Perspectives

A Life History Perspective on Skin Cancer and the Evolution of Skin Pigmentation

Daniel L. Osborne* and Raymond Hames

Department of Anthropology, University of Nebraska-Lincoln, Lincoln, NE

KEY WORDS  skin cancer; UVR; longevity; life history

ABSTRACT  The ancestral state of human skin pigmentation evolved in response to high ultraviolet radiation (UVR) stress. Some argue that pigmentation evolved to limit folate photolysis, therein limiting neural tube defects. Pigmentation also protects against sunburn which decreases the efficiency of sweating and potentiates skin infection. Pigmentation increases the efficacy of skin as a barrier to infection. Skin cancer has been rejected or minimized as a selective pressure because it is believed to have little or no effect on mortality during reproductive years. This argument ignores evidence of human longevity as a derived life history trait and the adaptive value of investment in offspring and kin, particularly during the post-reproductive lifespan. Opponents argue that lifespan in prehistoric hunter-gatherers was too short to be relevant to the evolution of skin pigmentation. This argument is flawed in that it relies on estimates of longevity at birth rather than adolescence. When appropriate estimates are used, it is clear that human longevity has a deep evolutionary history. We use a life history perspective to demonstrate the value of skin pigmentation as an adaptation to skin cancer with the following points: UVR exposure increases dysregulation of gene expression in skin cells leading to immortal cell lines; cutaneous malignant melanoma (CMM) affects individuals throughout reproductive years; and lifespan was longer than has previously been acknowledged, providing the opportunity for kin selection. This hypothesis is not at odds with the folate or barrier hypotheses. We stress that the evolution of skin pigmentation is complex and is an ongoing process. Am J Phys Anthropol 153:1–8, 2014. © 2013 Wiley Periodicals, Inc.

Beginning in the early 1950s a number of researchers have argued that human skin coloration is an adaptation to protect against skin cancer by blocking the harmful effects of UVA and UVB radiation (Daniels et al., 1972). A number of lines of evidence have been used to test this hypothesis. For example, Fear et al. (1976, cited in Beall and Steegman, 2000; p 199, Fig. 7.6) show that in the United States skin cancer rates and mortality are negatively correlated with latitude. In the state of Texas, skin cancer rates were approximately five times greater for light-skinned people compared with dark-skinned people. Other studies in Australia and New Zealand compared skin cancer rates of light-skinned individuals to aboriginal residents (e.g., Haynes et al., 2008; Sneyd and Cox, 2009; Olsen et al., 2012). The results were consistently the same: lighter-skinned individuals had higher skin cancer rates. To our knowledge no one disputes the association between skin color, the intensity of UV radiation, and skin cancer. Over the last 20 years there has been growing support for an alternative but not clearly contradictory hypothesis for skin coloration that we call the folate hypothesis as outlined by Jablonski and Chaplin (2000) and Jablonski (2010). The authors assemble impressive evidence that dark skin in high UV environments prevents the degradation of folic acid synthesis and ultimately folate production, thus preventing a host of problems from neural tube defects in infants to male infertility (see Elias and Williams, 2013, for a rebuttal). However, in low UV environments the problem may be allowing sufficient UV radiation in through the skin to stimulate vitamin D synthesis to prevent problems in bone formation, cognitive development, and immune function, leading to light skin as the adaptive solution. A more recent, intriguing hypothesis is that depigmentation evolved as an energy-sparing mechanism (Elias and Williams, 2013). In the process of promoting the folate hypothesis Jablonski (2010) argues that although skin cancer is reliably associated with UV radiation and skin color, the typical onset of skin cancer is at about the time when one’s reproductive career is ending; therefore, dark skin would not have a selective effect in preventing skin cancer. Elias and Williams (2013) dismiss the selective potential of skin cancer using this same reasoning. For a variety of reasons stemming from a new understanding of human life history and inclusive fitness theory, detailed below, we argue that preventing skin cancer after reproduction is likely adaptive. And while a full review of this literature is beyond the scope of this article, we provide a synthesis of recent research on the dangers of skin cancer and their likely impact on fitness.

