Medical Research Archives

ESMED
European Society of Medicine

OPEN ACCESS

Published: June 30, 2023

Citation: Smith DJM, 2023. The influence of visible light within the solar spectrum: How damaging is it to human skin and is it accounted for in sun protection measures? Medical Research Archives, [online] 11(6). https://doi.org/10.18103/mra.v11i6.3961

DOI: https://doi.org/10.18103/mra.v11i6.3961

ISSN: 2375-1924

RESEARCH ARTICLE

The influence of visible light within the solar spectrum: How damaging is it to human skin and is it accounted for in sun protection measures?

David John Mackay Smith

University of Queensland, St Lucia QLD 4072, Australia

djmsmith8@bigpond.com

Abstract:

Public health messages clearly state the risks of solar radiation and how the risk can be mitigated. This is supported by the availability of creams that effectively block out the ultraviolet component of solar radiation. Why then does the incidence of skin cancer and particularly melanoma remain so disturbingly high in Caucasian populations?

Almost all organisms on the planet have had to adapt to the presence of solar radiation since the beginning of evolutionary time. There are beneficial effects as well as risks in exposure, not the least of which is that it is the ultimate energy source for living species.

We need to re-examine attitudes and exposure patterns with an appreciation that some exposure is essential for good health. A balance needs to be found between benefits and risks. This can only be done by understanding that there are a range of wavelengths of light with different effects rather than a focus solely on the adverse effects of the ultraviolet component.

Introduction

Skin plays a role as an active barrier to the external environment, including sun exposure. The melanocytes and keratinocytes form a cooperative unit to asses and manage this exogenous energy source through paracrine and autocrine signalling. In response melanocytes transfer melanin to the keratinocytes to shield their nuclei. The tanning response. Different wavelengths produce different responses in the skin. Skin pigmentation is considered to be an important adaptive response because melanin has a number of features that can have a protective effect.

Part of the problem of exposure and risk in Australia is that the majority of the population are of Northern European ancestry. Moving closer to the equator en masse over a short evolutionary time span we have unfortunately carried with us a polymorphic melanocortin receptor (*MC1R*) gene in our melanocytes better adapted to a more temperate climate and responsible for an incomplete tanning response to a varying degree. The indigenous population evolved from darker skinned African hominoids that underwent a slow migration to an equally tropical environment. They have also had over 50,000+ years of human habitation on this continent with a more complete tanning response and naturally better suited to this new environment with a much lower incidence of skin cancer.

It is clear that occupation and recreation can result in excessive sun exposure but this is confounded by the fact that the incidence of melanoma is higher in indoor rather than outdoor workers. There are differences in exposure patterns and protective responses that help explain this enigmatic situation. We need to be more successful at negotiating the potentially harmful effects by relooking at solar radiation and instead of focusing on the most harmful wavelengths look at the overall effect of the whole spectrum. We also need to re-examine our behavior and exposure patterns. Prolonged periods indoors under artificial light punctuated with short bursts of intense irradiation outdoors is maladaptive.

Creams aim to block the ultraviolet component, ignoring 90% of solar photons, including visible light. The protective effect is incomplete, yet their use encourages more prolonged exposure. Extreme protective behaviors are necessary for the most sensitive skin types but they are still at risk. For the rest of the population evolutionarily developed natural protective mechanisms can also be employed. I want to reexamine these processes with a particular emphasis on the effects of visible light.

The electromagnetic spectrum

The electromagnetic spectrum that results from solar radiation produces a range of wavelengths which express an inverse relationship between wavelength and energy radiated, with resulting variation in biological activity.

Of interest to life on the planet, including humans, is the range from the shorter wavelength ultraviolet, to visible and on to the longer infrared wavelengths but it is important to remember that this is spectrum and there is no absolute division between these

wavelengths. The arbitrary divisions of solar energy at sea level are: 3-7% Ultraviolet (UV), 290-400nm, divided into UVA, B and C. UVC and a large percentage of UVB is absorbed by the ozone layer in the atmosphere; 40% visible light (VL); and 53% infrared (IR), (700-1440nm)[1]. Another important concept is that, although sunlight is polychromatic, its final effect on human skin is the result of not only the action of each wavelength individually, but also the interaction between these wavelengths.

Visible light (VL) is defined as the portion of the spectrum visible to the human eye. That is 400-700nm with the maximum in the green range of the spectrum at 555nm.

The early fixation on reaction to the specific UVB (280-320nm) wavelengths, led to an overestimation of its biological importance. This has been followed by a change in focus to include longer UV wavelengths with an appreciation of the underestimation of UVA damage. All the attention has been on UV effects, consequentially, the additive, synergistic or antagonistic interactions between different wavelengths have been largely overlooked.

This is particularly the case with VL, lying outside of what photobiologists defined as a deleterious spectral range.

Skin optics

When photons enter the skin there are differences in absorption, penetration and scattering due to variation in wavelength and level of irradiation producing differences in biological affects and requiring particular physiological responses.

On absorption there is initiation of chemical changes in the cells with energy transferred to chromophores. This is dependent on the position of the cell within the skin strata and the absorption spectrum of the chromophore. The absorption spectrum is the probability of absorption of the photon against wavelength. The chromophores that absorb in the VL range are melanin, water, riboflavin, haemoglobin, bilirubin, β carotene and protoporphyrin. Fig.1. The photon wavelength determines the depth of penetration[2]. UVB is absorbed by the epidermal keratinocytes with potential damage and subsequent mutation to their DNA, compared with energy from UVA, which penetrates more deeply into basal epidermal and superficial dermal layers. VL and IR penetrates more deeply again but in contrast to extensive research into the damaging effects of UVR, there has been little attention payed to the effects of VL on skin in relation to its less energetic wavelengths. Effects of UVA1(340-400nm) have an enhanced effect at the basal layer, possibly through back scatter from the dermis[3].

