ISSN: 2577 - 8005

Review Literature

Medical & Clinical Research

Management of Vitiligo, Narrative Review

Mohammed Al Abadie[1*], Zinah Sharara[2]

[1]*Medical School, University of Central Lancashire (UCLAN) and Department of Dermatology, North Cumbria Integrated Care NHS Foundation Trust.*

[2]*Community Dermatology Clinics, National Health Service, (Health Harmonie), United Kingdom.*

[*]Corresponding Author
Mohammed Al Abadie, PhD, FRCP, Department of Dermatology, North Cumbria Integrated NHS Care Foundation Trust, UCLAN Medical School. United Kingdom.

Submitted: 04 Apr 2024; **Accepted**: 11 Jun 2024; **Published**: 18 Jul 2024

Citation: *Mohammed Al Abadie, Zinah Sharara (2024) Management of Vitiligo, Narrative Review. Medical & Clinical Research, 9(7), 01-05.*

Abstract

Vitiligo is a prevalent autoimmune depigmenting skin disorder, affecting 0.5–2% of the global population. While often believed a cosmetic issue, vitiligo can have profound psychological impact on the patients. The disease is marked by the loss of functional melanocytes, driven by complex interactions between the innate and adaptive immune systems, leading to various proposed mechanisms of melanocyte destruction. This paper provides a narrative overview of vitiligo treatments, encompassing established therapies, unconventional approaches, and recently licensed molecular-targeted treatments. Additionally, highlighting emerging therapeutic strategies currently under investigation, aiming to provide a broad perspective on the management and potential future directions in vitiligo care.

Keywords: Vitiligo, Topical treatment, Surgical treatment, Stem cells, Exosome, Excimer lamps, Phototherapy

Introduction

Introduction

Vitiligo can present with one to several achromic macules with chalk- or milk-white in colour. Patches are likely symmetrical in distribution, well demarcated show centrifugal spreading with time [1].

Vitiligo Global Issues Consensus Conference clinically classified vitiligo into non-segmental, segmental, and mixed types, based on lesions crossing the midline. Non segmental included further variant according to the distribution and extent of lesions, these are generalized vitiligo, acrofacial vitiligo, universal vitiligo) moreover another category has been allowed unclassified for further observation [2].

There are several treatment options available for vitiligo, treatment algorithm suggested by Gawkrodger et al. [3].

No Treatment Option

After thorough discussion with the patient, it is sensible to provide the option of not to use an active treatment in adults with skin types I and II and the suggestion of camouflage cosmetics and sunscreens [3].

Treatment

Topical, systemic treatment, and phototherapy are helpful for stabilization and repigmentation of vitiligo. Treatment choice is established according to disease severity, and activity (stable versus progressive disease), distribution, skin phototype, impact on quality of life and incentive for treatment [4].

Topical Treatment

A) Potent or very potent topical steroid TCS are considered. Skin atrophy has been a common side-effect. There are no studies estimating the optimal duration of treatment with TCS. Some authors suggest daily application for a period not exceeding 2 months [3], while others suggest a discontinuous pattern (Applied once daily for 15 days of each month for 6 a maximum of months) [5].

B) Topical calcineurin inhibitors TCI (pimecrolimus or tacrolimus) show evident therapeutic effects on vitiligo and over 3 months treatment period and have established at least mild, moderate and marked response in 55.0%, 38.5% and 18.1% of patients respectively, the metanalysis pooled the data from a total of 46 study with a total of 1,499 vitiligo patients [6]. Moreover, in another metanalysis with a total of 13 studies including 509 patients TCIs showed comparable results to TCS in reaching at least 50% or at least 75% regimentation [7].

Currently both topical steroid and calcineurin inhibitors are commonly used as first-line treatments [8].

Topical Vitamin D

The existing evidence on the role of topical vitamin D for the treatment of vitiligo, as a monotherapy or in combination, is

currently limited and inadequate.

Recent systematic review has highlighted the role of cholecalciferol, calcipotriol, and tacalcitol in the treatment of vitiligo [9], and it was found that the combination of calcipotriol or tacalcitol with (NB-UVB) can enhance therapeutic outcomes. However, their effectiveness in combination with (PUVA) and Monochromatic Excimer Light (MEL) treatment for vitiligo is limited. Cholecalciferol was also combined with microneedling with some success. Moreover, combining topical corticosteroids with vitamin D analogues has shown superior efficacy in management of vitiligo as compared to vitamin D analogues alone [9].

