Female predominance also raises biological questions; it does not by itself prove that a hormone treatment can reverse Sjögren's. [2]

Infections are being studied as possible triggers. An investigation of Epstein–Barr virus (EBV) provides a detailed example of immune changes around infection, but it cannot establish the same cause in everyone. A past infection and a current infection requiring treatment are different situations. Ask what evidence shows an infection is active now before interpreting an antiviral proposal as treatment for autoimmune disease. The event that starts an illness may differ from what keeps it going. [3]

Could changes in gut or mouth microbes be important?

The microbiota is the community of microbes living in a particular part of the body. Researchers have found reasons to investigate its contribution to Sjögren's. Experiments transferring human microbiota into mice have affected immune and eye findings. These experiments do not establish that changing the microbiota is an effective treatment for Sjögren's in people. [4]

The direction of the relationship is difficult to untangle. Dry mouth can change the oral environment, eating difficulties can change diet, and medicines can change microbes. A commercial report labeled "dysbiosis" does not show which change caused your illness or how to reverse it. For a proposed intervention, ask whether it was tested in people with Sjögren's, against a comparison group, with meaningful benefits and harms measured. Nutritional care can help nutrition without needing to claim a microbiome cure.

What are interferon and immune pathways?

Interferons are signaling proteins used by the immune system. An immune pathway is a chain of signals that changes how cells behave. Researchers can measure how strongly certain genes respond to interferon; this pattern is often called an interferon signature. It describes cell activity, not a change in your inherited genes. Other signals, including BAFF, support B cells, which are involved in antibody production. These pathways provide possible treatment targets, but a target being active does not guarantee that blocking it will help every symptom. [5, 6]

One trial analysis found that hydroxychloroquine changed interferon-related measurements without demonstrating corresponding clinical improvement. This illustrates why both laboratory and patient outcomes are needed. It is not a reason to stop a prescribed medicine: its purpose in your own care may be different. Ask which problem the medicine is intended to treat and how you and your clinician will judge its effect. [7]

Do SSA, ACA or negative antibodies identify my disease subtype?

SSA, also called anti-Ro, and ACA, meaning anti-centromere antibodies, are names you may see on a blood-test report. These antibodies are useful clues, but they are not a complete map of the disease. Tissue research has found biological differences between anti-SSA-positive and anti-centromere-positive Sjögren's. Those results have not established an antibody-based rule for choosing a particular drug. [8]

Negative SSA does not explain away persistent symptoms or automatically exclude Sjögren's. It also does not mean that every person with dryness has seronegative Sjögren's. The clinical assessment must bring together the history, examination and appropriate objective findings. When reading about a new treatment, check whether people with your antibody pattern and organ problems were represented. A result from a narrowly selected group may not apply in the same way to you.

Can nerves contribute to dryness, pain or other symptoms?

Glands need nerve signals to release fluid. Nerves also influence sensation, heart-rate responses and digestive function. Some of these functions run automatically through the autonomic nervous system. Studies have linked autonomic symptoms with the burden of Sjögren's, which is a reason to take such symptoms seriously and assess them appropriately. A questionnaire alone cannot identify their cause. [10]

Receptors are parts of cells that receive signals. Some research asks whether antibodies interfere with receptors involved in nerve signaling. Laboratory support exists, but test methods have

produced conflicting results. A positive commercial receptor-antibody result is therefore not a complete explanation or an automatic reason for immune treatment. The clinician still needs to establish what is happening. A research test that measures an antibody's effect on cells is different from a routine test that detects its presence; the results cannot simply be treated as equivalent. [11, 12]

Why can I feel very unwell when my activity score is low?

A disease activity score measures selected features. It does not measure every cause of fatigue, pain, dryness or difficulty functioning. Conversely, some organ problems require attention even when a person does not feel especially unwell. Neither situation means that the other person's experience is more valid.

