Genitourinary Syndrome of Menopause: A Bibliometric Analysis of the Top 100 Cited Articles

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ABSTRACT Genitourinary syndrome of menopause (GSM) has gained increasing attention in recent years, with growing literature on its pathophysiology, clinical presentation, and treatment options. A bibliometric analysis helps identify high-quality research based on citation rates and journal impact factors. In this review, our objective was to analyze the key themes and topics in GSM literature. We conducted a bibliometric analysis using the Thomson Reuters Web of Science database to identify the top 100 most-cited articles on GSM published over the past 50 years. Data were categorized into manuscript type, theme, author, country of origin, journal impact factor, and citation rate. The mean citation count per article was 67, ranging from 405 to 5. The most-cited paper, authored by the North American Menopause Society, had the highest citation rate of 45.0 citations per year. The majority of articles (n=65) were published between 2010 and 2019. Randomized controlled trials comprised the largest publication type (29%). Most articles (n=65) were published in Q1-ranked journals. Although GSM is a relatively recent concept, the most-cited articles from the past 50 years generally focus on its medical and surgical treatments, as well as its epidemiology. This bibliometric analysis is the first to evaluate the top 100 most influential publications on GSM.

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KEY WORDS: genitourinary syndrome of menopause (GSM), vulvovaginal atrophy, atrophic vaginitis, bibliometric review

Genitourinary syndrome of menopause (GSM), previously known as vulvovaginal atrophy or atrophic vaginitis, is a progressive condition that negatively affects health and quality of life of many women after menopause. GSM is a relatively new term that was established in 2014 by the International Society for the Study of Women's Sexual Health and the North American Menopause Society (NAMS) [1]. GSM describes a broad range of menopausal symptoms mostly attributed to the decline of estrogen levels in postmenopausal women. The anatomical and pathophysiological changes caused by GSM affect the vagina, vulva, lower urinary tract system, and the musculature of the pelvic floor organs that are characterized by a very high concentration of estrogen receptors [2]. The decline in estrogen levels after menopause causes anatomical, biochemical, and histological changes in these organs and tissues. Reduction in collagen and hyaluronic acid content, significant thinning of the mucosal epithelium, marked increases in the density of connective tissue, and a reduction in the number of blood vessels supplying these organs are some of the changes that result in increased vaginal pH, reduced vaginal elasticity and disruption of normal vaginal flora. These changes consequently lead to the characteristic symptoms of GSM that include vaginal burning, irritation, bleeding and discharge, dysuria, and recurrent urinary tract infections as well as impairment in sexual function (loss of libido, lack of lubrication, discomfort, and pain with intercourse) [3].

More than 50% of postmenopausal women experience some degree of symptoms caused by GSM [4].

The therapeutic options for treatment of GSM, include lifestyle changes such as exercise, pelvic floor muscle training, and smoking cessation, have been shown to improve symptoms [5]. In addition, hormonal (estrogen, DHEA) as well as non-hormonal treatments (vaginal lubricants, moisturizers, micro ablative CO_2, or YAG laser) may be offered.

Bibliometric analysis is a popular method for exploring and analyzing large volumes of scientific data with the goal of uncovering publication patterns and research landscape concerning a specific topic. Previous bibliometric reviews were published on different topics in gynecology and women's health such as urinary incontinence, female sexual dysfunction, and menopausal syn-

drome [6-8]. However, a bibliometric analysis on GSM and its associated symptoms has not yet been conducted, to the best of our knowledge. The aim of this review is to present a bibliometric overview of a vast amount of literature concerning the presentation, pathophysiology, and management of GSM and to identify those articles of key relevance and greater clinical significance according to their bibliometric properties.

GENITOURINARY SYNDROME OF MENOPAUSE HAS GAINED SIGNIFICANT ATTENTION, WITH GROWING RESEARCH ON ITS PATHOPHYSIOLOGY, CLINICAL FEATURES, AND TREATMENTS.

METHODS

We relied on bibliometric information that was extracted from the Web of Science citation indexing database on journal articles that were published between 1971 and 2021. The Web of Science is among the largest citation databases in the world that covers almost 1.9 billion cited references from over 171 million records.

