The consequences of environmental and artificial ultraviolet radiation exposure on the epidermis increases the risk of basal cell carcinoma

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Introduction

Research Background

- Basal cell carcinoma (BCC) is the most commonly occurring skin cancer worldwide
- Ultraviolet B (UVB), a type of UV radiation (UVR) is known to increase the risk of basal cell carcinoma through natural sun exposure or human-induced activities
- UVB is a carcinogen that damages the DNA inside skin cells which leads to the abnormal function of the DNA repair system and alters the immune system resulting in progressive genetic alterations
- As UV exposure is known to increase the chances of development of BCC, the public should be urged to use sunscreen, wear protective apparel, and avoid harmful artificial UV exposure to decrease BCC incidence

Introduction

Research Purpose

- To discover the processes and the impacts of environmental and artificial Ultraviolet B exposure that increase the risk of Basal Cell Carcinoma

Research Question

- How does environmental and artificial Ultraviolet B exposure on the skin increase the risk of Basal Cell Carcinoma?

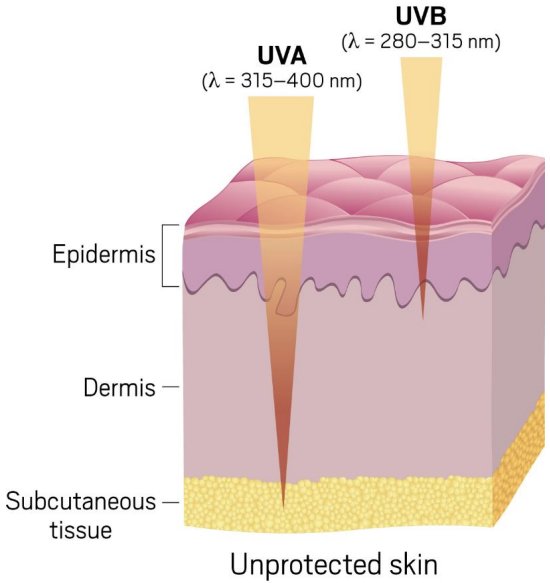
Research Hypothesis

- Environmental and artificial Ultraviolet B exposure increases the risk of BCC by damaging the outermost skin layer, causing gene mutations

Literature Review

UVB versus UVA Radiation

- Ultraviolet B (UVB) is the most significant environmental risk factor for the occurrence and progress of BCC due to its short wavelengths, causing skin damage on the epidermis whereas UVA has longer wavelengths
- Specifically, cumulative high-grade UVB exposure (strong exposure over a long period of time) could promote the uncontrolled replication of skin cells



UVB exposure from sunlight

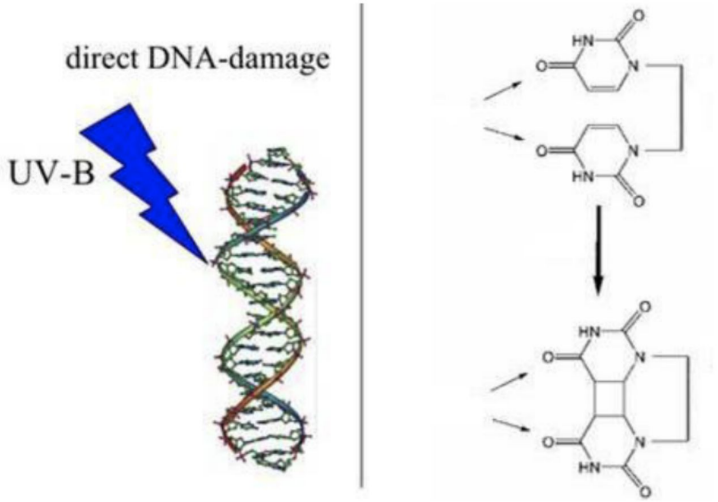
- Sun exposure is the most common factor associated with BCC and depends on the characteristics of sun exposure, such as pattern, timing, and amount (Gallagher et al. 2012)
- A study conducted in Australia delved deeper into the significance of sun exposure patterns (intermittent or continuous) and age (childhood or adulthood) in BCC: “We observed a statistically significant increase in [the] risk of BCC, with increasing proportion of weekly sun exposure obtained [on] the weekend, especially in late teenagers, exposure of the site of skin cancer during holidays and sunburn to the site” (Kricker et al. 1988)
- This data suggests that a particular amount of sun exposure delivered in infrequent, intense increments will increase the risk of BCC more than a similar dose delivered more continuously over the same total period of time