Phototherapy

NB-UVB has superior rate of regimentation as compared to PUVA [10], generally phototherapy can be tried as treatment option in patients with darker skin types who cannot be cured effectively with the above topical options and only when have widespread vitiligo, however if significant impact on QoL can also considered for localised vitiligo [3].

Phototherapy has been effectively combined with various treatments to enhance its efficacy in repigmentation [11]. It has been used in conjunction with topical tacrolimus, intramuscular betamethasone injections, Erbium laser therapy, and topical 5% 5-fluorouracil (5-FU). Additionally, the integration of antioxidant supplements, including Polypodium leucotomos, lipoic acid, vitamin C, and vitamin E, has shown significantly better outcomes compared to phototherapy alone [12].

These antioxidants are believed to mitigate oxidative stress, thereby augmenting the therapeutic effects of phototherapy. This synergistic approach underscores the potential of combining phototherapy with both pharmacological and nutraceutical interventions to achieve superior clinical results.

Excimer Lamps or Lasers

Targeted phototherapy methods using high-intensity 308-nm monochromatic light have shown efficacy in treating vitiligo, as they avoid exposure of healthy skin and lower the cumulative UVB dose. Excimer was found significantly effective and safe in inducing regimentation in vitiligo patients, with no statistically differences noted between Excimer lamps and laser [13]. It was found that the total number of treatment sessions has an essential role in ultimate repigmentation rather than their frequency [14]. Additionally, when combined with calcineurin inhibitors, excimer therapy has proven to be more effective than when used alone as monotherapy [15]. Furthermore, a novel combination of 308 nm excimer laser and a surgical needling technique has been found effective in treatment of moderate to severe vitiligo [16].

Surgical Treatment

Variable surgical methods have been suggested as therapeutic options to treat patients with Segmental Vitiligo and non segmental lesions who have stable disease for at least 12 months, characterized by the lack of new lesion development, no response to conventional medical interventions, and the absence of Koebner's phenomenon [3].

Surgical methods in vitiligo can be categorised into

A) Tissue grafts which including (full-thickness punch, split-thickness and suction blister grafts) whole transplanted pigmented epidermis and dermis into depigmented areas; the techniques are suitable for treating smaller areas [17]. Of note split full thickness punch graft have the potential disadvantages of gobblestoning and graft displacement, while split thickness graft technique and suction blister grafts are found to have the highest cosmetic outcome and repigmentation success rate [18]. On the other hand, studies reported that suction blister grafts are effective in sites that are difficult to treat, and cosmetically sensitive like the angles of the lips and areola, the drawbacks are it can only be used for small areas and time consuming [19]. After a successful grafting, complementary treatment in the form of phototherapy can be applied [20].

B) Cellular grafts, including non-cultured epidermal cellular grafts, autologous melanocyte cultures, and cultured epidermal suspensions [21], all have yielded excellent repigmentation [22]. Hair follicle transplantation presents a promising option due to its reservoir of melanocytes and stem cells [23], however, intraoperative bleeding and inclusion cyst are reported side effects [23, 24].

In general, the cellular transplants involve complex processing of the grafts prior to surgery.

Target Therapy

There is an emerging role of the JAK/STAT pathway in pathogenesis of vitiligo, the activation of JAK system leads to a sequences of gene transcriptions by the phosphorylated STAT1 in a complex cascade, and JAK inhibitors are widely studied as new treatment modality of vitiligo. Thre are 4 key types: JAK1, JAK2, JAK3 and TYK2. Once activated, the JAK system then leads to a series of gene transcriptions via the phosphorylated STAT1 in a complex cascade [25].

Multiple JAK inhibitors have been tried, in a recent publication we conducted a summative review [25], it was concluded these were successful in reducing the depigmented area percentage and were well tolerated, however, the limitation involved lacking head-to-head trials comparing the effectiveness and safety between biologics used in the treatment of vitiligo. The following have been tried and reviewed: JAK1/JAK2 Inhibitors; including Ruxolitinib and baritininb and JAK1/JAK3 Inhibitors; including Tofacitinib and JAK3/TEC inhibitor including; Ritlecitinib.

PDE-4

Phosphodiesterase inhibitor type 4 (PDE-4), prevents the activation of (Th1 and Th-17) lymphocytes and increases the expression (IL-2 and IL-10) which are anti-inflammatory chemokines, this is done by preventing the degradation of cAMP [26]. In a case series; Apremilast was found effective in managing the progression of adult vitiligo [27], while one case report has documented the effectiveness of crisaborole 2% ointment in vitiligo [28]. However due to sample size, results cannot be generalised.