*Correspondence to: Daniel L. Osborne, Department of Anthropology, University of Nebraska-Lincoln, 810 Oldfather Hall, P.O. Box 880368, Lincoln, NE 68588-0368, USA. E-mail: dosborne2@unl.edu

Received 1 May 2013; accepted 9 October 2013

DOI: 10.1002/ajpa.22408

Published online 31 October 2013 in Wiley Online Library (wileyonlinelibrary.com)

© 2013 WILEY PERIODICALS, INC.
Skin cancer types

Skin cancer presents as a range of disorders associated with abnormal growth of skin cells which develop into lesions classified as preskin cancer or skin cancer. Some skin cancers occur more frequently than others and are more relevant to fitness. The most common skin cancers are named for the cutaneous cells from which they arise and include the nonmelanoma skin cancers (NMSC) basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), and cutaneous malignant melanoma (CMM).

Exposure to ultraviolet radiation (UVR) increases risk of developing NMSC and CMM, though there is also a genetic predisposition (Lacour, 2002; Epstein, 2008; Nun et al., 2009; Scherer and Kumar, 2010). Rates of NMSC are estimated to have increased by 77% from 1992 to 2006 (Scherer and Kumar, 2010; Stern, 2010). This increase could be due to atmospheric changes, migration of lightly pigmented populations to lower latitudes, improvements in diagnosis, changes in sun-seeking behavior, and access to artificial UVR.

On a general scale, likelihood of metastasis in CMM is greater than in NMSC and if not treated early this cancer has high mortality. Like all skin cancers, lightly pigmented populations are at greater risk of developing CMM, although it is present in more darkly pigmented populations in lower proportions (Table 1; also see Camain et al., 1972; Soeripto et al., 1977; Bang et al., 1987; Neugut et al., 1994; Yakubu and Mabogunje, 1995; Sneyd and Cox, 2009). Accordingly, one cannot easily dismiss skin cancer as a selective pressure in the adaptation to UVR. The literature on skin cancer contains relatively few publications on risk and pathophysiology in more darkly pigmented populations (Yakubu and Mabogunje, 1995; Sneyd and Cox, 2009). Because moles present at birth can develop into CMM, some have questioned whether or not UVR has an effect on CMM (Tucker, 2008). This rejection of UVR as a driver of CMM rests largely on the heritability of this disease.

Skin cancer genetics

Genes associated with skin cancer risk remain poorly understood. Some genetic markers (e.g., MC1R, ASIP, TYR, EXOC2, UBAC2, OCA2, SLC24A5, SLC24A4, MATP, IRF4, and the 1p36 and 1q42 loci) have been identified as risk factors independent of skin pigmentation, though they only explain a small amount of variation in skin cancer risk (Han et al., 2008; Scherer and Kumar, 2010). Because genome-wide associations studies (GWAS) have not identified regions that explain heritability, some have proposed that many “small-effect” genes are responsible for this variation—although others contest that current models do not include large enough regions of the genome to conclude anything about the genetic basis of skin cancer (Vazquez et al., 2012).

One possible reason that genes with strong effects on skin cancer have not been identified could be the focus on coding regions. Mutations in the promoter regions of genes can affect trait expression and are affected by UVR, providing a clear gene × environment interaction (Greenman, 2007; Ikehata et al., 2008; Singh et al., 2012; Tewari et al., 2012; Huang et al., 2013). Mutations in telomerase reverse transcriptase (TERT) gene promoter regions are more likely to produce immortal cell lines conducive to oncogenesis than are mutations to coding regions (Huang et al., 2013). Two byproducts of UVR exposure are cyclobutane pyrimidine dimers (CPDs)—mainly thymine dimers (TTs)—and 6,4-photoproducts (6,4 pyrimidine-pyrimidones) (Ikehata et al., 2008; Rünger, 2008; Tewari et al., 2012). Both CPDs and 6,4-photoproducts are associated with melanoma oncogenesis. Cyclobutane pyrimidine dimer (CPD) formation from UVB exposure has been suggested as a strong selective pressure for dark pigmentation, but UVA was not considered a source of CPD or an important factor in the evolution of skin pigmentation (Jablonski and Chaplin, 2010). Based on these results UVA may be more carcinogenic than was previously assumed. This is especially important in evolutionary contexts because UVA is more abundant than UVB, increasingly so at higher latitudes, and may have played a more significant role in the evolution of skin pigmentation than was previously thought.