UVB exposure from indoor tanning

- Indoor tanning affects a smaller percentage of the population, but it has recently become more prevalent among young adults in Asian countries who traditionally preferred lighter skin tones
- A large case study revealed that “indoor tanning was correlated with a 69% increase in the risk of early-onset BCC, and this was more evident in women” (Teng et al. 2021)
- Another case study suggested that the risk of BCC from indoor tanning during high school/college was shown to be higher than the risk for people between the ages of 25 and 35 (An et al. 2021)

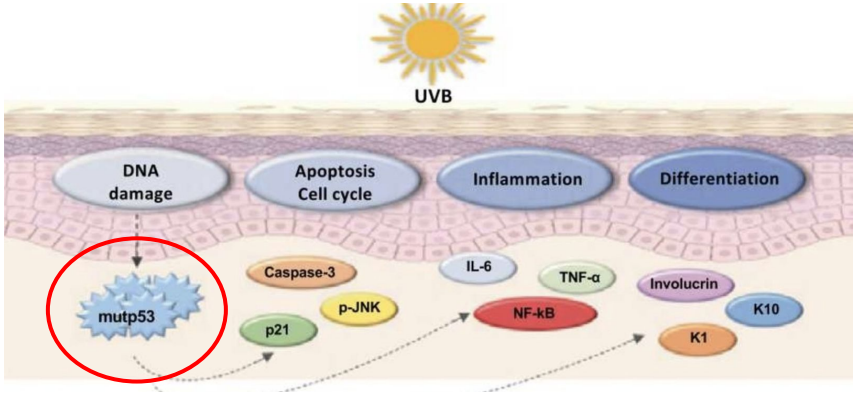
Effect of UVB on the DNA repair system

- Since DNA is the main target of UVB damage, when UVB damages the skin, it slows down the process of the DNA repair system and increases the risk of mutations in DNA
- Without the DNA repair mechanisms, damaged strands of DNA won't be able to be repaired and will cause greater genetic mutations in the future



Mutation of the p53 tumor suppressor gene

- BCC from exposure to UVB also causes mutations in the p53 suppressor gene (Journal of National Cancer Institute)
- According to one source added that “most of the TP53 mutations in BCC are [a] transition from C to T, and the frequency of double base changes from CC to TT is relatively high, which indicates alterations [were] induced by UVR” (Bakshi et al. 2017)
- The p53 suppressor gene’s main purpose is to stop the formation of tumors and the loss of the p53 function caused by UVR plays a central role in causing development of BCC



Hedgehog Signaling Pathway

- Hedgehog signaling pathway in BCC is a major regulator of many fundamental processes including the development of cellular embryos, tissue polarity which is the organization of cellular proteins and membranes of the tissue, as well as cell proliferation which is the division of cells
- Blocking this by small molecules such as Vismodegib and Sonidegib inhibits tumor growth of BCC which is done by blocking Smoothened (SMO), a key transmembrane protein that is a key component of the hedgehog signaling pathway
- Vismodegib and Sonidegib molecules work by slowing down the cell proliferation of cancer cells while also shrinking tumors

Research Methodologies

Methods (1)

What did this project do?

