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# In Silico Bioinformatic Analysis of Glucose Transporter 1 (GLUT1/SLC2A1) Gene in Vitiligo

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## Abstract

***Background:*** **Vitiligo is a common autoimmune dermatological disorder characterized by the progressive loss of pigmentation in the skin and/or mucosal surfaces. Recent advances in research have focused on elucidating the molecular mechanisms underlying vitiligo pathogenesis, with particular emphasis on epidermal–immune cell interactions, structural alterations in cutaneous cellular components, and dysregulation of immune cell metabolism. Glucose transporter 1 (GLUT1), a key mediator of cellular glucose uptake, has been increasingly recognized for its elevated expression in proinflammatory and autoimmune conditions. Notably, upregulation of GLUT1 has been documented in diseases such as rheumatoid arthritis, systemic lupus erythematosus, psoriasis, vitiligo and chronic spongiotic dermatitis, suggesting a potential role in the immunopathogenesis of these disorders.** ***Methods:*** **This study assesses the role of GLUT1 (encoded by SLC2A1) in vitiligo as an example of autoimmune skin disorders via in silico bioinformatic analysis, integrating gene expression, genetic polymorphisms, and inflammatory signaling correlations.** ***Conclusion:*** **Our findings highlight elevated GLUT1 expression in vitiligo regulatory impacts of pro-inflammatory cytokines on melanocyte, keratinocyte, fibroblast and immune cells GLUT1 expression, and the potential functional impact of intragenic SNPs on gene regulation, underscoring GLUT1 as a promising target for novel therapeutic interventions.**

**Key Words:** GLUT1, SLC2A1, Vitiligo, Bioinformatics

## Introduction

In recent years, the integration of bioinformatics into dermatological research and clinical practice has significantly advanced our understanding of skin diseases. Bioinformatics, which involves the application of computational tools to manage and analyze biological data, plays a crucial role in decoding the complex genetic, molecular, and environmental interactions involved in

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dermatological conditions with multifactorial pattern of inheritance. Next-generation sequencing (NGS) is a powerful high-yield technology that enabled researchers to identify genetic variants associated with diseases like psoriasis, vitiligo, atopic dermatitis, and melanoma [1,2]. Bioinformatics investigates interactions that facilitate the development of predictive models for disease susceptibility and progression, as well as the identification of potential biomarkers and therapeutic targets [3]. Bioinformatics can pave the way for a personalized approach to diagnosis, prognosis, and treatment optimizing patient care.

Vitiligo is an acquired depigmenting disorder characterized by the selective destruction of epidermal melanocytes. Its pathogenesis is multifactorial, involving intricate interactions among genetic predisposition, dysregulated immune responses, oxidative stress, environmental factors, and metabolic impairments [4,5]. Among the metabolic pathways implicated, glucose metabolism has gained much attention, particularly the role of glucose transporters such as GLUT1 (encoded by *SLC2A1*), which facilitates basal glucose uptake across multiple tissues including the epidermis [6]. Bioinformatics analyzing gene expression profiles in vitiliginous skin revealed differential expression of metabolic genes [7]. Transcriptomic analysis and immunohistochemical staining have shown altered GLUT1 expression in lesional vs. non-lesional skin, potentially linking metabolic dysregulation to melanocyte vulnerability and immune activation in vitiligo [6]. Furthermore, bioinformatic modeling of transcription factor binding sites and microRNA regulation suggests that melanocyte vulnerability may be under complex regulatory control in vitiligo, offering potential avenues for targeted therapy and diagnostic biomarkers [8]. This study aims to integrate bioinformatics and literature data to elucidate the role of GLUT1 in skin autoimmunity.

## Methods

**Bioinformatic verification of the molecular function of GLUT1:** The protein that are showed possible interaction with GLUT1 was studied by using the String database last accessed on 3-9-2024 through using: https://string-db.org/ Also, the molecular pathway associated with GLUT1, the site of expression and the related transcription factors were verified using FUNRICH software.