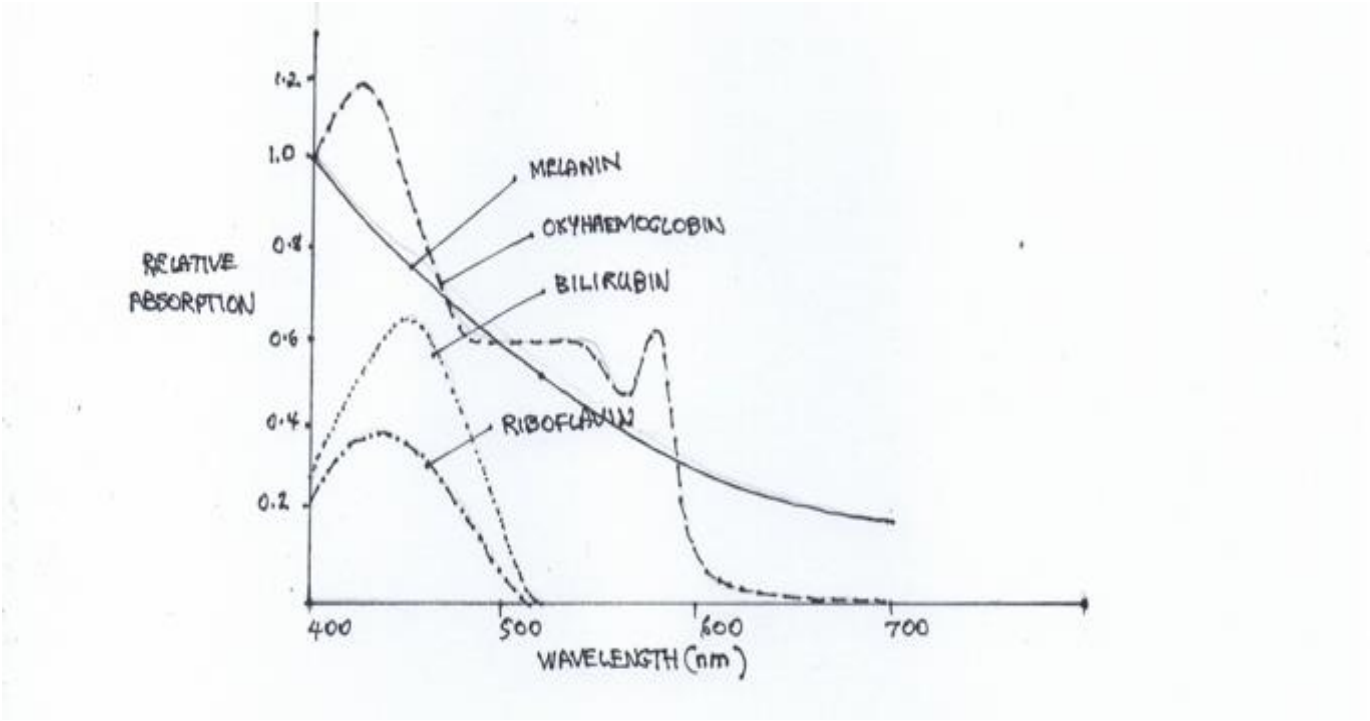

Figure 1. Skin Chromophore absorption spectra (Adapted from Mahmoud et al, 2008)

Biological effects of visible light

Early studies by Mahmoud and Liebel demonstrated defined biological effects of VL.

Although the contribution of the UV component of solar radiation to skin damage is well established through photoproducts producing direct cellular DNA damage, it is clear that indirect oxidative effects of reactive oxygen species (ROS) produced by solar radiation also contribute to skin damage. Considering that the UV comprises <10% of solar radiation, the effects of non-UV radiation on skin physiology now need to also be taken into consideration.

Erythema

Mahmoud found that erythema was mainly caused by UVB but UVA and VL are also capable of causing erythema but at much higher doses. UV erythema (250-297nm) causes superficial dermal capillary dilation but long UV (366nm) and VL (405/436nm), with deeper penetration, cause dilatation of vessels in the subpapillary plexus[4,5].

Pigmentation

Traditionally, pigmentation is believed to be the most important photoprotective response because of the multiple protective properties of melanin. Broadband UV absorbent, antioxidant and radical scavenging properties. UVA induces immediate pigment darkening (IPD) and at higher doses, persistent pigment darkening (PPD) which can last days to weeks. UVB induces an immediate erythematous response followed by delayed pigmentation (DP). IPD and PPD can be induced by a single UV dose in skin types I and II. Randhawa et al demonstrated that multiple

exposures to VL can also produce transient and long-lasting pigmentation in human skin, although a single exposure induces very little pigmentation. They termed this a photoadaptive response. The mechanism of increased melanin formation was L-dopa oxidation and altered pigment related gene expression increasing tyrosinase enzyme activity[6]. They concluded that "VL can induce photodamage pathways in a similar manner to UV".

Interestingly, Ragazzetti et al reported that VL (blue light) stimulated an opsin 3-regulated microphthalmia-associated increasing pigment gene expression in response, causing clustering of melanocytic enzymes, and thus contributing to hyperpigmentation in melanocompetent skin. These finding suggest physical agents, such as zinc oxide sunscreens may protect skin from solar radiation-induced hyperpigmentation, in Fitzpatrick skin types (FSTs) IV to VI, at least[7]. This also reignites the controversial issue of whether non-retinal opsins, in skin melanocytes, are able to sense, and directly act on, solar radiation. There is no doubt that they contain the light responsive proteins, opsins, and the phototransduction cascades[8,9].

Reactive oxygen species, pro-inflammatory cytokines and matrix degrading enzymes.

Free radicals are necessary for normal metabolic processes but their production results in a cascade of events with positive and negative consequences. The destructive end point is skin cancer, particularly melanoma but they also have important signalling and defence activation functions utilised to maintain cellular homeostasis.

In 2012 Liebel et al examined the physiological responses of skin equivalents to visible light (400-700nm) irradiation. They found that the production of ROS initiates events affecting skin health, including induction of pro-inflammatory cytokines, and matrix -metalloproteinase (MMP-1), resulting in DNA and tissue damage associated with photoaging and melanogenesis. They also demonstrated that the ROS production stimulated cell proliferative pathways, EGFR-ERK as an example. This pathway is implicated in UV-induced keratinocyte hyperplasia in the epidermis[10]. Zastrow et al, in *ex vivo* skin explant studies, estimated that 50% of total skin oxidative burden was generated by VL, compared to UVB-4% and UVA-46%[11]. Figure 2. This significant VL-induced component suggests that other portions of the solar spectrum contribute to skin damage and that sunscreens, aimed purely at UV wavelengths, may be providing an incomplete protective effect. Also, of significance is that these reactive oxygen and nitrogen species can cause radiation-independent pyrimidine dimer formation and alternations in endogenous antioxidant levels important in preventing additional skin damage[12].