- This was a research project that used quantitative, qualitative data to investigate the research question

Research Method

- After a more generic study was done, case studies were applied to further investigate the consequences of UVB exposure on the skin
- Description approach: used to describe and analyze the case studies to support the hypothesis

Methods (2)

Data

- Data content and sources:

	Environmental UVB Data	Artificial UVB Data
Methodology	Stratified sampling: used to differentiate patterns of sunlight exposure and age	Stratified sampling: used to distinguish categories of age groups
Sources	Journal of the National Cancer Institute	American Academy of Dermatology

How data was collected

- Journals collected and published their data in databases
- I collected the data by downloading the data tables from their databases

Data & Analysis

Sunlight UVB exposure

- Participants included 218 BCC cases recruited from a university dermatology clinic in Florida and 316 controls with no history of skin or other cancers
- Compared two different patterns of UVB sunlight exposure: Continuous and intermittent by age categories
- Results suggested that sunlight UVB exposure is associated with BCC regardless of the pattern in which the exposure was received (i.e. intermittent vs. continuous). The data also suggests that sunlight exposure at a younger age may be more significant for BCC

	Controls (n = 316)	Basal cell carcinoma (n = 218)		
Variable	**n (%)**	**n (%)**	**OR (95% CI)[1]**	**OR (95% CI)[2]**
Patterns by age at exposure				
Teens				
<1 hour	18 (6.0)	12 (6.0)	1.00 (reference)	1.00 (reference)
Continuous hours	151 (50.0)	113 (56.8)	1.04 (0.45-2.41)	0.97 (0.38-2.48)
Intermittent hours	133 (44.0)	74 (37.2)	1.08 (0.46-2.54)	1.10 (0.42-2.83)
Twenties				
<1 hour	34 (11.3)	18 (9.0)	1.00 (reference)	1.00 (reference)
Continuous hours	102 (33.9)	91 (45.5)	1.36 (0.68-2.71)	1.58 (0.75-3.36)
Intermittent hours	165 (54.8)	91 (45.5)	1.30 (0.66-2.56)	1.56 (0.74-3.26)
Thirties				
<1 hour	60 (20.5)	27 (13.6)	1.00 (reference)	1.00 (reference)
Continuous hours	85 (29.0)	79 (39.9)	1.31 (0.72-2.40)	1.77 (0.90-3.49)
Intermittent hours	148 (50.5)	92 (46.5)	1.38 (0.79-2.41)	2.09 (1.11-3.93)
Past 10 years				
<1 hour	63 (28.6)	52 (30.2)	1.00 (reference)	1.00 (reference)
Continuous hours	74 (33.6)	83 (48.3)	0.88 (0.51-1.52)	1.14 (0.62-2.12)
Intermittent hours	83 (37.7)	37 (21.5)	0.57 (0.32-1.03)	0.67 (0.35-1.28)

95% CI: 95% confidence of data

Indoor tanning UVB exposure

- This meta-analysis provides evidence of the association between indoor tanning and melanoma and non-melanoma skin cancer, particularly early-onset skin cancer diagnosed before age 50 years
- Stratified sampling: taking samplings of data from different age categories of patients
- This study showed that the first exposure at an early-age to indoor tanning, and frequent use of indoor tanning is significantly associated with an increased risk of BCC

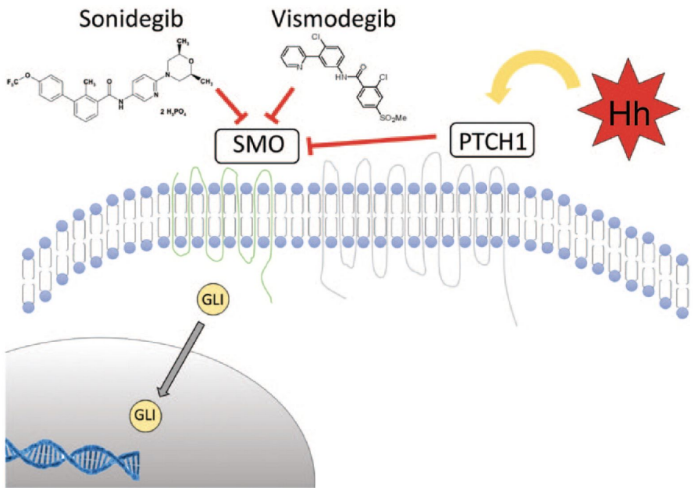
Exposure	Study N	Summary RR (95% CI)		Heterogeneity I^2 (%)	*p*-Value
Basal cell carcinoma					
First exposure at early age to indoor tanning (year)					
<20	2	1.86 (1.44–2.41)	0	0.61	
≥20	2	1.51 (1.19–1.92)	0	0.69	
Annual frequency of indoor tanning (times)					
<10	2	1.29 (1.01–1.65)	40	0.20	
≥10	2	1.46 (1.28–1.66)	18	0.27	