Researchers group symptom patterns to improve study design and explore why treatments help some people more than others. These groups are not labels saying symptoms are psychological or imagined. In everyday care, the useful question is what is limiting you: surface damage, low secretion, nerve pain, sleep disturbance, inflammatory disease or several factors together. Naming the problem makes the treatment goal clearer. [14]

What exactly is a biomarker?

A biomarker is a measurable feature of a biological process, such as the level of a protein in blood. Its usefulness depends on the question. A test that helps identify a disease may not predict which treatment will help. A result associated with future risk may not show that a particular medicine reduces that risk. [1]

Question	What the test would need to show
Does this support the diagnosis?	Reliable separation from relevant alternative explanations
What may happen later?	Validated information about future outcomes
Is the medicine acting on its target?	A reproducible biological change
Which medicine is more likely to help?	A difference in comparative treatment benefit

Before paying for an additional panel, ask what decision the result would change. A technically sophisticated report can still lack evidence for the decision you need.

What can the tests already used in care tell me?

Routine tests help assemble a picture rather than deliver a single verdict. Antibodies, blood counts, immunoglobulins (antibody proteins) and complement (a group of immune proteins) may contribute different information alongside eye tests, secretion measurements and organ assessment. An abnormal number needs to be interpreted in that context. [19]

A risk marker is not a diagnosis of a future complication. Equally, a reassuring blood result should not be used to dismiss a new persistent gland swelling or another important change. Discuss new findings rather than trying to calculate personal risk from a research table. Ask whether a test is

being used to diagnose, monitor treatment safety, follow an organ problem or assess a specific concern; the answer explains why and when it might be repeated.

Why do biopsy, ultrasound and saliva tests sometimes disagree?

They look at different things. A biopsy examines a small tissue sample. Ultrasound shows structural patterns. A saliva test measures fluid produced under particular conditions. None is a perfect substitute for all the others, and symptoms describe an additional part of the picture.

New research measures many proteins or genes in saliva, tears, blood or tissue. Those results can depend on collection methods and which cells are present. A study analyzing thousands of cells may still include only a few people. Before a new test becomes useful, it needs reliable results across laboratories and patients similar to those who will actually receive it. Disagreement should lead to interpretation, not an automatic conclusion that one test or the person is wrong. [8, 9]

Are “early Sjögren” antibody panels reliable?

A panel checks several antibodies together. Tests for antibodies such as SP1, PSP and CA6 arose from promising discovery work. Some early studies reported useful associations. A later study in a rheumatology outpatient population found that the tested panel did not distinguish Sjögren’s well from relevant comparison groups. [16, 17, 18]

These results explain why an “early” label on a panel is not proof that it can confirm your diagnosis before standard testing. They do not mean that all new biomarker research is worthless. Ask which exact test was validated, against which alternative illnesses, and whether it adds useful information to your assessment. A positive panel should not replace a structured evaluation; a negative panel should not end an appropriate investigation of persistent symptoms.

Could a molecular profile choose my medicine?

That is an important goal of research. A phenotype describes what is observed, such as symptoms and examination findings. An endotype aims to describe the biology behind it. A molecular profile may measure which genes are active in a sample. Molecular studies and reanalyses of previous trials suggest that some groups may respond differently. They have not yet established a universal routine test that selects the best Sjögren treatment for each person. [13, 15]

A promising result should be checked in a new group and ideally in a trial that plans the test-based decision in advance. Searching through completed trials can find useful clues and chance patterns. Also, “healthy-like” in a molecular paper means similar results in the measured features; it does not mean a patient is healthy or their symptoms are unreal. A research label should not determine access to otherwise indicated care.

How can treatment be personalized now?

Start with your priorities and the clinical problems that need treatment. Different plans may be appropriate for someone whose main difficulty is eating with dry mouth, someone with inflammatory organ disease and someone whose function is limited by nerve pain. Previous benefit, side effects, other illnesses and practical burdens all matter.

