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Title

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Journal

Dermatology Online Journal, 26(11)

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Publication Date

2020

DOI

10.5070/D32611048118

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Saccharomyces cerevisiae as a skin physiology, pathology, and treatment model

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Abstract

Saccharomyces cerevisiae serves as a useful model in experimental biology. Within dermatology research, several studies have examined this organism's role in skin physiology, pathology, and treatment. *Saccharomyces cerevisiae* has been used to explore the mechanisms of melanogenesis as its extract inhibits key enzymes involved in melanogenesis and melanosome transfer. Additionally, the lack of probiotic intestinal *Saccharomyces cerevisiae* has been associated with psoriasis, potentially related to the anti-inflammatory effects of the yeast. Furthermore, antibodies against *Saccharomyces cerevisiae* have been observed in skin conditions, including atopic dermatitis. *Saccharomyces cerevisiae* may even cause skin infections, such as septic emboli in a patient with acute myelogenous leukemia. Lastly, *Saccharomyces cerevisiae* has potential use in vaccine development against melanoma and is utilized to study various treatment modalities such as zinc pyrithione, an ingredient often used in anti-dandruff shampoo.

Keywords: *Saccharomyces cerevisiae*, melanogenesis, psoriasis, atopic dermatitis, melanoma

Introduction

Saccharomyces cerevisiae (*S. cerevisiae*), also known as baker's yeast, is a eukaryotic organism that has served as a very useful cell model in experimental

biology. Many proteins are highly conserved between yeast and human genomes, which allows for the study of the functional significance of different proteins. For example, the yeast model has been very helpful in investigating the RAS pathway and its role in tumorigenesis [1]. Although *S. cerevisiae* has not been widely used in the field of dermatology, we will highlight the studies in which these yeast cells have been used to examine skin physiology, pathology, and treatment. We hope to empower dermatologic researchers to further utilize this tool to uncover additional mechanisms underlying dermatological conditions.

Discussion

Studies related to *S. cerevisiae* and skin physiology, pathology, and treatment were searched on PubMed using the following terms: "Saccharomyces cerevisiae dermatology," "Saccharomyces cerevisiae skin," "Saccharomyces cerevisiae skin physiology," "Saccharomyces cerevisiae skin pathology," "Saccharomyces cerevisiae treatment," and "Saccharomyces cerevisiae skin disorders" (Table 1).

Skin physiology

Use of *Saccharomyces cerevisiae*'s as a cell model revealed important findings related to skin physiology. When a natural yeast extract was added to a culture of melanoma cells, tyrosinase (a key enzyme in melanogenesis) activity was inhibited.

This inhibitory effect was a result of inhibition of enzyme activity; it did not decrease tyrosinase protein levels. Melanogenesis and melanosome transfer was reduced in the presence of the yeast extract, potentially related to the downregulation of PAR-2, an important protein in the melanosome transfer process [2]. Another study used yeast cells to elucidate the localization and function of the ocular albinism 1 (Oa1) protein. This protein co-localized with Pep12p, a late endosomal marker. Ocular albinism 1 is important for melanosome biogenesis by trafficking proteins from the late endosome to melanosomes [3].

Skin pathology

Saccharomyces cerevisiae has also been used as a cell model to study pathological mechanisms. *Sporothrix schenckii* is a dimorphic fungus that infects the skin and causes pink-to-purple nodules to develop. A study identified that phenotypic switching of the fungus was in part related to the *Sporothrix schenckii* silent information regulator 2 gene (*SsSir2*), which silences transcription. Higher levels of *SsSir2* were present in the yeast stage of the fungus relative to the mycelial phase. This marker shares significant homology with the *Sir2* gene, which is involved in phenotypic switching in *S. cerevisiae*. In this way, initial findings from yeast were used to find a related marker in a different organism [4]. Another group used *S. cerevisiae* to study the role of GPR18, a GPCR protein that was abundantly overexpressed in melanoma metastases. After expressing GPR18 cDNA constructs in *S. cerevisiae* cells, GPR18 was constitutively active, revealing its important role in the malignant potential of melanoma [5]. Additionally, *S. cerevisiae* has been used to