Of cosmetic concern to FST IV to VI is hyperpigmentation and melasma that will not be prevented by popular sunscreen formulations.

Visible light on melanin

Melanin, despite its involvement in photoprotective mechanisms, is the most

abundant endogenous photosensitiser in human skin. This is particularly significant for the red hair phenotypes that have a relatively high pheomelanin to eumelanin ratio. This skin type is the strongest expression of the MC1R polymorphic variant. Approximately 50% of the Anglo-Saxon derived Australian population carry at least one of these genes. Photoexcitation by sunlight culminates in the formation electronic excited states, such as ROS and reactive nitrogen species, severely increasing the phototoxicity of VL to skin cells. This induces significant oxidative damage in nucleic acids, lipids and proteins triggering apoptosis and accumulation of premutagenic DNA lesions. In response, cells release pro-inflammatory cytokines and MMPs, promoting further apoptosis and aging[13].

Synergistic effects

There can be protective effects of longer wavelengths against damaging shorter wavelengths. Menezes et al described the protective effect of IR light against damaging effects of UV irradiation in human dermal fibroblasts. He noted that, in the natural environment, cells are first irradiated by solar VL-IR wavelengths due to the combined effect of solar zenith angle and absorbance properties of atmospheric components and concluded that this was a "natural process of cell protection against solar UV, acquired and preserved through evolutionary selection"[14].

Accumulation of melanin can be considered to be a photoprotective response by melanocytes to reduce DNA damage induced by UVR. It is known that excess UVA radiation induces modification and degeneration in both eumelanin and pheomelanin. Ito et al investigated the role of VL, alone or in combination with UVA, in the photodegradation of both types of melanin in human epidermal melanocytes. Exposure to excess UVA induces the degradation of melanin that may be deleterious to pigmented tissues. Although the spectrum of solar energy is nearly half VL, few studies have examined its role in this sort of effect. In this study, they examined the effects of physiological doses of VL (150- 300J/cm^2) alone or in combination with UVA (20J/cm^2) in melanocytes. Their results showed that VL accelerates UVA-induced changes in the structural changes in both types of melanin, although acting alone there were only minor changes[15].

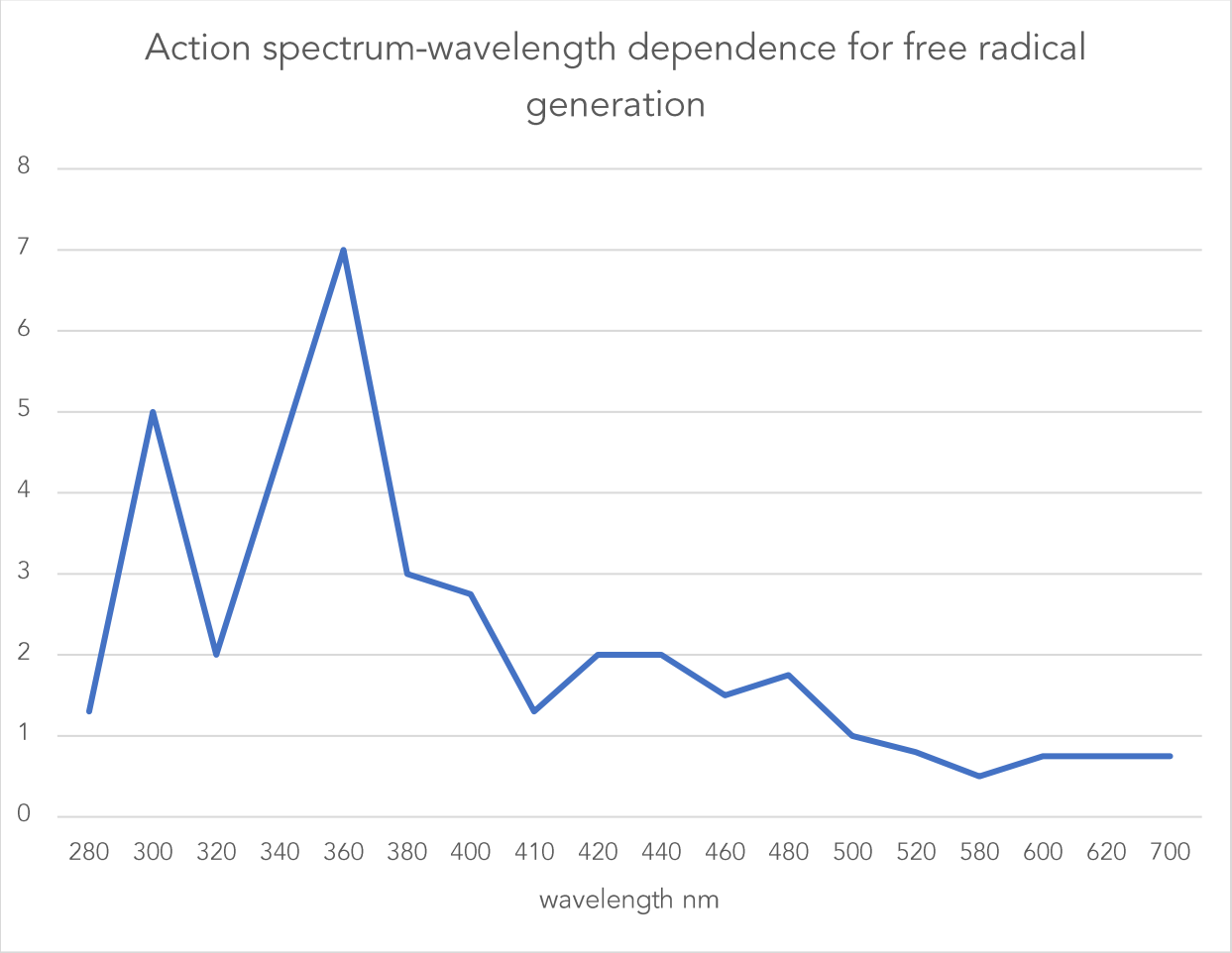

Figure 2. Free radical generation across the solar spectrum (adapted from Zastrow et al)

Photodermatoses

UVR is the action spectra of most photodermatoses, however, VL is the action spectra for solar urticaria, cutaneous porphyria and less commonly polymorphic light eruption and chronic actinic dermatitis.