## Results

**Bioinformatic analysis:**

The STRING database was used to construct a protein–protein interaction network centered around SLC2A1 (GLUT1) (Figure 1), revealing its functional associations with key regulators involved in glucose metabolism, hypoxia response, and cellular stress. Notable interactors include SLC2A2 and SLC2A4 (other glucose transporters), HIF1A (a hypoxia-inducible transcription factor), TP53 (a tumor suppressor gene with metabolic roles), and BSG (basigin, implicated in metabolic and inflammatory pathways). Line thickness indicates the confidence of the predicted interaction, with colored edges representing different types of evidence (e.g., experimental, co-expression, database annotations). The network highlights the centrality of SLC2A1 in metabolic and stress-response signaling pathways relevant to autoimmune and

inflammatory skin conditions such as vitiligo.

Pathway enrichment analysis associated with SLC2A1 expression. (Figure 2). Bar plot illustrates enriched and depleted biological pathways related to SLC2A1 based on fold change analysis. Pathways shown in orange represent significantly depleted processes, including TLR4 signaling cascades (e.g., IKK complex recruitment, IRF3/IRF7 activation, and MyD88-independent pathways), inflammatory signaling (e.g., NFκB and MAP kinase activation), and IL-3-mediated immune events. In contrast, pathways shown in blue are enriched in association with SLC2A1, such as HIF-2α transcriptional regulation, integrin-linked kinase signaling, EGFR (ErbB1) signaling, and thrombin/PAR pathway activation. These findings suggest a dual role for SLC2A1 in modulating both pro-inflammatory and cellular metabolic or survival pathways, underscoring its potential involvement in vitiligo pathogenesis and autoimmunity.

Tissue and cellular expression profile of SLC2A1 (Figure 3) Bar graph displaying the fold change in SLC2A1 expression across various tissues and cell types. Enriched expression (in blue) was observed in skin, skin cancer, oral mucosa, serum, and reproductive tract tissues (including vulva/anal skin and amniotic fluid), as well as in cancer cell lines such as OVCAR3 and CRC. In contrast, depleted expression (in orange) was noted in immune-related and vascular cells, including monocytes, macrophages, lymph nodes, spleen, HUVECs, and smooth muscle cells. This differential expression pattern highlights a potential role for SLC2A1 in cutaneous and mucosal tissues, possibly linking its metabolic functions to skin homeostasis and inflammatory skin diseases like vitiligo.

*Transcription Factor Enrichment and Depletion for SLC2A1 Gene.* (Figure 3) This bar chart presents the transcription factors associated with the regulation of SLC2A1 (which encodes the glucose transporter GLUT1), highlighting both enriched and depleted transcriptional regulators. On the x-axis, fold change values indicate the strength and direction of association, with positive values (blue bars) representing enrichment and negative values (orange bars) denoting depletion. Each transcription factor is labeled on the y-axis.

Four transcription factors ELK1, SPI1, OTX2, and GSC are significantly depleted (fold change = –101), suggesting reduced regulatory influence or binding affinity to the SLC2A1 promoter region in vitiliginous skin. In contrast, a larger panel of transcription factors including NFYA, STAT1, RXRA, NR1H3, SOAT1, MYC, ASCL2, ZNF143, HNF4A, KLF7, SP1, and PPARG are enriched (fold change = 101), indicating potential upregulation or enhanced transcriptional control over SLC2A1.(Figure 4)

These findings suggest a complex regulatory network involving both activating and repressing elements, with a skew toward positive regulation in vitiligo. This may reflect transcriptional adaptation mechanisms in response to metabolic or immunological signals.