95% CI: 95% confidence of data
Summary RR: risk ratio, also called relative risk
I^2: % of variation across studies due to heterogeneity rather than sampling error

Current Treatments

Current Treatments

- For superficial BCCs (seen mostly on the upper trunk and shoulders) less than 2 cm in diameter, the *Imiquimod* topical was approved by the FDA that had success rates of over 80% (Singal et al. 2016)
- Treatments for mild BCC: topical chemotherapies like 5-fluorouracil with a 70% cure rate for thin and small lesions or surgical excision with over 90% cure rate (Naik et al. 2016)
- Lesions unable to be removed by surgery, hedgehog pathway inhibitor drugs (Vismodegib, Sonidegib) with a 40% response rate is used (Dummer et al. 2020)



Future Research

Possible Future Areas of Research (1)

- It is important to address the harmful exposure to UVB from the sun and human-induced activities as there aren't enough preventative treatments that are reliable to reduce the risk of BCC
- It is crucial to find preventative measures other than wearing protective clothing and sunscreen to prevent UVB damage on the skin that could potentially induce BCC. While it is currently known that Vitamin B3 intake can reduce the risk of developing BCC, dermatologists are working to develop a more effective drug that could protect the skin's barrier
- For superficial BCCs (seen mostly on the upper trunk and shoulders) less than 2 cm in diameter, the *Imiquimod* topical was approved by the FDA that had success rates of over 80%

Possible Future Areas of Research (2)

- For patients with BCC, although it is known that BCC can be managed through surgical excision, it is not readily available in many places around the world. To resolve this issue, an algorithm could be developed to systemize existing techniques and direct surgical treatment of BCC. This could be very accessible and useful in places where surgery is not available.
- Overall, compared to the discoveries of the past, dermatologists and researchers have made a substantial improvement in developing treatments and surgeries to expand preventative measures and cure patients diagnosed with BCC.

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Slide 5 Quote: Totonchy, M., & Leffell, D. (2017). Emerging concepts and recent advances in basal cell carcinoma. *F1000Research*, *6*, 2085. https://doi.org/10.12688/f1000research.11314.1

Slide 8 Image: Boerner, L. K. (2021, July 21). What's in sunscreen, and how does it protect your skin from the sun's rays? [UV filters help prevent sunburn and cancer, while other ingredients encourage people to slather sunscreen on their skin]. *Chemical & Engineering News*, *99*(27). https://cen.acs.org/business/consumer-products/What-in-sunscreen-and-how-does-it-protect-your-skin-from-the-sun-rays/99/i27

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Slide 10 Case study:

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Slide 16 Graph: Sondak, V. K., Messina, J. L., Roetzheim, R. G., Cherpelis, B. S., Fenske, N. A., & Rollison, D. E. (2012). Patterns and timing of sunlight exposure and risk of basal cell and squamous cell carcinomas of the skin – a case–control study. *BMC Cancer*, *12*(1). https://doi.org/10.1186/1471-2407-12-417

Slide 17 Graph: Schulman, J. M., & Fisher, D. E. (2009). Indoor ultraviolet tanning and skin cancer: Health risks and opportunities. *Current Opinion in Oncology*, *21*(2), 144-149. https://doi.org/10.1097/CCO.0b013e3283252fc5

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Slide 19 Image: https://journals.sagepub.com/doi/10.1177/1758834016653605

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Acknowledgements

Acknowledgement

- Thank you to Dr. Anne Chang for joining me as my mentor, helping me with the data collection process, and giving me insightful comments
- Thank you to Mrs. Kaci for reviewing my drafts and offering me helpful suggestions and advice for my research
- Thank you to peers Michelle Lee and Emily Zhou for giving me beneficial feedback and suggestions on my project
- Thank you to Foothill College for allowing me to present my research

Thank you!

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