Phototherapy

Photobiomodulation uses Lasers, IPC, LEDs and fluorescent bulbs in VL treatment protocols with specific wavelengths used to treat a range of conditions, including acne, psoriasis, wound healing and hair growth. In Photo Dynamic Therapy (PDT) sunlight and red light are utilised to treat actinic damage and superficial skin cancers.

Photoprotection and the tanning response

In response to solar radiation, p53 accumulation in keratinocytes induces expression of the prohormone proopiomelanocortin (POMC) and subsequent increase in its neuroendocrine peptide products alpha-melanocortin stimulating hormone (αMSH) and adrenocorticotrophic hormone (ACTH), which regulate the function of melanocytes[16].

The melanocortin 1 receptor (MC1R) on melanocytes when stimulated by αMSH is a driver and principal regulator of melanogenesis and a major determinant of skin phenotype. Thus, the *MC1R* gene function is a major determinant of melanoma susceptibility. Eumelanin, the black-brown pigment, is an effective filter against solar radiation and scavenger of free radicals. Polymorphism of the *MC1R* gene can result in variants with reduced ability of MC1R to promote eumelanin after its activation, alternatively promoting the formation of pheomelanin, an endogenous photosensitiser, at the expense of eumelanin, making these individuals, having a higher pheomelanin to eumelanin ratio, more susceptible to melanoma and increasing their risk. MC1R/αMSH interaction stimulates a canonical cyclic adenosine monophosphate/ protein kinase A (cAMP/PKA) pathway activating microphthalmia-associated transcription factor (MITF), upregulating expression of melanogenic enzymes, increasing melanocyte dendricity and aiding in transfer of melanosomes to the melanocyte cell periphery[17].

MC1R/αMSH interaction through the cAMP/PKA pathway promotes eu-melanogenesis providing the cytoprotective effect of the tanning response but despite the poor tanning ability and the promotion of pheo-melanogenesis in MC1R allelic variants, non-canonical pathways can be stimulated by αMSH that contribute to control of oxidative stress through induction of antioxidant defences and activity of DNA repair pathways. This includes ERK, PI3K/AKT and PPAR-γ pathways. For example, MC1R coupling to the ERK pathway is differentially regulated from the cAMP pathway by transactivation of c-KIT, another transmembrane receptor, allowing MC1R allelic variants to effectively activate the ERK signalling cascade[18]. Figure 3.

Natural protective measures

Both Liebel and Zastrow advocate addition of antioxidants to sunscreen to reduce the negative impacts of VL on human skin[10,11]. Rather than adding more components to pre-existing sunscreen preparations, with the use of sunscreens already encouraging more prolonged exposure, I would like to advocate a more balanced approach to sun exposure by utilisation of pre-existing defence mechanism built into the skins' physiological response. Evolutionally refined and adapted over eons but unfortunately often by-passed with modern life-style pressures and choices. Firstly, photoadaptation by melanocompetent individuals and secondly, adapting a life-style better coordinated with endogenous circadian patterns of behaviour and response.

Photoadaptation

Humans have been exposed to solar radiation since our appearance on earth and evolution has enabled individuals, with the capacity to adapt to exposure, to show a decreased response after acclimatization, termed photoadaptation.

There are a number of natural protective responses. Pigmentation, thickening of the epidermis and stratum corneum, DNA repair, mobilisation of antioxidant systems and Vitamin D production.

Individuals with tanning ability notice that the skin burns more easily at the beginning of summer with sun exposure as opposed to exposure at the end of summer.

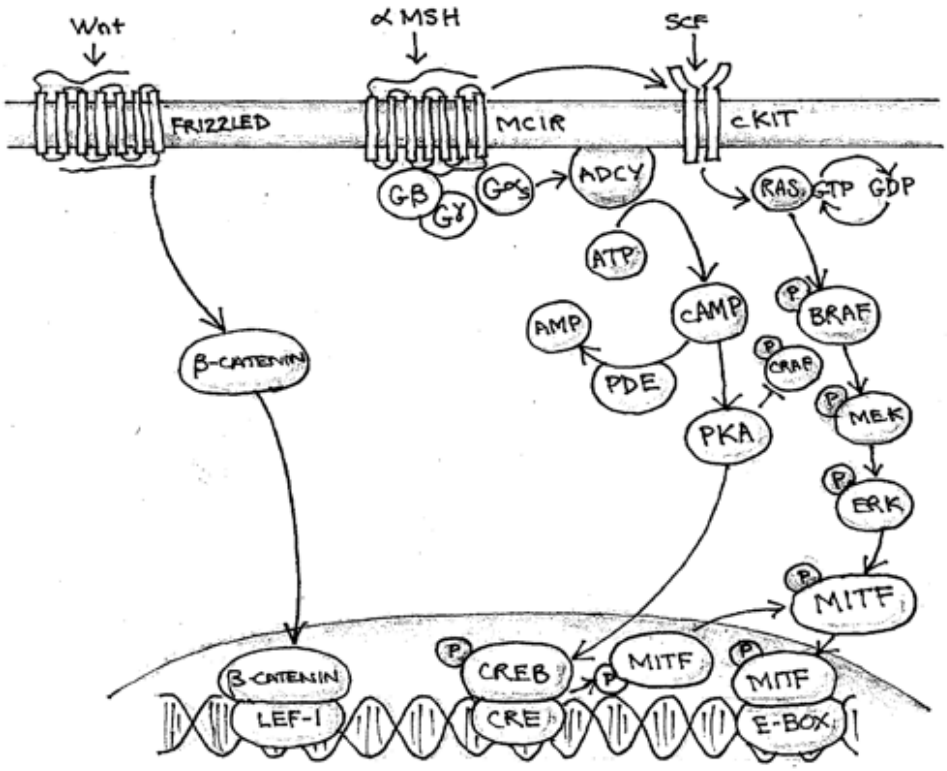

Figure 3. cAMP signalling showing cross-talk between cAMP and MAPK signalling.

MITF is regulated by three pathways. Frizzled-Wnt signalling (melanocyte development); MC1R-cAMP signalling; and cKIT-MAPK signalling (differentiation and proliferation). αMSH/MC1R signalling can activate the MAPK pathway in a cAMP-independent manner.