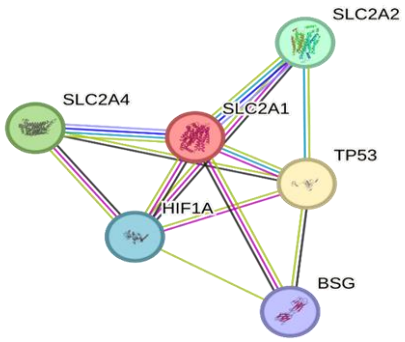


Figure 1: Protein- protein interaction with GLUT1

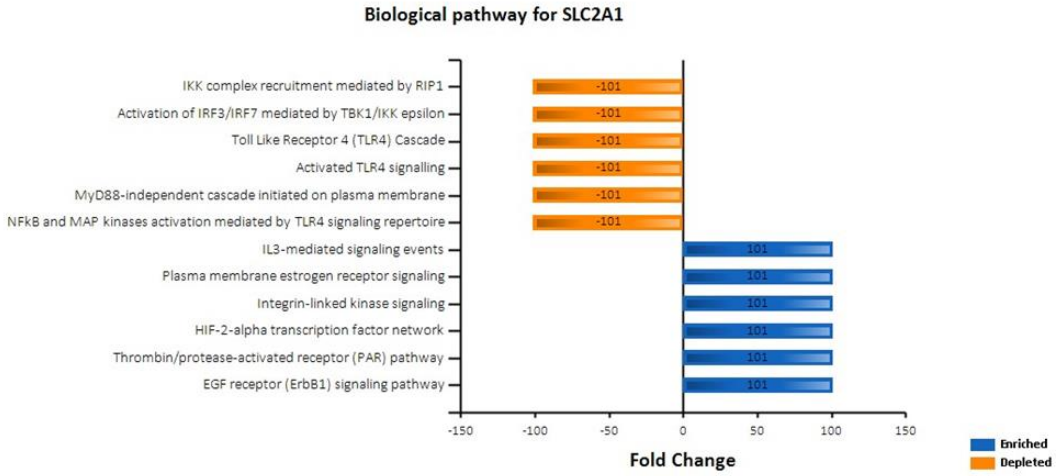


Figure 2. Biological pathway with up-regulation and down-regulation of GLUT1 expression.

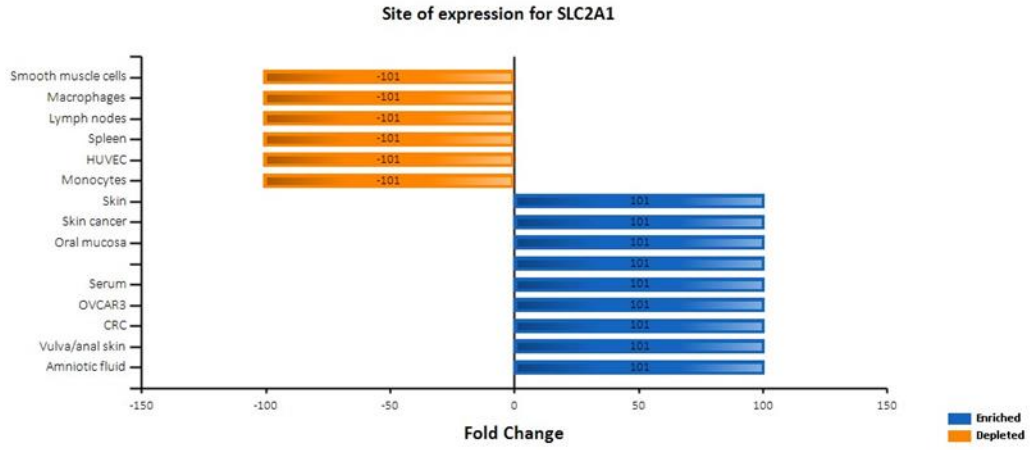


Figure 3. Site of up-regulation and down-regulation of GLUT1 expression.

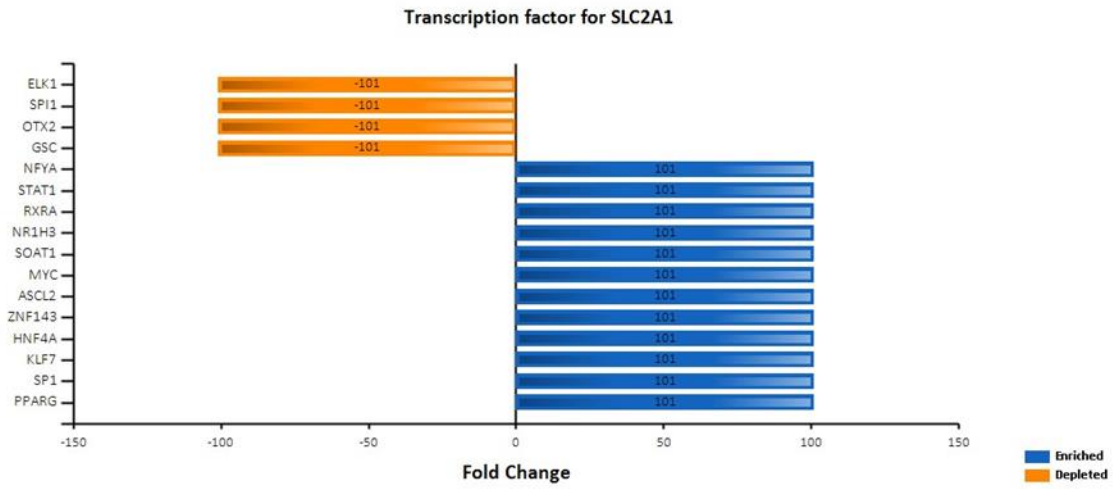


Figure 4. Transcriptional factors up-regulated and down-regulated with GLUT1.