Agree on a goal you can recognize, a time to review it and how side effects will be assessed. Examples include reading more comfortably, sleeping with fewer interruptions or improving an objectively measured organ problem. Ask what would prompt a change of plan. Personalization

already includes this careful matching of care to needs; it does not require an expensive molecular panel. A research test is useful only if it adds to that process.

Can a gland work better without growing back?

Yes. Less discomfort, increased output from surviving cells, recovery from a reversible problem and new tissue growth are different possibilities. Reducing inflammation can help the gland without proving that new tissue has grown. An increase in saliva may be valuable even when no new gland tissue has been demonstrated. Likewise, seeing cells with gland markers in a laboratory does not prove useful secretion into a person's mouth. [30]

Researchers must also consider ducts, blood supply, nerves and the surrounding tissue. Repeated function measurements under similar conditions are more informative than isolated readings. A low output does not reveal exactly how much tissue is permanently lost. Continue appropriate eye and mouth protection while discussing what recovery might realistically mean in your situation.

What does "premature aging" of gland cells mean?

Stem and progenitor cells are cells that can give rise to other cells and contribute to tissue maintenance. Researchers have observed aging-related changes in these gland cells and studied how inflammation affects them. This is a possible explanation for impaired repair, not proof that all of your gland cells have permanently stopped working. Here, "aging" describes changes in cells; it is not a measure of your age or a verdict on how much function you can regain. [20]

It also does not establish an "anti-aging" medicine, supplement or senolytic treatment for Sjögren's. Senolytics are intended to remove certain cells with aging-related changes; that idea alone does not establish a safe or useful treatment. A treatment would need to show that it changes the relevant cell process, improves useful gland function and has an acceptable safety profile. Ask what was actually measured: a cell marker, tissue structure, saliva output or everyday benefit. A claim about one of these should not silently become a claim about all of them.

What are gland organoids, and can they be transplanted?

Organoids are small three-dimensional groups of cells grown in a laboratory to reproduce selected features of a tissue. They can help researchers study Sjögren's and explore treatments. They are not miniature replacement organs already available for routine transplantation. Recent studies include models grown from patients' gland samples and human-cell organoids tested in mice. A model can reproduce part of a disease without reproducing the whole person. [21, 22]

"Made from human cells" is different from "successfully transplanted into patients." A future graft would need to survive, function, connect to the body's drainage system and remain safe. It would also have to cope with the disease environment. Organoids may become useful for treatment testing before they become useful for transplantation, but predicting an individual's response also needs clinical validation.

What do we know about stem-cell injections?

Cell treatments differ by cell source, processing, route and intended action. One approach uses mesenchymal stromal cells, which can be obtained from tissues such as fat. They may alter inflammatory signals without becoming new gland tissue. Evidence for one preparation cannot be transferred automatically to another.

A small randomized Sjögren trial assigned 74 people to receive adipose-derived cells or placebo; 64 completed treatment and follow-up. It reported early signals, but at 6 months there was no statistically significant difference between groups in unstimulated saliva flow—the saliva produced without deliberate stimulation. Durable gland regeneration was not established. [24]

This supports further research rather than a promise of regrowth. If considering a study, ask for the exact product, comparator, follow-up, harms and outcomes. An entry in a trial registry shows that a study is listed; it does not prove that it works or that recruitment is currently open. [32]

CAR-T is a different kind of cell treatment: T cells, a type of immune cell, are modified to recognize particular target cells. In autoimmune research the aim is to change the harmful immune response, not to supply new gland cells. Sjögren applications remain experimental. Better disease control would not itself prove gland regrowth, and the potential benefits must be assessed alongside serious risks. [33, 34]

Could gene therapy restore saliva?