ADCY, adenylate cyclase; cAMP, cyclic AMP; CRE, cAMP responsive element; CREB, cAMP responsive element binding protein; G proteins a,b,γ; P, phosphorylation; PDE, phosphodiesterase; MITF, microphthalmia associated transcription factor; SCF, stem cell factor; Wnt, wingless-type ligand. (Adapted from Rodriguez & Setaluri 2014).

Daily sub-erythemal doses produce less stratum corneum and epidermal thickening than less frequent exposure but the protective effect increases over time[19]. Repeated sun exposure affords the same protection against DNA photodamage and erythema[20]. The most important end point is protection against skin cancer. Based on epidemiological studies of solar exposure and risk of melanoma, there appears to be a reduced risk of melanoma in those individuals receiving chronic, occupational exposure Vs intermittent, recreational exposure. Thus, the pattern of exposure appears to be important in the etiology of melanoma[21,22]. Squamous

cell carcinoma (SCC) constantly shows a strong correlation with culminative UVR exposure[23], thus, photoadaptation against SCC has not been demonstrated. Solar radiation is impossible to completely avoid and must be balanced by the fact that all solar radiation leads to some level of DNA damage. Fair skinned individuals must always use photoprotection, clothing and sunscreen, with UV indices >3[24].

Coordination with the endogenous circadian system of physiological and homeostatic control.

The endogenous circadian system

Circadian rhythms are a feature of almost all living cells. Even though cells are capable of independent oscillation, and organisms when isolated from external stimuli sustain an approximately 24-hour cycle of physiology and metabolism. However, there is a master controller in the brain, the suprachiasmatic nucleus (SCN), that provides a coordinated response throughout the body, influenced by daily and seasonal patterns of light and dark. Photons stimulate intrinsically photosensitive ganglion cells in the retina. The neuronal signal passes directly to the SCN that sits above the chiasma in the hypothalamus. The SCN has multiple outputs to hypothalamic and thalamic nuclei, and including the Pineal gland. Neuronal and hormonal signals then pass to the periphery. Sunlight is used to entrain this endogenously generated rhythmicity to the earth's rotation, providing, in the case of visible light, a three-dimensional perception of the world plus the fourth external dimension, time. At a molecular level, the mammalian circadian system is driven by an autoregulatory feedback loop of transcriptional activators and repressors. Circadian regulated genes have widely varied functions but are significantly influential in DNA damage repair, the cell cycle, cellular proliferation and apoptosis, as well as metabolic function. This endogenous clock is designed to anticipate environmental changes in terms of available nutrients and tissue specific requirements and threats that might impact cellular homeostasis. An equivalent system is present in even the most primitive organisms throughout the kingdoms of life. Evolution has refined this adaptive process in mammals into a highly complex and integrated system of activators and suppressors with the overall function being protection of the genome. Normal circadian rhythms are essential for the body's natural defense against disease and cancer. However, deregulation through modern lifestyle choices can influence these biological processes and enhance the capacity for carcinogenesis.

DNA damage repair

Gadameeddhi et al demonstrated that Xeroderma pigmentosum A (XPA), a vital enzyme in the Nucleotide excision repair (NER) mechanism, oscillates with circadian rhythmicity. This gives NER, the dominant mammalian DNA repair mechanism responsible for UV-induced bulky photolesions, a temporal, varying expression in mice[25]. Further work by a range of investigators supported Gadameedhi's initial proposition that human DNA repair will be most effective and less prone to carcinogenic

effects of UVR in the morning[26,27]. This rhythmicity also applies to Base excision repair (BER) responsible for DNA damage repair through oxidative effects[28].

I think it is as reasonable to say that DNA repair capacity is as significant as radiation-induced DNA damage as exemplified by the condition Xeroderma pigmentosum, a genetic deficiency of NER enzymes, with an incidence of melanoma X2000 as compared to normal individuals[29].

Cell cycle control

There is evidence of a bidirectional control between the cell cycle and circadian systems with common regulators. The clock controls the expression of several cycle related genes and thus, having some control over the timing of cell division in proliferating cells[30]. This is particularly significant in the skin with the relatively high proliferative rate of most skin cells. Skin homeostasis is imperative to its protective function for the whole organism and similar to the circadian cycle of positive and negative regulators, the cell cycle is a closely regulated system with check-points placed at key transitions in the cycle to regulate fidelity of DNA replication and mitosis. Both systems are also influenced by post transcriptional modifications to further fine tune the relationship.

There was an early finding of an anti-phasic relationship between repair and proliferation in human tissue with the eventually proven correct suggestion of an intimate relationship between circadian and cell cycles[31]. Since then circadian gating of mitosis has been demonstrated in a range of multicellular organisms via circadian regulation of S phase duration[32,33].

Proliferation

Geyfman's study demonstrating circadian control of keratinocyte proliferation led him to ask the question "why do epidermal keratocytes proliferate in a circadian fashion?"

The current hypothesis, at that time, suggested that clock-controlled proliferation serves as a mechanism for protecting against UV-induced DNA damage by minimising DNA replication during exposure to solar radiation. However, in humans, maximum S phase and mitosis, in the epidermis, are occurring when UV intensity is high and DNA is most susceptible. In Geyfman's study they found many metabolic genes are antiphasic to cell cycle-related genes, the former peaked through the day and the latter at night. In contrast, ROS, as a by-product of oxidative phosphorylation, and S-phase are antiphasic. Their study argued that the clock functions to segregate epidermal keratinocyte proliferation from oxidative phosphorylation, protecting the genome from endogenous ROS-mediated DNA damage[34]. The maximum number of keratinocytes, in human epidermis, go through S-phase in the late afternoon. So, afternoon exposure, even though avoiding maximal UV exposure, is less advantageous than morning exposure with DNA more exposed during mitosis.

Central and peripheral clocks

The SCN receives photic input directly from the retina. It acts as a central pacemaker to coordinate peripheral clocks. Light has

traditionally been considered to be the main *zeitgeber* for the circadian system, but timing of food intake has an effect on liver, kidney, heart and pancreatic clocks[35] and scheduled exercise can induce phase shift in skeletal muscle and lung clocks[36]. Thus, a more complex system translates a range of signals with bidirectional communication between brain and peripheral organs, adapting physiology to environment.