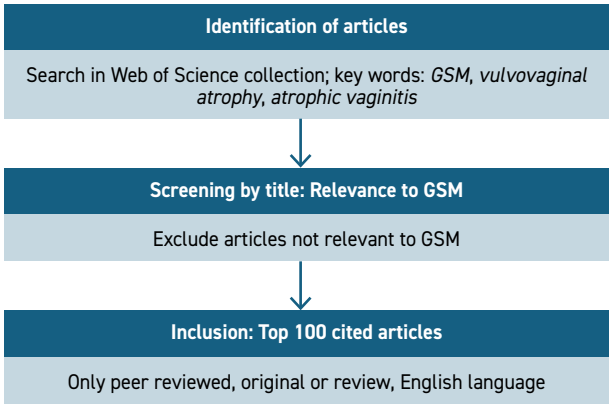
Since GSM is a relatively new term that was established in 2014, we entered it as well as its most previously used terms and synonyms into the Web of Science search. After performing a comprehensive search in the Web of Science Core Collection using the keywords *genitourinary syndrome of menopause*, *GSM*, *vulvovaginal atrophy*, and *atrophic vaginitis*, all retrieved articles were screened by title to assess their relevance. Articles that were not clearly related to GSM were excluded. From the remaining relevant articles, we selected the 100 most-cited papers for inclusion in the analysis. Search results were limited to articles written in English. The search was completed within one day, 19 July 2022, to avoid search errors from daily updates of the database. A total of 1558 articles were returned. We ranked publications by the number of citations, allowing us to identify and discuss the most influential and clinically significant articles on the topic of GSM. The Journal Citation Reports (JCR) database was used to identify the 2021 impact factor of each journal. We included only peer-reviewed original and review articles published in academic journals. We excluded conference abstracts, book chapters, and any other non-peer-reviewed materials [Figure 1].

RESULTS

Between 1971 and 2021, a total of 1558 articles were detected. Two assessors (EK, TE) independently performed the final database analysis. In addition, the citation rate was obtained by dividing the total number of citations by the number of years since publication. This variable was used to counter bias coming from the fact that older publications had more citations accumulating overtime. The top three articles with the highest citation rates were all published by the NAMS. The most cited article, with 405 citations and a citation rate of 45.0 per year, was "Management of Symptomatic Vulvovaginal Atrophy: 2013 Position Statement of The North American Menopause Society", [9] was published in 2013 in *Menopause: The Journal of the North American Menopause Society*. The objective of that article was to expand on the previously issued statement from NAMS on the management of symptomatic vulvovaginal atrophy (VVA) in postmenopausal women.

Figure 1. A PRISMA-style flowchart

GSM = genitourinary syndrome of menopause

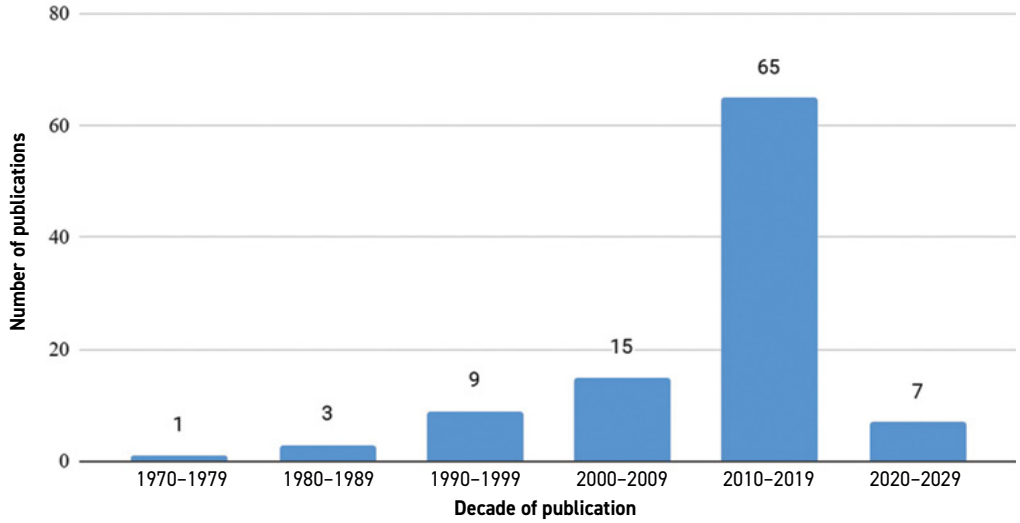


The second most cited article was "Genitourinary Syndrome of Menopause: New Terminology for Vulvovaginal Atrophy from the International Society for the Study of Women's Sexual Health and The North American Menopause Society" [10] with the second highest citation rate (42.4). The article with the third highest citation rate (41.0) was "The 2020 Genitourinary Syndrome of Menopause Position Statement of The North American Menopause Society" [11]. The mean number of citations was 67, ranging between 405 and 5.