Aquaporin is a protein that helps water pass through a cell membrane. Aquaporin gene transfer aims to give cells instructions to make this protein and release more fluid. A human phase 1 study of AAV2-hAQP1 followed 24 people with dry mouth after radiation treatment for 12 months. Phase 1 is an early stage of testing, with an emphasis on safety. The study was open-label: participants and researchers knew the treatment, and there was no randomized control group. Radiation injury is different from autoimmune Sjögren's. [25]

The work is relevant to the future of salivary treatment, but it does not establish benefit for Sjögren's. Improving the function of surviving cells is also different from rebuilding an entire gland. Ask which disease was studied and which outcome improved. A designation supporting drug development should not be confused with approval of a treatment for your condition.

Are peptides such as Lacripep a regeneration treatment?

Peptides are short chains of the building blocks of proteins. Lacripep is one specific peptide studied for the eye surface. Its first human Sjögren study compared Lacripep with the drop base without active peptide in 204 people. By day 28, Lacripep had not shown a statistically significant advantage over the drop base on the overall corneal staining and dryness measures. Staining uses a dye to show damage on the eye surface. Later subgroup and regional findings gave reasons for further study; they do not replace the overall result. [26]

Research on corneal nerve and surface repair addresses a different question from regrowing tear or salivary glands. A positive result for one named peptide cannot support every product sold as a "regenerative peptide." Ask about the exact molecule, preparation, route, anatomical target and human evidence. This allows promising research to be considered fairly without turning an early signal into a treatment guarantee. [27]

What about cell sheets, scaffolds and exosomes?

A cell sheet is a thin layer of cells; a scaffold is a structure intended to support tissue growth. Both explore ways to build tissue and connect it to the body. A study using human-derived salivary cell sheets achieved partial duct integration in mice; this remains preclinical work, before testing that use in people. Exosomes and other extracellular vesicles are tiny particles released by cells that carry biological signals. They are not interchangeable with intact cells, and a "cell-free" product is not automatically safe. [23]

For any proposed product, look for evidence and regulatory status for that particular product and use. Approval of a different cell therapy does not establish approval for gland regeneration. Reports of harm from unapproved exosome products are a reason to examine claims carefully, while legitimate research continues. [28, 29]

How would we know that regeneration really helps?

A credible claim needs more than a photograph of cells or a testimonial. It should show sustained useful function, meaningful benefit and adequate safety follow-up in the relevant patients. Tissue evidence can strengthen the claim, but should connect to function.

Ask	Why it matters
Were people with Sjögren's studied?	Other causes of gland injury may respond differently
Was there a comparison group?	Output and symptoms can vary for other reasons
What improved, and for how long?	A short signal is different from durable benefit
What harms and uncertainties remain?	A lasting intervention requires lasting observation

Early studies can answer limited questions honestly. The problem begins when their conclusions are expanded beyond what they measured.

For example, a lower inflammation score can support better disease control. More saliva on repeated testing can support improved gland function. Neither finding alone shows that new working gland tissue has formed. A claim of regeneration needs evidence for that additional step. [1, 30, 31]

What should I take to my next appointment?

Bring the exact report or study link, your current concerns and the outcome you hope to improve. For a test, ask: "What would we do differently with the result?" For a treatment, ask: "Which problem is it meant to help, and how will we measure benefit?" For a regenerative proposal, ask: "Was useful, lasting recovery shown in people with my disease?"

You do not need to become a molecular biologist to ask these questions. It is reasonable to be hopeful and to want clear evidence at the same time. Research uncertainty should be explained openly while your current symptoms, function and organ health receive appropriate attention.

Continue reading

Sjögren's module · Start with your question · Diagnosis and uncertainty · Choosing treatment goals · Eye, mouth and gland care · Anti-centromere antibodies · Fatigue, pain and function · Understanding clinical trials · Treatments in development

About this publication

Personal educational publication by Olga Goodman, MD. This is not a clinic portal or an emergency service. Any private expert service is separate from clinic accounts and insurance billing. Reuse requires attribution and a link to the original publication.