Melanocortin Peptides

Afamelanotide is a potent synthetic analogue of α-melanocyte-stimulating hormone, when administered subcutaneously it has achieved synergistic effect with NB-UVB in inducing repigmentation [29,30].

Unconventional Therapies

Oxidative stress has a role in the pathogenesis of vitiligo [31] and several products with antioxidant enzymes have been tried for the treatment of vitiligo with conflicting results.

Prostaglandin E2

Prostaglandin E2 controls the proliferation of melanocytes by means of stimulant and immunomodulatory effects. Topical preparation of prostaglandin E2 [32] and Bimatoprost, which is a synthetic analogue of prostaglandin F2α [33], have been tried with good success, however very limited studies are there in literature.

Pseudocatalase

This can act by reducing the free radicals and improving the catalase action. Psudocatalase introduced in a topical cream has been proposed as therapeutic modality for vitiligo. Results improved when pseudocatalase was combined to phototherapy [34], this outcome was contradicted in different study; as psudocatalase has not added any beneficial effect to the NB-UVB [35].

5-Fluorouracil

5-FU is a pyrimidine analogue of the antimetabolites family, with anticancer proprieties, recently shown pro pigmentary action when combined with therapeutic trauma [36], and can effectively induce skin repigmentation in vitiligo when applied topically in combination with fractional CO2 Laser [37], Er:YAG (2940 nm) laser [38], excimer laser, and microneedling [39].

Levamisole

Levamisole is an antihelminthic drug, which has shown immunoregulatory properties [40]. It has utilised in vitiligo, studies have proposed therapeutic role in arresting the activity and to induce repigmentation in patients who have limited and slow-spreading disease [41]. An open study demonstrated that levamisole may be used alone, or in combined with corticosteroids, and this seems to be more effective [42]. However, this result was then not proven in different study [43].

Levodopa

Levodopa is an amino acid precursor of dopamine and melanin and proposed to have melanogenic and antioxidant activities [44, 45].

Only few cases reported its efficacy in vitiligo, and repigmentation was described after treating Parkinson patients treated with L-DOPA [46, 47]. Then it was also reported effective in combination with UV light [48].

In a nationwide, population-based, case–control study, the association between levodopa use and vitiligo has been studied, levodopa intake was associated with a lower risk of vitiligo, suggesting a protective effect on the development of vitiligo [49].

Other Emerging Therapies: Stem Cells and Exosome

There is extensive Research work recently endeavoured about advanced modalities in disorders of pigmentation, based on enhancing and replacement of affected genes, damaged tissues, or cells, this is by implanting mesenchymal stem cells and multi-lineage differentiating stress enduring cells [50]. Implanting mesenchymal stem cells regulate cytokine secretion and the balance of T-cell as well as improving detoxification, cell proliferation and morphology of melanocytes [49, 51].

It is well known that Hair follicle melanocyte stem cells are situated in the bulge region of the hair follicle and these are one of the typical representatives of regenerative stem cells [52], the concept of implanting a melanocyte processing plant under the epidermis of vitiligo was researched and a significant outcome obtained in vitiligo patients when Stem cell transplantation was combined with 308-nm excimer laser therapy [53].

Exosomes are a subset of extracellular vesicles, which can transmit different biomolecules, such as proteins, lipids, and nucleic acids (RNA and DNA) to be incorporated in recipient cells [54], thus described as mediators in many biological activities, prompting cellular processes and gene expression [55]. Keratinocyte-Exosome vesicles found to transmit selected microRNAs (miRNAs) to modulate melanogenesis in melanocytes [56].

This process currently being explored in vitro and in animal experiments, and the clinical reports and human studies are not yet available in recent literature search. Hence, clinical value of these therapies cannot be assessed, especially with concerns about exosome and stem cells therapy raised by CDC about potential teratogenicity, and the risks of contamination of the product and the possibilities infections following these trials [57].

Conclusion

Vitiligo proven to have a significant impact on a person's psychological well-being and quality of life [58, 59]. Tailoring the treatment options to each patient`s specific immune and genetic and profile may enhance treatment outcomes and reduce side effects, however, these potential advancements require years of research to become broadly available.

Advanced method utilised like targeted immune therapy and the regeneration of melanocyte stem cell may replace phototherapy treatments or used in combination as adjuvants to produce more effective and newer armamentarium in vitiligo.

Conflict of Interest

None.

Financial Support

None.