This set of 100 top cited papers were published over the period of 50 years. There was a steady increase in the number of publications from 1970 onward, with a significant peak in GSM-related publications during the period between 2010 and 2019 [Figure 2]. Thereafter there was a

Figure 2. Publication trends in GSM-related research, divided by decades

GSM = genitourinary syndrome of menopause



notable decline in publications in 2020. The earliest manuscript in this set was "Treatment of Atrophic Vaginitis in Post-menopausal Women with Micronized Estradiol Cream-Follow Up Study" by Gordon et al. in 1979 [12]. It was published in the *Journal of the Kentucky Medical Association* and was cited 5 times. The most recent paper, "Pilot Study of Fractional CO_2, Laser Therapy in Genitourinary Syndrome of Menopause in Gynecologic Cancer Survivors" was published in 2021 in *Maturitas* and was cited nine times [13]. This study concluded that fractional CO_2, laser therapy was a feasible treatment in gynecological cancer survivors, with preliminary evidence of safety.

The articles in the 100 top cited list were published in journals from a variety of disciplines. The highest number of publications was divided between two journals: *Menopause: The Journal of North American Menopause Society* (23 publications, impact factor 3.31) and *Maturitas* (20 publications, impact factor 5.11).

Figure 3 shows the distribution of journal quartiles in a given year of publication. A quartile is the ranking of a journal based on the impact factor, citation, and indexing of that journal. The most prestigious journals within a subject area are those occupying the first quartile, Q1. Most publications (n=65) in the top 100 list are published in journals with Q1 ranking, followed by 32 in Q2 and 3 in Q3. Among the top 100 cited papers on GSM, none were published in a Q4 journal, although the lowest citation number was five.

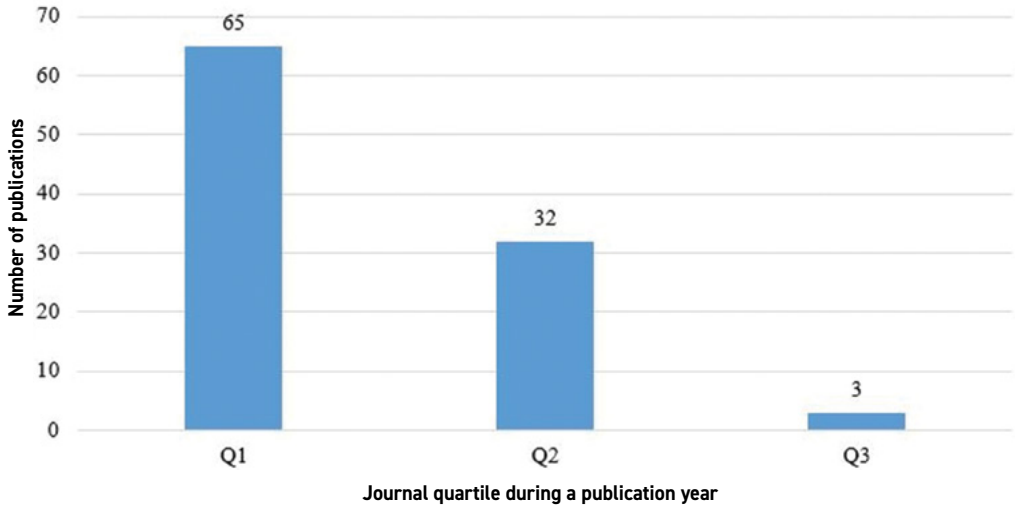
Geographic distribution was also evaluated. As shown in Figure 4, most articles originated from the United States (n=41), Italy (n=26), and Spain (n=11).

Regarding study design, we categorized the top 100 articles by document type. Most publications were randomized controlled trials (n=29), followed by review articles (n=14) and observational studies (n=10). The remaining manuscripts included cross-sectional studies, conference proceedings, and position papers.