Skin cancer as a selective force in skin pigmentation

Skin cancer has been dismissed or downplayed as a selective force in the evolution of skin pigmentation because it is argued to affect individuals as their
TABLE 2. Life Expectancy at birth, age 15, and age 45 in 5 Unacculturated Hunting and Gathering Societies and USA in 2008

<table>
<thead>
<tr>
<th>Group</th>
<th>$e_0$</th>
<th>$e_{15}$</th>
<th>$e_{45}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kung</td>
<td>36</td>
<td>38.1</td>
<td>19.7</td>
</tr>
<tr>
<td>Hadza</td>
<td>34</td>
<td>42.5</td>
<td>24.2</td>
</tr>
<tr>
<td>Hwi</td>
<td>27</td>
<td>32.5</td>
<td>17.9</td>
</tr>
<tr>
<td>Ache</td>
<td>37</td>
<td>38.5</td>
<td>21.1</td>
</tr>
<tr>
<td>Agta</td>
<td>21</td>
<td>28.6</td>
<td>13.7</td>
</tr>
<tr>
<td>USA 2008</td>
<td>78.1</td>
<td>63.8</td>
<td>35.5</td>
</tr>
</tbody>
</table>

Source: Kaplan and Gurven (1997; p 327, Table 2) for tribal groups and CDC (http://www.cdc.gov/nchs/data/nvss/nvars61/nvars61_03.pdf; p 4, Table B) for USA.

Longevity among hunter-gatherers. While it is abundantly clear that human life expectancy at birth has increased dramatically since 1900 (Finch, 2012; Burger et al., 2012) humans, prior to that time, were a long-lived species. There is good reason to believe that human longevity has not changed sufficiently in recent times such that early death in the context of evolved longevity would have no effect on fitness. Kaplan and Gurven's (2007) comparative sample of longevity among contemporary hunter-gatherers and horticulturalists (with a strong dependence on foraging) is the largest of its kind to date. They examined 19 different subsistence societies including 5 hunter-gatherer groups with little contact, 4...
different forager-horticulturalists, and 9 acculturated
hunter-gatherer groups. Claims about the recent ex-
tension of longevity and corresponding belief in short lon-
gevity of hunter-gatherers is often mistakenly
misrepresented by life expectancy at birth estimates (øe),
which range from 21 to 37 years among uncontacted
hunter-gatherers (Kaplan and Gurven, 2007; p 326).
However, if one examines life expectancy at age— the
average number of additional years of life—among tradi-
tional hunter-gatherers, 64% reach age 45 (Table 2).
And, on average, traditional hunter-gatherers who reach
age 45 will have two decades of life left (Kaplan and
conclude, “Post-reproductive longevity is a robust feature
of hunter-gatherers and of the life cycle of Homo sapi-
ens. Survivorship to grandparental age is achieved by
over two-thirds of people who reach sexual maturity and
can last an average of 20 years” (see also Finch, 2010; p
1723). More to the point, Levitis et al. (2013) developed
“Postreproductive Representation,” a measure ultimately
demonstrating that postreproductive life is a derived
evolutionary trait of humans and not a consequence of
modern increases in human lifespan. It is defined as “as
that proportion of adult-years lived which are post-
fertile” (2013; p 68). The figures for humans range from
0.315 to 0.5 in tribal populations and up to 0.76 in mod-
ern populations. The corresponding figure for wild
chimps is 0.018.