References

1. Migayron L, Boniface K, Seneschal J (2020) Vitiligo, from physiopathology to emerging treatments: a review. Dermatology and Therapy 10:1185-1198.
2. Ezzedine K, Lim HW, Suzuki T, Katayama I, Hamzavi I, et al. (2012) Revised classification/nomenclature of vitiligo and related issues: the Vitiligo Global Issues Consensus Conference. Pigment Cell & Melanoma Research 25(3):E1-3.
3. Gawkrodger DJ, Ormerod AD, Shaw L, Mauri-Sole I, Whitton ME, et al. (2008) Guideline for the diagnosis and management of vitiligo. British Journal of Dermatology 159(5):1051-1076.
4. Brazzelli V, Antoninetti M, Palazzini S, Barbagallo T, De Silvestri A, et al. (2007) Critical evaluation of the variants influencing the clinical response of vitiligo: study of 60 cases treated with ultraviolet B narrow-band phototherapy. J Eur Acad Dermatol Venereol 21(10):1369-1374.
5. Taieb A, Alomar A, Böhm M, Dell'anna ML, De Pase A, et al. (2013) Vitiligo European Task Force (VETF); European Academy of Dermatology and Venereology (EADV); Union Europe´enne des Me´decins Spe´cialistes (UEMS). Guidelines for the management of vitiligo: the European Dermatology Forum consensus. Br J Dermatol 168(1):5-19.
6. Chang HC, Hsu YP, Huang YC (2020) The effectiveness of topical calcineurin inhibitors compared with topical corticosteroids in the treatment of vitiligo: a systematic review and meta-analysis. J Am Acad Dermatol 82(1): 243–245.
7. Lee JH, Kwon HS, Jung HM, Lee H, Kim GM, et al. (2019) Treatment Outcomes of Topical Calcineurin Inhibitor Therapy for Patients With Vitiligo: A Systematic Review and Metaanalysis. JAMA Dermatol 155(8):929.
8. Dang YP, Li Q, Shi F, Yuan XY, Liu W (2016) Effect of topical calcineurin inhibitors as monotherapy or combined with phototherapy for vitiligo treatment: a meta-analysis. Dermatol Ther (Heidelb) 29(2):126-133.
9. Al-Smadi K, Ali M, Alavi SE, Jin X, Imran M, et al. (2023) Using a Topical Formulation of Vitamin D for the Treatment of Vitiligo: A Systematic Review. Cells 12(19):2387.
10. Mohammad TF, Al-Jamal M, Hamzavi IH, Harris JE, Leone G, et al. (2017) The Vitiligo Working Group recommendations for narrowband ultraviolet B light phototherapy treatment of vitiligo. J Am Acad Dermatol 76(5): 879-888.
11. Zhu B, Liu C, Zhang L, Wang J, Chen M, et al. (2023) Comparison of NB-UVB combination therapy regimens for vitiligo: A systematic review and network meta-analysis. Journal of Cosmetic Dermatology 22(3):1083-1098.
12. Jung HM, Jung YS, Lee JH, Kim GM, Bae JM (2021) Antioxidant supplements in combination with phototherapy for vitiligo: A systematic review and metaanalysis of randomized controlled trials. Journal of the American Academy of Dermatology 85(2):506-508.
13. Lopes C, Trevisani VF, Melnik T (2016) Efficacy and safety of 308-nm monochromatic excimer lamp versus other phototherapy devices for vitiligo: a systematic review with meta-analysis. American journal of clinical dermatology 17:23-32.