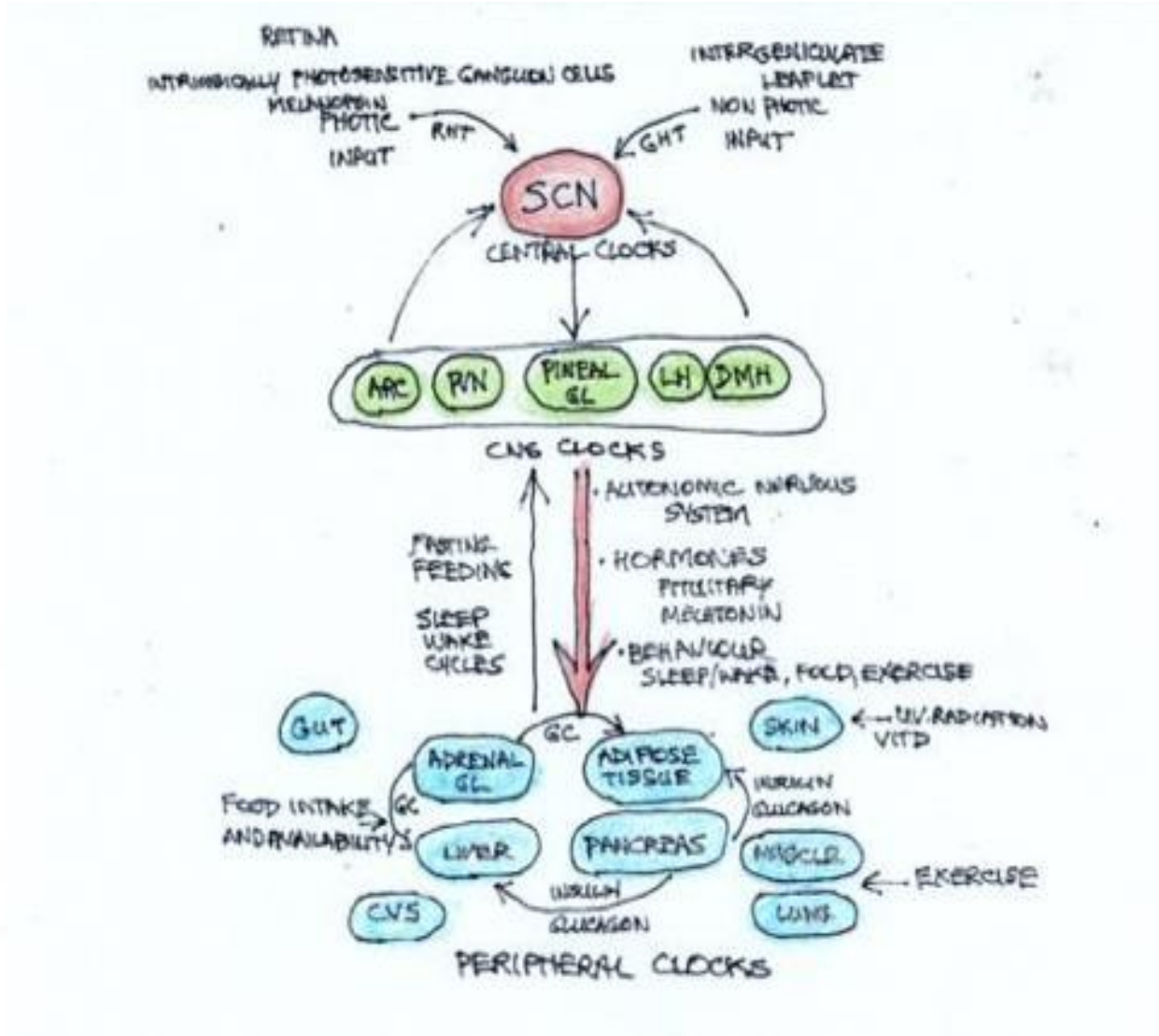

Figure 4. Central, CNS and peripheral clock communication.

Pathways and signals involved in clock-clock communication responsible for integration and stabilisation of biological rhythms at central and peripheral levels. An integrated response is translated from the brain, through neural projections via the autonomic nervous system and humoral signals, to peripheral tissues. Peripheral clocks receive the time

information, communicate with each other, and release signals that feedback to the clock in the brain. Arcuate nucleus (ARC); dorsomedial hypothalamus (DMH); glucocorticoids (GS); lateral hypothalamus (LH), paraventricular nucleus (PVN).

Light pollution, melatonin suppression and disease

Light during normal periods of darkness (light pollution) is becoming an increasing problem in industrialised nations. Artificial light at night has the potential to disrupt the intimate relationship between circadian rhythms, sleep/wake cycles and metabolic cascades. One consequence is suppression of melatonin rhythms[37,38], a significant hormone in the circadian system, but there are also changes in gene and protein expression, neuronal firing thresholds and other hormones such as glucocorticoids[39].

Shift work is associated with an increased incidence of obesity, diabetes and metabolic syndrome[40]. Epidemiological studies suggest that women working night shift work have an increased incidence of breast cancer[41-43], and possibly other hormone related cancers such as prostate in male shift workers[44,45].

Vitamin D and melanoma

It is accepted that sun exposure is the major environmental causative factor in melanoma incidence, however sun exposure is critical for Vitamin D synthesis. Sub-optimal levels are associated with reduced bone health and increasing literature linking increased risk of other diseases, so that a balance between exposure and protection is needed. Overall, genetic-epidemiological data suggests intermittent exposure and sun-burn have been responsible for the drastic increase in melanoma in Caucasian populations this century[46]. Excluding the high-risk phenotypes, the epidemiological data is complex but suggests that exposure can be protective in some circumstances, possibly through photoadaptation or higher Vitamin D levels[47].

Vitamin D is anti-proliferative *in vitro* for some melanoma cell lines[48]. At melanoma diagnosis, lower Vitamin D levels are associated with thicker tumors and poorer prognosis[49,50]. Sun-sensitive people have lower Vitamin D levels[51] and patients with a previous diagnosis of melanoma are likely to practice sun-avoidance behaviors. Should we be measuring levels and suggesting supplementation for our melanoma patients? Shield's English study suggested optimal level of 60nmol/L and supplemented dose of 1000 IU daily for levels < 40 nmol/L and 400 IU for 40-60. This is for a population that generally had a low intake of fatty fish and the evidence is lacking for supplementation reducing melanoma risk.