One could argue that contemporary hunter-gatherers
are not representative of prehistoric populations because
paleodemographic estimates of longevity based on
human remains generally show significantly lower survi-
vorship than those attained by Kaplan and Gurven. As
noted by Kaplan and Gurven (2007; p 334) paleodemo-
graphic estimates are beset by a variety of problems
such as sampling biases (e.g., Wood et al., 1992) that
typically lead to lower estimates than documented in
contemporary hunter-gatherers. And it is not unreason-
able to argue that contemporary hunter-gathers exist in
a more difficult epidemiological landscape because of
STDs, tuberculosis, and other diseases that have
recently entered their populations through contact with
more complex societies. More to the point, there is little
evidence that the subsistence landscapes in the past
were significantly different than the landscapes of con-
temporary hunter-gatherers. The environment of current
hunter-gatherers sampled by Kaplan and Gurven
(Hadza, Ache, Kung, Hiwi, and Agta) ranges from desert
to savannah to tropical forest locations which the first
humans occupied, suggesting that their results apply to
a moderately wide range of low-latitude, evolutionarily
relevant environments.

**Longevity and individual and kin effects.** The
obvious question one must answer is that given that lon-
gevity is not an artifact of modern conditions what can
humans do to enhance their reproductive success after
direct reproduction is no longer possible or sharply
diminished? The short answer to this question is the
enhancement of inclusive fitness through one’s positive
effects on the reproductive success of kin (Hamilton,
1964). There is now considerable evidence that humans
behave in ways to enhance the fitness of close kin
(Cronk, 1991; Voland, 1998; Barrett et al., 2002; Gaulin
and McBurney, 2003; Hames, in preparation). This is
especially critical for females because of menopause,
whereby they lose the ability to reproduce directly
between the ages of 40 and 45 even though they will live
another two decades, on average. We will first examine
this issue from a female perspective and then turn to
males.

As noted by Hawkes et al. (1997), the problem of
female longevity in the context of menopause was first
considered by G. C. Williams (1957), who argued that
the riddle of human menopause could be solved through
investment in children or grand offspring. A particular
version of this view became known as the “grandmother
hypothesis” that argues that grandmothers enhanced
their inclusive fitness by either enhancing the fertility of
daughters or the survivorship of grand offspring
(Hawkes et al., 1997) through food transfers, child care
and other acts of assistance. In a modified version of
this hypothesis known as the “mother hypothesis” Pecccei
(2001) argues that since a woman’s last child is not fully
independent of parental investment for about 16 to 18
years, the survivorship of a woman’s last child would be
diminished if she were not to live long enough to
assure her children a lifetime of food transfers. Compari-
tative data on economic independence (when food produc-
tion is equal to or greater than consumption) shows Pecccei
(2001) is reasonably accurate (Kaplan, 1997; Kramer
2005).

Over the last 10 years or so considerable evidence has
accumulated to support the grandmother hypothesis,
showing that postreproductive women are able to
enhance their inclusive fitness through such means as
increasing the fertility of daughters and ensuring the
survivorship of grandoffspring. This research highlights
the adaptive value of longevity-inclusive fitness effects
even when direct reproduction ceases. Sear and Mace
(2008) reviewed 45 studies investigating the presence of
mostly senior kin (mothers, fathers, grandparents, older
siblings) on the fertility of reproductive-aged women and
the survivorship of their children. The presence of a
maternal grandmother was associated with an increase
in her grandchildren’s probability of surviving in 69% of
the cases (9 of 13), and for paternal grandmothers it was
55% (9 of 17 studies) (2008; Table 3, p 8).

It is consistently shown that since males do not go
through menopause and marry polygynously or engage in
serial monogamy they continue to engage in direct repro-
duction until near the end of their lives. For example,
among the polygynous Yanomamó, male fertility peaks
between ages 25 and 55 and steadily declines thereafter
(Melancon, 1982; p 175, Fig. 9.2). Furthermore, polygyny
is more frequently allowed by foragers than in other eco-
nomic formations (Marlowe, 2003). Consequently, male
reproductive careers through polygyny or serial monog-
amy can last decades beyond that of females (See Joseph-
son, 2002 for a cross-cultural survey).