Following the analysis of article types and impact factors, we examined the distribution of research themes among the top 100 publications. Most articles focused on medical treatment (n=34) and epidemiology (n=19), together accounting for over half of the top 100 papers. These two themes account for more than half the publications in the top 100 list, making them a significant focus of research and publication. The highest cited medical treatment themed paper "The Role of Local Vaginal Estrogen for Treatment of Vaginal Atrophy in Postmenopausal Women: 2007 Position Statement of The North American Menopause Society" [14] discussed the high effectiveness of local vaginal estrogen treatment for vaginal atrophy and concluded that this therapy should be continued for as long as distressful

A BIBLIOMETRIC ANALYSIS IDENTIFIED THE 100 MOST CITED GSM ARTICLES, FOCUSING ON CITATION RATES, JOURNAL RANKINGS, AND KEY THEMES SUCH AS TREATMENTS AND EPIDEMIOLOGY.

Figure 3. The distribution of journal quartiles



symptoms remain [14]. Sixteen articles discussed the role of surgical laser treatment, and another 16 articles compared the effectiveness of laser and medical treatment on associated outcomes of patients suffering from GSM. We also analyzed the distribution of publications based on the impact factor of each journal. More than a quarter (26%) of publications were published in journals with an impact factor higher than five. *JAMA: Journal of The American Medical Association* had the highest impact factor (157.335) and had one article published that was included in the top 100 publications: "Vaginal Atrophy in the Post-menopausal Woman. The Importance of Sexual Activity and Hormones" [15] that was cited 235 times.

To the best of our knowledge, this is the first bibliometric analysis of the most influential papers on the topic of GSM. Key themes identified were pathophysiology, clinical presentation and approaches to treatment of GSM. Most publications in this analysis dealt with the use of estrogen based vaginal creams and novel carbon dioxide lasers. Most articles mentioned in this review were society guidelines or systematic reviews.

DISCUSSION

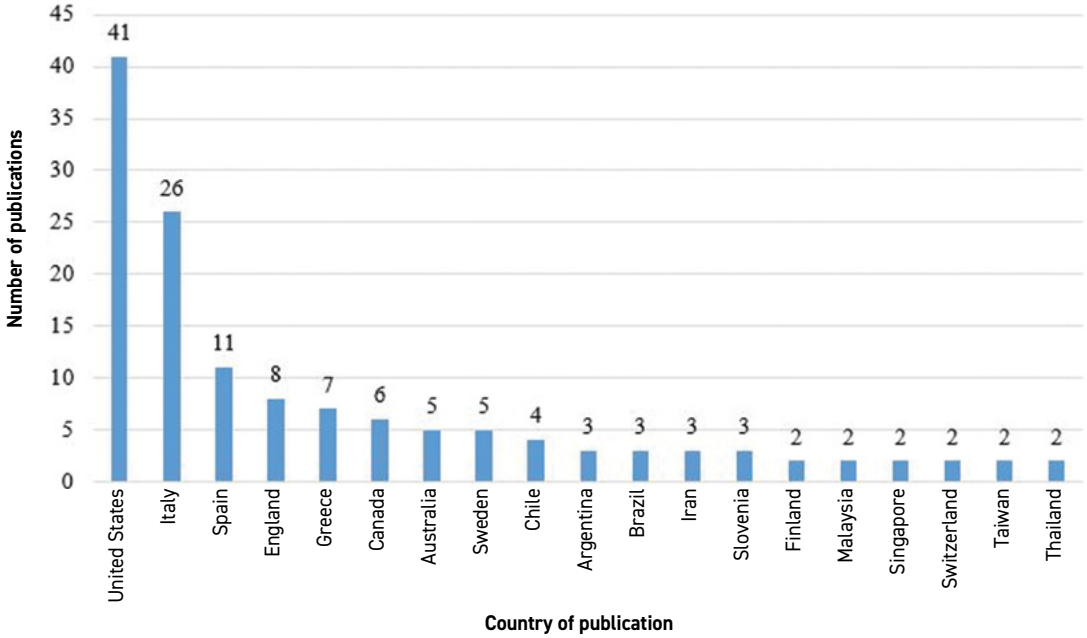
We conducted a bibliometric analysis of the 100 most cited publications on GSM. We analyzed publications based on the number of citations, impact factors of the journals, years of publication, and geographical distribution, as well as medical fields and document types.