14. Hofer A, Hassan AS, Legat FJ, Kerl H, Wolf P (2005) Optimal weekly frequency of 308-nm excimer laser treatment in vitiligo patients. Br J Dermatol 152(5): 981-985.
15. Nisticò S, Chiricozzi A, Saraceno R, Schipani C, Chimenti S (2012) Vitiligo treatment with monochromatic excimer light and tacrolimus: results of an open randomized controlled study. Photomed Laser Surg 30(1):26-30.
16. BinSheikhan S, Al Abadie M (2017) Improvement in moderate to severe vitiligo using a novel combination of 308 nm excimer laser and a surgical needling technique. Clinical & Experimental Dermatology 42(3).
17. Frączek A, Kasprowicz-Furmańczyk M, Placek W, Owczarczyk-Saczonek A (2022) Surgical treatment of vitiligo. Int J Environmental Research and Public Health 19(8):4812.
18. Mulekar SV, Isedeh P. Surgical interventions for vitiligo: an evidence-based review. British Journal of Dermatology. 2013 Oct 1;169(s3):57-66.
19. Kar BR, Raj C (2018) Suction blister epidermal grafting for vitiligo involving angles of lip: Experience of 112 patients. J Cutaneous and Aesthetic Surgery 11(1):13.
20. Iwanowski T, Szlązak P, Rustowska A, Sokołowska-Wojdyło M (2018) Efficacy of suction blister epidermal grafting with concomitant phototherapy in vitiligo treatment. Advances in Dermatology and Allergology/Postępy Dermatologii I Alergologii 35(6):592-598.
21. Chen YF, Yang PY, Hu DN, Kuo FS, Hung CS, et al. (2004) Treatment of vitiligo by transplantation of cultured pure melanocyte suspension: analysis of 120 cases. J American Academy of Dermatology 51(1):68-77.
22. Tyagi S, Malhotra SK, Kaur T (2021) Comparative evaluation of efficacy of non-cultured epidermal cell suspension and epidermal curettage in stable vitiligo. Journal of Cutaneous and Aesthetic Surgery 14(1):32.
23. Thakur P, Sacchidanand S, Nataraj HV, Savitha AS (2015) A study of hair follicular transplantation as a treatment option for vitiligo. J Cutaneous and Aesthetic Surgery 8(4):211.
24. Malakar S, Dhar S (1999) Repigmentation of vitiligo patches by transplantation of hair follicles. International Journal of Dermatology 38(3):237-238.
25. Al Abadie M, Tukmatchy H, Al Abadie M, Anthony Ball P, Morrissey H (2023) An Update on Vitiligo Target Therapy: A Semi-Structured Systematic Review. Medical & Clinical Research, 8(11), 01-06.
26. Li H, Zuo J, Tang W (2018) Phosphodiesterase-4 inhibitors for the treatment of inflammatory diseases. Frontiers in Pharmacology 9:1048.
27. Majid I, Imran S, Batool S (2019) Apremilast is effective in controlling the progression of adult vitiligo: a case series. Dermatologic Therapy 32(4):e12923.
28. Tam I, Kahn JS, Rosmarin D (2021) Repigmentation in a patient with vitiligo on crisaborole 2% ointment. JAAD Case Reports 11:99-101.
29. Lim HW, Grimes PE, Agbai O, Hamzavi I, Henderson M, et al. (2015) Afamelanotide and narrowband UV-B phototherapy for the treatment of vitiligo: a randomized multicenter trial. JAMA Dermatology 151(1):42-50.
30. Toh JJ, Chuah SY, Jhingan A, Chong WS, Thng ST (2020)