While there are numerous studies showing how post-
menopausal women can enhance their direct fitness by
continuing to survive and invest in current dependent
offspring or grandoffspring there are few showing the
same for men. However, recent research by Scelza (2010)
shows that fathers play important social roles for their
sons among Martu hunter-gatherers. Her Martu data
show that men who have fathers are likely to go through
ritual initiation to manhood earlier (a prerequisite for
marriage) and marry earlier, and have higher fertility at
age 30 compared with males who lacked living fathers
who could sponsor them and therefore went through ini-
tiation later.
We have shown that human longevity is not a recent phenomenon and that postreproductive humans can enhance their inclusive fitness by increasing the survivorship and fertility of offspring and close kin. Therefore, we believe that the evidence cited above casts serious doubts on claims that skin coloration’s protective value is not an adaptation for the prevention of relatively late onset skin cancer.

Modern rates of skin cancer and tests of adaptive hypotheses

Jablonski and Chaplin (2010:2) acknowledge the value of dark skin in protecting against skin cancer in the following: “Skin cancers are mostly a consequence of modern human migrations and resulting mismatches between skin pigmentation and geography or lifestyle.”

We agree with their mismatch hypothesis. The key point they make is that dark skin protects against skin cancers. To understand the value of dark skin, we can think of no better natural experiment (Beall and Steegman, 2000; p 201) than to examine skin cancer rates of those whose ancestral homelands were in low UV environments but who currently grew up and live in higher UV environments. If dark skin coloration is a protective response to skin cancer then light skinned individuals should show greater skin cancer rates than their dark-skinned ancestors who continue to live in their aboriginal homelands.

Skin cancer incidence rates for darkly pigmented populations living at low latitudes are few. This is due in part to the lower incidence rates in these groups relative to lightly pigmented populations—since the latter have higher mortality rates from skin cancer, research is focused on combating this issue. The limited data suggest that both NMSC and CMM are present in equatorial populations (Camain et al., 1972; Soeripto et al., 1977; Yakubu and Mabogunje, 1995). Yakubu and Mabogunje (1995) tracked incidence in a Nigerian sample (n = 721) over an 11-year period, including comparative data in their analysis. The authors report 24% of subjects developed skin cancer on the head and neck with 85% of those cases being SCC—their ages ranged from 4 months to 75 years, with a median age of 39 years. While BCC normally dominates cancer of the head and neck, this does not appear to be the case for this Nigerian sample. Camain et al. (1972) report that SCC was the most frequent type of skin cancer in their sample from Senegal, though most tumors presented on the lower limbs rather than the head and neck. Soeripto et al. (1977) report skin cancer frequency in Indonesians, finding that skin cancer accounted for 17.6% of tumors in males and 9.6% in females—though the authors note that the value for females is suppressed due to high frequencies of genital tumors. Some have argued that disparate skin cancer rates between African albinos and non-albinos support skin cancer as a selective pressure for pigmentation (e.g., Lomas et al., 2012). Body modification occurs in contemporary human cultures and is likely not a novel behavior in humans. For example, Sosis et al. (1997; p 242) show that tattooing and scarification occur in over half of the societies in the HRAF probability sample. Because modification of the skin—both intentional and accidental—can decrease the amount of melanin present at the site of injury (Chadwick et al., 2012), this suggests the opportunity for CMM to be a selective agent associated with body modification and may help explain oncogenesis in skin not normally subjected to UVR. This may also support the claim that skin pigmentation evolved in response to infection, as more darkly pigmented skin is more resilient to this stress.