While journal impact factors may influence citation count, journal quartile ranking often better reflects a journal's standing within its field. The most cited article and the article with the highest citation rate (45.0) was published in 2013 by NAMS. The objective of this publication was to update and expand on the previous statement of the NAMS on the management of symptomatic vulvovaginal atrophy in postmenopausal women. The dominance of NAMS publications among the top-cited articles reflects the NAMS's central role in shaping GSM research and clinical practice, especially through its position statements on local estrogen therapy.

The second most cited article with citation rate of 42.4 was published in 2014 in *Menopause: The Journal of the North American Menopause Society*. The article was cited 320 times. The goal of the article was to discuss the results of a conference sponsored by ISSWSH and NAMS. The aim of the 2013 conference was to review the clinical science related to genitourinary symptoms associated with menopause and to determine whether the term vulvovaginal atrophy should be revised to better describe the condition for medical care, treatment, clinical research, and teaching. The 2014 redefinition of vulvovaginal atrophy as GSM, proposed by ISSWSH and NAMS, marked a significant shift toward more inclusive and patient-sensitive terminology [1].

The third most cited article with citation rate of 25.3 was published in 2010 in *Climacteric*. It was cited 276 times. Several treatment options were proposed

Figure 4. Country of origin of articles



in the article. Non-hormonal treatments such as lubricants and moisturizers for relieving vaginal dryness during sexual intercourse, systemic estrogen therapy for successful restoration of the vaginal pH levels and for alleviating vaginal atrophy-related symptoms such as dryness, irritation and urinary urgency, and local estrogen therapy. The key recommendations for clinical care listed in the article also included an early, open and sensitive discussion of the health care providers with postmenopausal women about their urogenital health to make sure that symptoms of vaginal atrophy are detected early and correctly managed [16].

MOST INFLUENTIAL ARTICLES WERE PUBLISHED BETWEEN 2010 AND 2019, WITH RANDOMIZED CONTROLLED TRIALS AS THE LEADING PUBLICATION TYPE AND Q1 JOURNALS DOMINATING.

A significant number of publications in the top 100 list discussed the use of innovative carbon dioxide laser in the treatment of genitourinary syndrome of menopause. Of the top 100 cited publications, 19 contained the term *laser therapy* in the title, the earliest of which was published in 2015 and the most recent was published in 2020. In addition, six articles were published in journals with a specific focus on medical lasers. Four articles were published in *Lasers in Surgery and Medicine* and two articles were published in *Lasers in Medical Science*.

The most cited article on the use of carbon dioxide laser was "Microscopic and Ultrastructural Modifications of Postmenopausal Atrophic Vaginal Mucosa after Fractional Carbon Dioxide Laser Treatment" [17]. It was published in *Lasers in Medical Science* in 2015 and was cited 154 times [17]. This study was conducted on 50 postmenopausal women affected by severe atrophy symptoms including dryness, itchiness, burning, dysuria, and dyspareunia. Carbon dioxide laser treatments were performed without anesthesia since they are completely painless. Biopsies were then taken from each patient after 30 and 60 days from different sites on the vaginal wall and subsequently compared to the biopsies taken before the treatment. The study showed reassuring microscopic evidence of morphologic changes following carbon dioxide laser treatment on atrophic postmenopausal vaginal mucosa. Pre-treatment biopsy showed vaginal mucosa containing very few cell layers and appeared very thin, while post-treatment biopsy showed very thick stratified squamous epithelium forming many layers. This study was one of the earliest published on the use of lasers in vulvovaginal atrophy and opened new perspectives on the use of electromagnetic energy for restoring the functionality of atrophic vaginal mucosa.

Another similar studs published in 2015 and cited 152 times, "Sexual Function after Fractional Microablative CO_2 Laser in Women with Vulvovaginal Atrophy" [18], concluded that fractional microablative CO_2 laser treatment was associated with a significant improvement of sexual function and satisfaction with sexual life in postmenopausal women with vulvovaginal atrophy symptoms [18]. This study was published in *Climacteric*.

The recent article discussing the use of laser therapy in genitourinary syndrome of menopause was published in 2021 in *Maturitas*: "Pilot Study of Fractional CO_2 Laser Therapy for Genitourinary Syndrome of Menopause in Gynecologic Cancer Survivors" [19]. The study showed preliminary evidence of improvement in sexual function compared with sham treatment in gynecologic cancer survivors.