Afamelanotide implants and narrow-band ultraviolet B phototherapy for the treatment of nonsegmental vitiligo in Asians. J American Academy of Dermatology 82(6):1517-1519.
31. Laddha NC, Dwivedi M, Mansuri MS, Gani AR, Ansarullah M, et al. (2013) Vitiligo: interplay between oxidative stress andimmune system. Experimental Dermatology 22(4):245-250.
32. Kapoor R, Phiske MM, Jerajani HR (2009) Evaluation of safetyand efficacy of topical prostaglandin E2 in treatment of vitiligo. British J Dermatology 160(4):861-863.
33. Grimes PE (2016) Bimatoprost 0.03% Solution for the Treatment of Nonfacial Vitiligo. J Drugs in Dermatology: JDD 15(6):703-710.
34. Schallreuter KU, Salem MA, Holtz S, Panske A (2013) Basic evidence for epidermal H2O2/ONOO−-mediated oxidation/nitration in segmental vitiligo is supported by repigmentation of skin and eyelashes after reduction of epidermal H2O2 with topical NB-UVB-activated pseudocatalase PC-KUS. The FASEB Journal 27(8):3113-3122.
35. Bakis-Petsoglou S, Le Guay JL, Wittal R (2009) A randomized, double-blinded, placebo-controlled trial of pseudocatalase cream and narrowband ultraviolet B in the treatment of vitiligo. British Journal of Dermatology 161(4):910-917.
36. Liao ZK, Hu SH, Han BY, Qiu X, Jiang S, et al. P(2021) Propigmentary action of 5-fluorouracil through the stimulated secretion of CXCL12 by dermal fibroblasts. Chinese Medical J 134(20):2475-2482.
37. Weshahy R, Abdelhamid MF, Sayed KS, El Desouky ED, Ramez SA (2022) Efficacy and safety of combined fractional ablative CO2 laser and 5 fluorouracil in the treatment of acral vitiligo: An open, uncontrolled study. J Cosmet Dermatol 21(11):5636-5641.
38. Abdelwahab M, Salah M, Samy N, Rabie A, Farrag A (2020) Effect of topical 5-fluorouracil alone versus its combination with erbium: YAG (2940 nm) laser in treatment of vitiligo. Clinical, Cosmetic and Investigational Dermatology 23:77-85.
39. Jha AK, Sonthalia S (2019) 5-Fluorouracil as an adjuvant therapy along with microneedling in vitiligo. J American Academy of Dermatology 80(4):e75-76.
40. Goldstein G (1978) Mode of action of levamisole. The Journal of rheumatology. Supplement 4:143-148.
41. Pasricha JS, Khera V (1994) Effect of prolonged treatment with levamisole on vitiligo with limited and slow-spreading disease. International J Dermatology 33(8):584-587.
42. Khondker L, Khan SI (2013) Efficacy of levamisole for the treatment of slow spreading vitiligo. Mymensingh Med J 22(4):761-766.
43. Agarwal S, Ramam M, Sharma VK, Khandpur S, Pal H, et al. (2005) A randomized placebo-controlled double-blind study of levamisole in the treatment of limited and slowly spreading vitiligo. British Journal of Dermatology 153(1):163-166.
44. Komagamine T, Suzuki K, Hirata K (2013) Darkening of white hair following levodopa therapy in a patient with Parkinson's disease. Movement Disorders: Official Journal of the Movement Disorder Society 28(12):1643.
45. Zhong SY, Chen YX, Fang M, Zhu XL, Zhao YX, et al. (2014) Low-dose levodopa protects nerve cells from oxidative stress and up-regulates expression of pCREB and CD39. PLoS One 9(4):e95387.
46. Reynolds NJ, Crossley J, Ferguson I, Peachey RD (1989) Darkening of white hair in Parkinson's disease. Clinical and Experimental Dermatology 14(4):317-318.
47. Grainger KM (1973) Pigmentation in Parkinson's disease treated with levodopa. Lancet i:97-98.
48. Goolamali SK (1973) Levodopa in vitiligo. The Lancet 301(7804):675-676.
49. Bae JM, Kim M, Han JH, Lee S, Ju HJ, et al. (2022) Preventive effect of levodopa on vitiligo development: a nationwide case–control study. British Journal of Dermatology 187(2):259-261.
50. Ghashghaei S, Abbaszadeh M, Karimi S, Ataie-Fashtami L, Bajouri A, et al. (2023) Advanced therapy medicinal products in vitiligo; current status, future prospect, and approved treatments. Cell Journal (Yakhteh) 25(3):143.
51. Yang RL, Chen SY, Fu SP, Zhao DZ, Wan WH, et al. (2023) Antioxidant mechanisms of mesenchymal stem cells and their therapeutic potential in vitiligo. Frontiers in Cell and Developmental Biology 2023:11.
52. Nishimura EK, Jordan SA, Oshima H, et al. (2002) Dominant role of the niche in melanocyte stem-cell fate determination. Nature 416(6883):854-860.
53. Liu J, Chen Q. Clinical effect of stem cell transplantation combined with 308-nm excimer laser therapy for 56 cases of vitiligo. Journal of Cosmetic Dermatology. 2023 Dec;22(12):3276-81.
54. Ha DH, Kim HK, Lee J, Kwon HH, Park GH, et al. (2020) Mesenchymal stem/stromal cell-derived exosomes for immunomodulatory therapeutics and skin regeneration. Cells 9(5):1157.
55. Wong PM, Yang L, Yang L, Wu H, Li W, et al. (2020) New insight into the role of exosomes in vitiligo. Autoimmunity Reviews 19(11):102664.
56. Takano K, Hachiya A, Murase D, Tanabe H, Kasamatsu S, et al. (2020) Quantitative changes in the secretion of exosomes from keratinocytes homeostatically regulate skin pigmentation in a paracrine manner. The Journal of Dermatology 47(3):265-276.
57. https://www.cdc.gov/hai/outbreaks/stem-cell-products.html
58. Thompson AR, Eleftheriadou V, Nesnas J (2022) The mental health associations of vitiligo: UK population-based cohort study. BJPsych Open 8(6):e190.
59. Kobori C, Takagi R, Yokomizo R, Yoshihara S, Mori M, et al. (2023) Functional and long-lived melanocytes from human pluripotent stem cells with transient ectopic expression of JMJD3. bioRxiv. 2023:2023-03.