Conclusion

It is important to bear in mind that as humans we are part of nature, not above it, and subjected to its laws. We need to be cognitive of natural circadian patterns of light and dark, and to the best of our ability, employ a life-style synchronised with these patterns of nature.

This will engage a range of natural protective measures provided and refined through adaption and evolution.

Rising at dawn to entrain the endogenous time-keeping mechanism, as much as possible restricting recreational exposure to early morning where longer wavelengths of light will not only be less damaging but also providing maximally effective DNA repair. There is also the suggestion that these longer wavelengths provide conditioning of the skin for exposure latter in the day. Afternoon exposure is still preferable to overhead sun exposure but this risks exposure that may intersect more with the proliferative skin cell phase where DNA is more exposed during mitosis. If there is involvement in recreational activities that require more prolonged sun exposure then it is advantageous to have a pattern of regular mild exposure to allow for skin photoadaptation. Eating nutritious meals at regular intervals and finding time for some regular exercise can also influence circadian hormonal patterns. Modest regular solar exposure as well as conditioning skin will provide adequate biosynthesis of vitamin D. Restricting light at night will avoid interfering with melatonin levels and risking further deregulation of the circadian system.

These simple measures will provide a happier, healthier and possibly longer life than ignoring them. The products of industrialisation and technological advances can provide additional protective responses but, at this stage, the protection afforded is incomplete. This has shown to be significant in the case of the effects of visible light on the skin and its involvement in the incidence of skin cancer and particularly melanoma.

Corresponding author:
David John Mackay Smith
University of Queensland
St Lucia QLD 4072, Australia
Email: djmsmith8@bigpond.com

Funding:
None

Conflicts of Interest:
None

References:

1. Frederick, J., Snell, H., Haywood, E. **Solar ultraviolet radiation at the earth's surface**. 1989. *Photochem & Photobiol*; 50: 443-570.

2. Diffey, B., Kochevar, I. **Basic principles of photobiology**. 2007. *Photodermatology*: 15-17.

3. Tewari, A., Sarkany, R., Young, A. **UVA1 induces cyclobutene pyrimidine dimers but not 4-6 photoproducts in human skin in vivo**. 2012. *J Invest Dermatol*; 132: 394-400.

4. Mahmoud B, Hexel C, Hamzavi I, et al. **Effects of visible light on the skin**. 2008. *Photochem. & Photobiol*; 84(2): 450-462.

5. Mahmoud B, Ruvolo E, Hexel C, et al. **Impact of long wavelength UVA and visible light on melanocompetent skin**. 2010. *J. Invest. Dermatol*; 130(8): pp. 2092-2097.

6. Randhawa, M., Seo, I., Liebel, F., et al. **Visible light induces melanogenesis in human skin through a photoadaptive response**. 2015. *PLOS ONE*/DOI:1371/pone 0130949.

7. Ragezzetti, C., Sormani, L., Delayle, D., et al. **Melanocytes sense blue light and regulate pigmentation through the opsin-3**. 2018. *J. Invest. Dermatol.*;138:171-178.

8. Monteiro de Assis, L., Tonolli, P., Baptista, M., et al. **How does the skin sense sunlight? An integrative view of light sensing molecules**. 2021. *J Photochem & Photobiol C: photochem reviews*; 47. Doi.org/10.1016/j Photochem reviews.2021.10043.

9. Smith, D. **Photosensory function, reception and response in human skin**. 2021. *J Clin Cosmetic Dermatol*; 5(2). Doi.org/10.16966/2576.2826.164.

10. Liebel, F, Kaur S, Ruvolo E, et al. **Irradiation of skin with visible light induces reactive oxygen species and matrix degrading enzymes**. 2012. *J Invest Dermatol*; 132(7): pp. 1901-1907.

11. Zastrow, L., Lademann, J. **Light-instead of UV protection: new requirements for skin cancer protection**. 2016. *Anticancer research*; 36:1389-1394.

12. Vandersee, S., Beyer, M., Ladermann, J., et al. **Blue violet light irradiation dose dependently decreases carotenoids in human skin, which indicates the generation of free radicals**. 2015. *Oxid Med Cell* 2015:579675.

13. Tonolli, P., Baptista, M., Chiarelli-Neto, O. **Melanin, lipofuscin and the effects of visible light in the skin**. 2021. *J Photochem & Photobiol* 7: 1000044.

14. Menezes, S., Coulomb, B., Lebreton, L., et al. **Non-coherent near infrared radiation protects normal human dermal fibroblasts from solar ultraviolet toxicity**. 1998. *J Invest Dermatol*; 111: 629-633.

15. Ito, S., Kolbe, L., Wakamatsu, K., et al. **Visible light accelerates the ultraviolet A-induced degeneration of eumelanin and pheomelanin**. 2018. DOI:10.1111/pcmc.12754; 32(3):441-447.

16. Abdel-Malek, Z., Knittel, J., Kadekaro, A., et al. **The melanocortin 1 receptor and the UV response of human melanocytes -a shift in paradigm**. 2008. *Photochem & photobiol*; 84(2);501-508.

17. Adehmann, C., Trambaurer, A., Chem, B., et al. **MFSD12 mediates the import of cysteine into melanosomes and lysosomes**. 2010. *Nature*; 588: 699-704.

18. Herraiz, C., Jiménez-Cervantes, C., Zauna, P., et al. **Melanocortin 1 receptor mutants impact differentially on signaling to the cAMP and the ERK 2 mitogen-activating protein kinase pathway**. 2009. *FEBS letters*; 583: 3269-3274.

19. Gonzalez, S., Hegyi, V., Bager, A., et al. **Development of cutaneous tolerance to ultraviolet B during ultraviolet B phototherapy**. 1996. *Photoderm Photoimmunol Photomed*; 12(2): 73-78.

20. Sheehan, J., Cragg, N., Chadwick, C. **Repeated ultraviolet exposure affords the same protection against DNA photodamage and erythema in human skin type II and IV but is associated with faster DNA repair in skin type IV**. 2002. *J Invest Dermatol*; 118: 825-829.

21. Elwood, J. **Melanoma and sun exposure: contrasts between intermittent and chronic exposure**. 1992. *World J Surg*; 16: 157-165.