References

01. FDA–NIH BEST: Biomarkers, EndpointS, and other Tools · living resource

02. Genome-wide association study identifies Sjögren's risk loci with functional implications in immune and glandular cells · 2022

03. Hudson et al. Evidence that autoantibody production may be driven by acute Epstein–Barr virus infection in Sjögren's disease · 2024 online

04. Gut microbiota from Sjögren syndrome patients causes decreased T regulatory cells and desiccation-induced corneal barrier disruption in mice · 2022

05. Inhibition of JAK–STAT pathway corrects salivary gland inflammation and interferon driven immune activation in Sjögren's disease · 2024

06. Lee et al. JAK-1 inhibition suppresses interferon-induced BAFF production in human salivary gland · 2018

07. Bodewes et al. Hydroxychloroquine treatment downregulates systemic interferon activation in the JOQUER randomized trial · 2020; online 2019

08. Inamo et al. Comparative single-cell and spatial profiling of anti-SSA-positive and anti-centromere-positive Sjögren's disease · 2025

09. Nayar et al. Molecular and spatial analysis of tertiary lymphoid structures in Sjogren's syndrome · 2025

10. Autonomic symptoms are common and associated with overall symptom burden and disease activity in primary Sjögren's syndrome · 2012

11. A novel luminescence-based method for detecting functionally active M3 muscarinic receptor antibodies · 2014

12. Peptide-based ELISAs are not sensitive and specific enough to detect muscarinic receptor type 3 autoantibodies in Sjögren's syndrome · assay validation study

13. Soret et al. A new molecular classification to drive precision treatment strategies in primary Sjögren's syndrome · 2021

14. Tarn et al. Symptom-based stratification of primary Sjögren's syndrome: cohorts and trial reanalyses · 2019

15. Chevet et al. Transcriptomic stratification predicts response to rituximab, abatacept, or hydroxychloroquine–leflunomide in three randomized trials · 2026; online December 2025

16. Novel autoantibodies in Sjogren's syndrome · 2012

17. Tissue-specific autoantibodies improve diagnosis of primary Sjögren's syndrome in the early stage · 2019

18. Johr et al. Diagnostic use of testing for novel murine autoantibodies for Sjögren disease in the rheumatology outpatient setting · 2026; online 2025

19. British Society for Rheumatology guideline on management of adult and juvenile onset Sjögren disease · 2024 online; 2025 issue

20. Pringle et al. Salivary gland stem cells age prematurely in primary Sjögren's syndrome · 2019; online 2018

21. Development of salivary gland organoids derived from patient biopsies: a functional model of Sjögren's disease · 2025

22. Functional human salivary gland organoids for tissue regeneration in chemically defined culture systems · 2026

23. Human iPSC-derived salivary gland cell sheets integrate with injured glands to form glandular structures · 2025

24. Li et al. Effect of adipose tissue-derived stem cells therapy on clinical response in primary Sjögren's syndrome · 2023

25. Brennan et al. Phase 1 open-label dose-escalation study of AAV2-hAQP1 for radiation-induced late xerostomia and parotid hypofunction · 2026

26. Tauber et al. Lacripep for primary Sjögren-associated ocular surface disease: first-in-human study · 2022 online; 2023 issue

27. A synthetic tear protein resolves dry eye through promoting corneal nerve regeneration · 2022

28. FDA: Approved cellular and gene therapy products · current list checked 23 September 2026

29. FDA: Public safety notification on exosome products · 2019 notification; checked September 2026

30. NIDCR: Saliva and salivary gland disorders · official patient resource

31. FDA: Surrogate endpoint resources for drug and biologic development · official resource

32. NCT06805448: Intraglandular adipose-derived mesenchymal stem cells for Sjögren-related xerostomia · registry record

33. National Cancer Institute: CAR T Cells—Engineering Patients' Immune Cells to Treat Their Cancers · mechanism and safety background; updated 26 February 2025; checked 21 November 2026

34. NCT06428188: Sequential CAR-T Cells Targeting BCMA/CD19 in Patients With Relapsed/Refractory Autoimmune Diseases · includes Sjögren's; registry description, not evidence of benefit or confirmation of current recruitment