Even though GSM affects more than half of the general population of women experiencing post-menopausal symptoms, it is seen more frequently in women affected by breast cancer [20]. Earlier symptom onset is often explained by chemotherapy-induced ovarian insufficiency, oophorectomy and/or radiation therapy. In the top 100 cited publications on GSM, five publications contained the word 'cancer' in the title. The most cited article on GSM and cancer was "Management of Genitourinary Syndrome of Menopause in Women with or at High Risk for Breast Cancer: Consensus Recommendations from NAMS and the International Society for the Study of Women's Sexual Health" [20]. It was cited 80 times and published in 2018 in *Menopause: The Journal of the North American Menopause Society*. The article reviewed pharmacological and non-pharmacological treatment options for women with a history of breast cancer and presenting with vulvovaginal atrophy. The authors concluded that there are significant gaps in the scientific literature about the evidence of safe and effective therapies. Some of the reasons for this gap, as the authors discussed, included lack of evidence for safety of current GSM treatments for cancer patients, as well as U.S. Food and Drug Administration (FDA)-required labeling of all products containing estrogen. As per FDA requirements, the boxed warning of all estrogen products must include the following text: *Warning: Endometrial Cancer, Cardiovascular Disorders, Breast Cancer, and Probable Dementia* [21]. This warning often leads health care providers to refrain from providing treatment for GSM, thus leaving patients untreated.

Based on this bibliometric analysis, there are no highly cited papers on the pharmacological treatment of GSM or vulvovaginal atrophy in patients with cancer. This situation shows a significant deficit in literature and may guide further research in this area. Additional research is needed to evaluate safety and efficacy of existing therapies including intravaginal estrogen, different lasers as well as non-pharmacological treatments. This is important in providing data regarding the most effective treatment of GSM in patients suffering from cancer.

A bibliometric review is a useful tool in analyzing large datasets of published literature and evaluating trends related to a certain scientific topic. It is important to address the limitations of a bibliometric review. Unfortunately, metrics such as citation rate can be exploited by researchers and the journals to artificially raise bibliometric scores. Self-citations, for example, may significantly distort actual citation rates. Studies have found that author self-citations can account for up to one-third of the total number of citations received within the first few years of publication [22]. The number of citations of an article is often influenced by the journal's impact factor. The impact factor is an index calculated by Clarivate's Web of Science database that reflects the yearly average number of citations of all articles published in a given journal in the previous 2 years. The impact factor is often used as an indicator of the relative value and importance of a journal in its scientific field. Impact factor as a metric also has its limitations. A study that analyzed 7528 journals showed that as few as 300 journals account for more than 50% of the total number of citations, and approximately 38 million articles were not cited at all [23]. These circumstances mean that impact factor is often driven by a small number of highly cited articles and may not be a good enough indicator of an article's scientific merit. This limitation does not significantly alter the results of our study since the majority of journals included in this review had an impact factor of less than 5. Another limitation of this study is the predominance of cited literature from North America and Western Europe. Although relevant studies from other regions were included where applicable, the global research landscape may be underrepresented due to the historical imbalance in publication volume and visibility.

CONCLUSIONS

This bibliometric review highlights key advances and prevailing gaps in GSM research. The prominence of society guidelines underscores their influence on clinical practice, particularly in promoting local estrogen therapy. At the same time, the emergence of laser therapies provides promising non-hormonal alternatives, particularly

for patients with contraindications to hormonal treatment. Notably, the lack of high-impact studies on GSM treatment in breast cancer survivors reveals an urgent need for focused research in this population. Addressing this gap may significantly improve therapeutic options and quality of life for these patients.

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Capsule

Tissue residency determinant

Tissue-resident memory T (TRM) cells provide defense against recurring infections, but their dysfunction can lead to disease. Although transcriptional programs associated with the formation of $CD8^+$ TRM cells have been defined, much less is known about the development of $CD4^+$ TRM cells. **Kiuchi** et al. identified a transcription factor, hepatic leukemia factor (HLF), that promoted the differentiation of $CD4^+$ TRM cells in the lungs of mice during chronic inflammation. Based on its DNA-binding profile, HLF coordinated the up-regulation of genes required for tissue residency and a pro-inflammatory phenotype while suppressing the expression of genes that are required for tissue egress. Mice that lacked HLF expression in $CD4^+$ T cells had less lung pathology during long-term exposure to a fungal antigen.

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