22. Vuong, K., McGeechan, K., Armstrong, B., et al. **Occupational sun exposure and risk of melanoma according to anatomical site**. 2014. *Int J Cancer*; 134(11): 2735-2741.

23. Kricker, A., et al. **Early life UV and risk of basal and squamous cell carcinoma in New South Wales, Australia**. 2017. *Photochem Photobiol*; 93(60): 1483-1491.

24. Garmyn, M., Young, A., Miller, S. **Mechanisms and variables affecting UVR photoadaption in human skin**. 2018. *Photochem & Photobiol Sciences*; 17: 1932.

25. Gaddameedhi, S., Selby, C., Kaufmann, W., et al. **Control of skin cancer by the circadian rhythm**. 2011. *PNAS*; 108(46): 18790-18795.

26. Sancar, A., Lindsay-Boltz, L., Kang, T., et al. **Circadian clock control of the cellular response to DNA damage**. 2010. *FEBS letters*; 584:2618-2625.

27. Sarkar, S., Gaddameedhi, S. **UV-B-induced erythema in human skin: the circadian clock is ticking**. 2018. *J. Invest. Dermatol*; 138:248-251.

28. Manzella, N., Bracci, M., Strafella, E., et al. **Circadian modulation of 8-oxo guanine DNA damage repair**. 2015. *Sci. Rep.* 5 13752; doi: 10.1038/srep13752.

29. Bradford, P., Goldstein, A., Tamara, D. et al. **Cancer and neurological degeneration in Xeroderma Pigmentosum: long term follow-up characterises the role of DNA repair**. 2011. *J. Med. Genetics*; 48(3): 168-176.

30. Masri, S., Cervantes, M., Sassone-Corsi, P. **The circadian clock and cell cycle: interconnected biological circuits**. 2013. *Current Opinion in Cell Biol*; 25: 730-734.

31. Bjarnsoon, G., Jordan, R., Wood, P., et al. **Circadian expression of clock genes in human oral mucosa and skin: association with specific cell-cycle phases**. 2001. *Am. J. of Path*; 158(5): 1793-1801.

32. Laranjeiro, R., Tamal, K., Peyric, E. et al. **Cyclin-dependent kinase inhibitor p20 controls circadian cell-cycle timing**. 2013. *PNAS*; 110(17): 6835-6840.

33. Matsuo, T. et al. **Control mechanisms of the circadian clock for timing of cell division in vivo**. 2003. *Science*; 302: 255-259.

34. Geyfman, M. et al. **Brain and muscle Arnt-like protein-1 (BMAL1) controls circadian cell proliferation and susceptibility to UVB-induced DNA**

damage in the epidermis. 2012. *Proc. Nat. Acad. Sci. USA*; 109: 11758-11763.

35. Damiola, F. **Restricted feeding uncouples circadian oscillators in peripheral tissues from the central pacemaker in the suprachiasmatic nucleus.** 2000. *Genes Dev*; 14: 2950-2961.

36. Wolff, G., Esser, K. **Scheduled exercise phase shifts the circadian clock in skeletal muscle.** 2012. *Sci. Sports Exerc; Med*; 44: 1663-1670.

37. Brainard, G., Lewy, A., Menaker, M., et al. **Effect of light wavelength on the suppression of nocturnal plasma melatonin in normal volunteers.** 1985. *Ann N Y Acad Sci*; 453: 376-378.

38.Gooley, J., Chamberlain, K., Smith, K., et al. **Exposure to room light before bedtime suppresses melatonin onset and duration in humans.** 2011. *J Clin Endo Metab*; 96: E463-E472.

39. Emmer, K., Russart, G., Walker, W., et al. **Effects of light at night on laboratory animals and research outcomes.** 2018. *Behav Neurosci*; 132: 302-314.

40. Fonken, L., Nelson, R. **The effect of light at night on the circadian clock and metabolism.** 2014. *Endcr Rev*; 35(4): 648-670.

41. Hansen, J. **Increased breast cancer risk among women who work predominantly at night.** 2001. *Epidemiology*; 12: 74-77.

42. Davis, S., Mirick, D., Stevens, R. **Night shift work, light at night and the risk of breast cancer.** 2001. *J Natl Cancer Inst*; 73: 1557-1562.

43. Schernhammer, E., Laden, F., Speizer, F. **Rotating night shifts and risk of breast cancer in women participating in the nurses' health study.** 2001. *J Natl Cancer Inst*; 93: 1563-1568.

44. Kubo, T., Ozasa, K., Mikain, K., et al. **Prospective cohort study of the risk of prostate cancer among rotating shift workers: Findings from the Japan collaborative study.** 2006. *Am J Epidemiol*; 164: 549-555.

45. Ayesha, A., McNair, C., McCann, J., et al. **The circadian cryptochrome, CRY1, is a pro-tumorigenic factor that rhythmically modulates DNA repair.** 2021. Doi.org/ 10.1038/s41467-020-20513-5.

46. Chang, y., Barrett, T., Bishop, D et al. **Sun exposure and melanoma risk at different latitudes: a pooled analysis of 5700 cases and 7216 controls.** 2009. *Int. J. Epidemiol;* 38:814-830.

47. Gandini, S., Sera, F., Cattaruzza, M., et al. **Meta-analysis of risk factors cutaneous melanoma II sun exposure.** 2005. *Euro. J. Cancer;* 41: 45-60.

48. Reichrath, J., Rech, M., Moeini, M., et al. **In vitro comparison to the endocrine system in 1,25(OH)2D3-responsive and -resistant melanoma cells.** 2007. *Cancer Biol. Ther;* 6: 48-55.

49. Newton-Bishop, J., Beswick, S., Randerson-Moor, J., et al. **Serum 25 hydroxyvitamin D3 levels are associated with Breslow thickness at presentation and survival from melanoma.** 2009. *J. Clinic. Oncol*; 27: 5439-5444.

50. Nümberg, B., Gröber, S., Gärtner, B., et al. **Reduced serum 25OH vitamin D levels in**

stage IV melanoma patients. 2009. *Anticancer Res*; 29: 3669-74.

51. Fields, S., Davies, J., Bishop, T., et al. **Vitamin D and melanoma**. 2013. *Dermatol.-Endo*; 5(1): 121-129.