characterize the functional aspects of the bovine papillomavirus E2 transcriptional activation domain. Bovine papillomavirus E2 is an important component of the pathogenesis of papillomavirus, which causes warts on the skin. E2 mutants had functional relevance to the transcriptional activation domain [6]. Moreover, *S. cerevisiae* can be helpful in the diagnosis of skin conditions. *Saccharomyces cerevisiae* was used to produce the bullous pemphigoid antigen 230 (BP230); 12 of 17 bullous pemphigoid sera recognized the resulting BP230 antigen [7].

Saccharomyces cerevisiae may also play role in the pathogenesis of psoriasis. The intestinal microbial content of psoriasis patients treated with dimethylfumarate (DMF) was compared to psoriasis patients with no treatment, and healthy controls; fecal *S. cerevisiae* was attenuated in psoriasis patients compared to healthy controls ($P < 0.001$), but DMF use raised their levels back to appropriate levels ($P < 0.001$). Since *S. cerevisiae* has immunomodulatory properties related to its β -glucan cell wall, which lowers TNF (a pro-inflammatory cytokine) and increases IL10 (an anti-inflammatory cytokine), the absence of *S. cerevisiae* may contribute to the inflammatory processes of psoriasis [8].

However, another study associated a pro-inflammatory effect with *S. cerevisiae*, so the exact mechanism of *S. cerevisiae*'s role in psoriasis may not be exactly clear. When mice were administered a single intraperitoneal injection of mannan from *S. cerevisiae*, symptoms of both psoriasis and psoriatic arthritis arose. Upon repeated administration, both conditions worsened in severity. The researchers proposed this was a result of uncontrolled activation

Table 1. Summary of the major roles of *Saccharomyces cerevisiae* in skin physiology, pathology, and treatment.

Area	Major Findings	Reference
Skin Physiology	Demonstrates inhibitory affect in melanogenesis.	[3]
Skin Pathology	Linked with psoriasis.	[8]
	Anti- <i>Saccharomyces cerevisiae</i> antibodies titers found in Behcet disease and X-linked chronic granulomatous disease.	[11]
	Antibodies against gp200, a <i>Saccharomyces cerevisiae</i> protein, found in atopic dermatitis patients.	[12,13]
	Found in the cutaneous septic emboli in a patient with relapsing acute myeloid leukemia.	[15]
Skin Treatment	Vaccine formulations against melanoma contain <i>Saccharomyces cerevisiae</i>	[16,17]
	Zinc pyrithione induced iron starvation in <i>Saccharomyces cerevisiae</i> cells.	[18]

of macrophages, leading to secretion of TNF and downstream T-cell activation, and IL17A production [9]. Further studies are needed to examine how a lack of *S. cerevisiae* in the gut, and the injected mannans from *S. cerevisiae*, can each contribute to psoriatic phenotypes.

Although some conditions are a result of immunomodulation by *S. cerevisiae*, others are characterized by a presence of *S. cerevisiae* antibodies. An eight-year-old boy with X-linked chronic granulomatous disease presented with cheilitis, oral ulcers, erythematous macules, erythematous and violaceous papules throughout the body, and hyperkeratotic papules on the palms and heels. Laboratory results revealed the presence of anti-*S. cerevisiae* antibodies (IgA 42.5U/ml; IgG 81.2U/ml), [10]. Moreover, *S. cerevisiae* antibodies were found in patients with Behcet disease, a multisystemic inflammatory disease characterized by oral and genital ulcers. Anti-*S. cerevisiae* antibodies may be a diagnostic tool for Behcet disease, but the direct effect between *S. cerevisiae* and skin lesions has not been well characterized [11].