Further, Moan et al. (2008) argue that vitamin D3 has a protective effect on cancers—including skin cancers. The negative relationship between latitude and CMM is well established. The relationship between skin cancer death rate and latitude, however, is more complicated. The authors evaluated skin cancer incidence and death rate in individuals of European descent living in Australia, New Zealand, Sweden, Denmark, Norway, and the UK (Moan et al., 2008). As an additional control, the authors only included individuals that either never tan and always burn (type I skin), or those who almost always burn and occasionally tan (type II skin). Not surprisingly, subjects living in Australia and New Zealand were affected by CMM at a higher rate than were subjects living in Europe. But incidence rates relative to death rates of Australian and New Zealand subjects
were actually lower than subjects living in Europe. This suggests that while CMM incidence rates are higher in Australia and New Zealand, individuals who develop CMM at higher latitudes have higher mortality. The authors owe this relationship in part to the greater availability of UVB-induced vitamin D3 synthesis. These samples share common ancestries and had lightly pigmented skin, providing some degree of control, but variation in exposure to carcinogens, diet, and healthcare cannot be ruled out as possible factors. Darkly pigmented individuals tend to present with thicker tumors and suffer from faster disease progression than lightly pigmented individuals (Johnson et al., 2003; Gloster and Neal, 2006; Haynes et al., 2008; Sneyd and Cox, 2009; Wu et al., 2011), which may be due to lower levels of vitamin D3 though delayed diagnosis and differential access to healthcare may also be at play.

Muirne models support the relationship between vitamin D3 and skin cancer. BCC, SCC, and CMM all have the vitamin D (1,25-dihydroxyvitamin D3) receptor—VDR—suggesting that vitamin D3 plays some role in development and progression of skin cancer (Bikle, 2012). Mice lacking the VDR develop skin tumors after exposure to a carcinogen (Zinser et al., 2002) or UVB (Ellison et al., 2008). Other murine models have demonstrated that vitamin D3 suppresses Hedgehog (HH) proliferation and signaling responsible for BCC, independent of the VDR (Tang et al., 2011). Additionally, topi¬cal application of vitamin D3 to cancerous lesions also slows HH proliferation and signaling. Bikle (2012) argues that in addition to controlling proliferation and differ¬entiation of HH, the wnt/β-catenin pathways, immunoregulation, and DNA repair are also likely medi¬ated by vitamin D3. Higher levels of D3 increase repair capacity. Complicating matters further, folate also repairs DNA damage, with capacity for DNA repair being highest with increased folate (Williams et al., 2012). High UV-induced D3 might share a negative relation¬ship with folate, all things being equal. If D3 and folate are low, then DNA repair is seriously hindered. So disentangling the relationship between D3, folate, and skin cancer complicates matters, but does not necessi¬tate rejecting the skin cancer hypothesis.

CONCLUSIONS

We have presented several lines of evidence in support of skin cancer as a selective agent in skin pigmentation. Rejected by some due to its perceived delayed age at onset, data now support CMM as a disorder affecting individuals throughout their reproductive years. It is also now clear that longevity has a deeper evolutionary history than once assumed and that kin selection can have a positive effect on fitness. Though less deadly, the late-developing NMSCs could be selective when viewed through the lens of life history theory and kin selection. The evidence for epigenetic change provides a model demonstrating the adaptive value of dark skin in high UVR environments. Epigenetic change can produce comparatively rapid changes in phenotype in response to environmental cues and is consistent with claims of skin pigmentation as a labile trait. Many issues remain, how¬ever, as future research must disentangle the relation¬ships between UVR, skin cancer, skin damage, barrier functions, vitamin D3, and folate. Research on the evolu¬tion of skin pigmentation in groups who underwent some degree of selection for depigmentation would offer interesting perspectives on this matter—particularly in populations living at high altitudes where UVR intensity is high.

ACKNOWLEDGMENTS

The authors thank the anonymous reviewers for useful commentary on earlier versions of this article.

LITERATURE CITED


Rünger TM. 2008. CeT transition mutations are not solely UVB-signature mutations, because they are also generated by UVA. J Invest Dermatol 128:2138–2140.