## Discussion

Our tissue expression analysis revealed a distinct dichotomy in SLC2A1 (GLUT1) distribution: significant enrichment in skin, oral mucosa, vulvar/anal skin, and biological fluids (including serum and amniotic fluid) as well as certain cancer cell lines. Conversely, depletion was observed in immune cell populations (e.g., monocytes, macrophages, lymph nodes, spleen), HUVECs, and smooth muscle cells. This pattern underscores a specialization of SLC2A1 in cutaneous and mucosal glucose uptake, highlighting its potential role in maintaining skin homeostasis and mediating metabolic stress in vitiligo lesions.

Cibrian and his colleagues illustrated that immune cells metabolic reprogramming underlie autoimmune processes [9]. As a facilitative glucose transporter, SLC2A1 is pivotal for basal glucose uptake in metabolically active cells, such as keratinocytes and melanocytes. Elevated GLUT1 levels have been detected in vitiligo lesional skin relative to healthy controls ($p < 0.001$)[6], suggesting metabolic reprogramming in these cells and surrounding fibroblasts that may contribute to disease onset, persistence, or progression through metabolic crosstalk.

The reduced SLC2A1 expression in monocytes, macrophages, lymphoid organs, HUVECs, and smooth muscle suggests that these cell types may rely on alternative glucose transporters or metabolic pathways when under oxidative or inflammatory stress [10]. In vitiligo, where autoreactive CD8+ T cells and innate responses are key drivers of melanocyte destruction decreased GLUT1 might reflect altered metabolic states or a compensatory mechanism in these immune populations.

Dysregulated glucose metabolism in vitiligo is increasingly recognized as a component of its multifaceted pathogenesis, alongside genetic, oxidative, and autoimmune factors. Notably, impaired IGF-1/insulin signaling in vitiligo keratinocytes manifesting as low ATP levels, metabolic imbalance, and proinflammatory phenotype supports a metabolic origin for localized

inflammation[7]. These findings align with our data where analysis of protein-protein interactions reveals that GLUT1 is co-expressed with proteins associated with hypoxia, immunologic reactions, and apoptosis, including Hypoxia-Inducible Factor (HIF)-1, Basigin (BSG), and TP53. Using the FUNRICH software to study the biological pathways involving GLUT1, we found that it is upregulated in Interleukin-3-mediated signaling, Integrin-linked kinase signaling, and the HIF transcription factor network. This upregulation confirms its involvement in tissue hypoxia and immunological functions. Furthermore, GLUT1 expression was found to be elevated in the skin, and this upregulation correlates with increased levels of other transcription factors, such as HIF-1 and SP1, which supports its association with immunological infiltration and tissue resident memory cells in vitiliginous skin.

Beyond vitiligo, GLUT1 (SLC2A1) is also upregulated in other inflammatory and proliferative skin conditions, notably psoriasis and chronic spongiotic dermatitis. This consistent overexpression supports the hypothesis that metabolic reprogramming via GLUT1 is a shared pathogenic mechanism in dermatologic diseases characterized by hyperactive cellular metabolism and immune activation[11,12,6].

Collectively, our findings highlight SLC2A1 as a metabolic link at the skin immune axis in vitiligo. Enrichment in epidermal tissues aligns with increased metabolic demand, while depletion in immune cells may reflect altered metabolic strategies during inflammation. These divergent patterns reinforce the concept that metabolic reprogramming particularly via glucose transport is a key event in vitiligo pathogenesis.

## Conclusion

Our in silico and literature analysis places GLUT1 at a nexus of metabolic and immune dysfunction in autoimmune skin disease. Upregulation by cytokines and functional SNPs compels consideration of GLUT1 as both a biomarker and therapeutic target. Future in silico work should explore eQTL datasets, transcription factor binding predictions, miRNA interactions (e.g. miR-22), and 3D protein–ligand docking focused on GLUT1 inhibitors.

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