Saccharomyces cerevisiae has also been studied in patients with atopic dermatitis (AD). Gp200 is a heat-stable glycoprotein that is present in the cell wall of *S. cerevisiae*. It has been associated with antibody production and inflammation in Crohn disease. Individuals with varying severity of atopic dermatitis were assessed based on the presence of anti-gp200 IgE/IgG. IgE and IgG antibodies were found in 55% and 55% of healthy controls, 67% and 89% of individuals with atopic predispositions, 63% and 100% of patients with mild AD, and 86% and 79% with severe AD, respectively [12].

Increases in total serum IgE levels against *S. cerevisiae* were also seen after skin prick testing of patients with AD. Of those studied, 94% of patients with severe AD, 76% with moderate AD, and 25% with mild AD had a positive test reaction [13]. Additionally, there was cross reactivity between IgE and IgG in AD patients in the presence of mannans from other yeast such as *C. albicans*, *P. ovale*, and *C. albidus* [14].

Although there is little direct evidence of baker's yeast causing infections, yeast was found on a skin

biopsy, and in the Hickman line of a case of cutaneous septic emboli in a patient with acute myeloid leukemia. The patient could have been infected from yeast overgrowth resulting from broad-spectrum antibiotics, or her Hickman line (the more likely cause) from where the organism was isolated [15]. However, nearly all dermatological cases were noted to include infections of other microorganisms along with *S. cerevisiae*. More research is needed to determine the exact cause and effect relationship between *S. cerevisiae* and its role in specific infections.

Treatment

Saccharomyces cerevisiae may be useful for making vaccines [16,17]. For individuals at risk for melanoma, providing protective immunity in the form of a vaccine is a valuable preventative measure that could greatly reduce the incidence of this major dermatological problem. Owing to *S. cerevisiae*'s non-pathogenic nature to humans and the ability for researchers to efficiently genetically modify the organism, the yeast has been suggested as a potential vector to provide immunity against this form of cancer [16]. The inclusion of a melanocyte antigen within the *S. cerevisiae*'s genome prevented tumor formation in a melanoma mouse model [16]. This yeast vaccine delayed tumor development, induced antitumor immunity, and prolonged survival rates within a melanoma mouse model [17].

Saccharomyces cerevisiae has also been used to understand the mechanism of skin therapies [18]. Zinc pyrithione reduces dandruff and is widely used as an ingredient in many anti-dandruff shampoos [19]. To further understand this compound's mechanism of action, *S. cerevisiae* was used to examine zinc pyrithione effects on expression of iron-related genes [18]. The result was zinc pyrithione-induced iron starvation [18].

Conclusion

Saccharomyces cerevisiae has been utilized in a number of studies in dermatology (**Table 1**). It has broad uses in studies of skin physiology, pathology, and treatment, but its utilization in the field of dermatology can be increased. In the future,

researchers may be able to take advantage of this biological tool to further explore important findings of skin disorders.

Potential conflicts of interest

Dr. Feldman has received research, speaking and/or consulting support from a variety of companies including Galderma, GSK/Stiefel, Almirall, Alvotech, Leo Pharma, BMS, Boehringer Ingelheim, Mylan, Celgene, Pfizer, Ortho Dermatology, Abbvie, Samsung, Janssen, Lilly, Menlo, Merck, Novartis, Regeneron, Sanofi, Novan, Qurient, National

Biological Corporation, Caremark, Advance Medical, Sun Pharma, Suncare Research, Informa, UpToDate and National Psoriasis Foundation. Dr. Feldman also consults for others through Guidepoint Global, Gerson Lehrman and other consulting organizations. Dr. Feldman is founder and majority owner of www.DrScore.com. Dr. Feldman is founder and part owner of Causa Research, a company dedicated to enhancing patients' adherence to treatment. Shahzeb Hassan, Christian Poulos, Junaid Bhatti, Sean Rangwani, Zonair Khan, Ali Mahmoud, and Taha Osman Mohammed do not have conflicts to disclose.

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