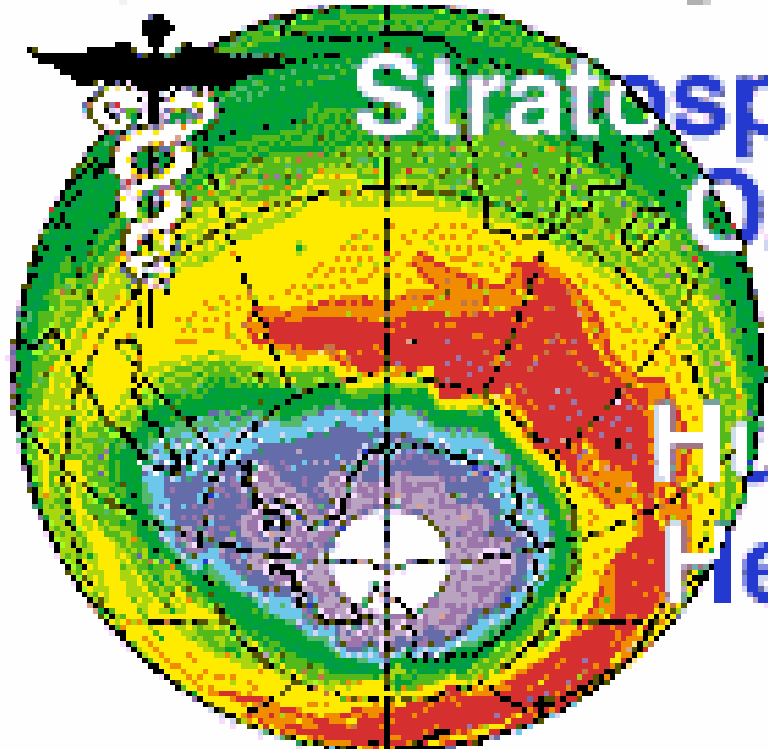
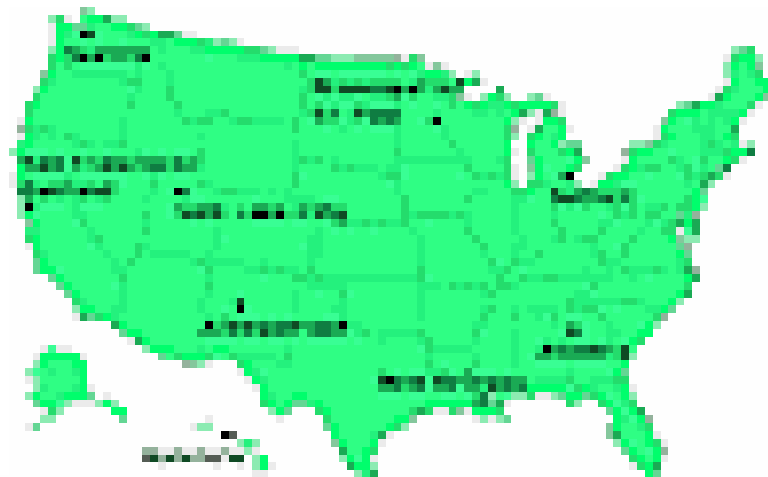


Breakup Of The Ward Ice Shelf Antarctica 2004





Stratospheric Ozone and Human Health



<http://sedac.ciesin.org/ozone/docs/uvd-home.html>

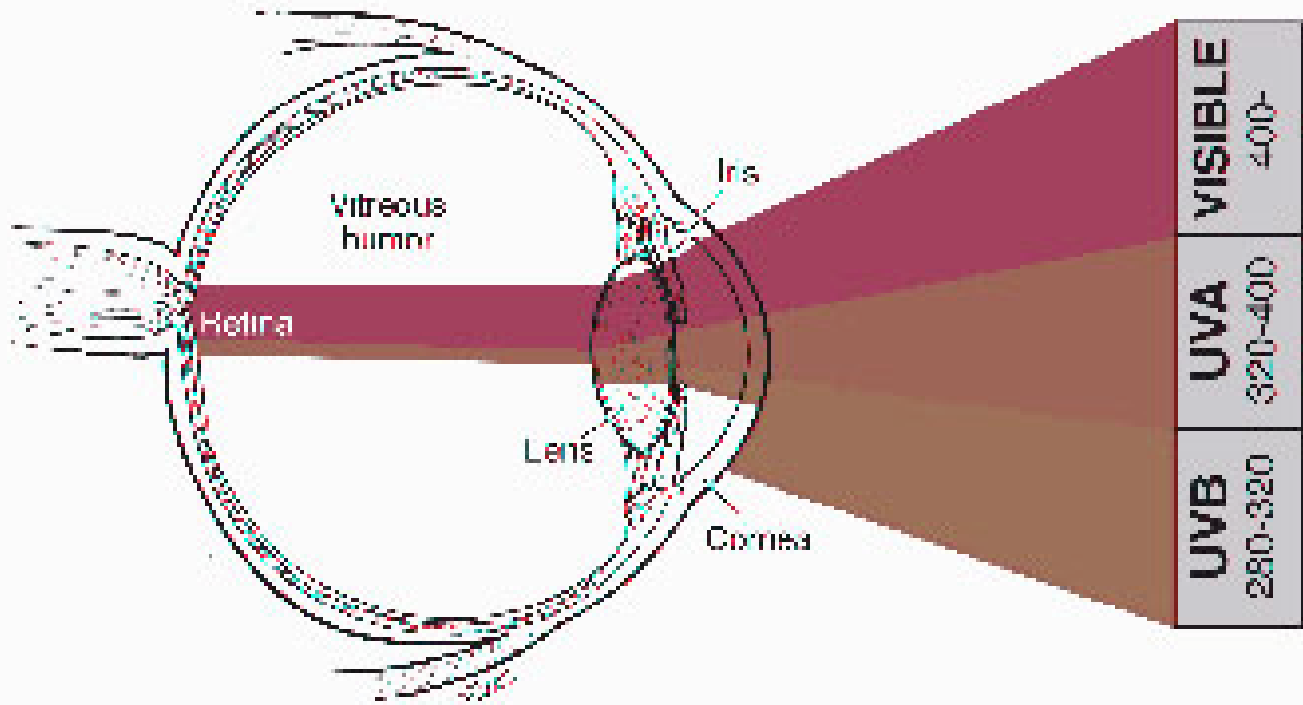
Medical Ecology Of
Stratospheric Ozone Depletion:
Impacts on the Human Condition

Photo Aging



Some 20 million people worldwide are currently blind as a result of cataracts. Of these, WHO estimates that as many as 20% may be due to UV exposure. Experts believe that each 1% sustained decrease in stratospheric ozone would result in an increase of 0.5% in the number of cataracts caused by solar UV.





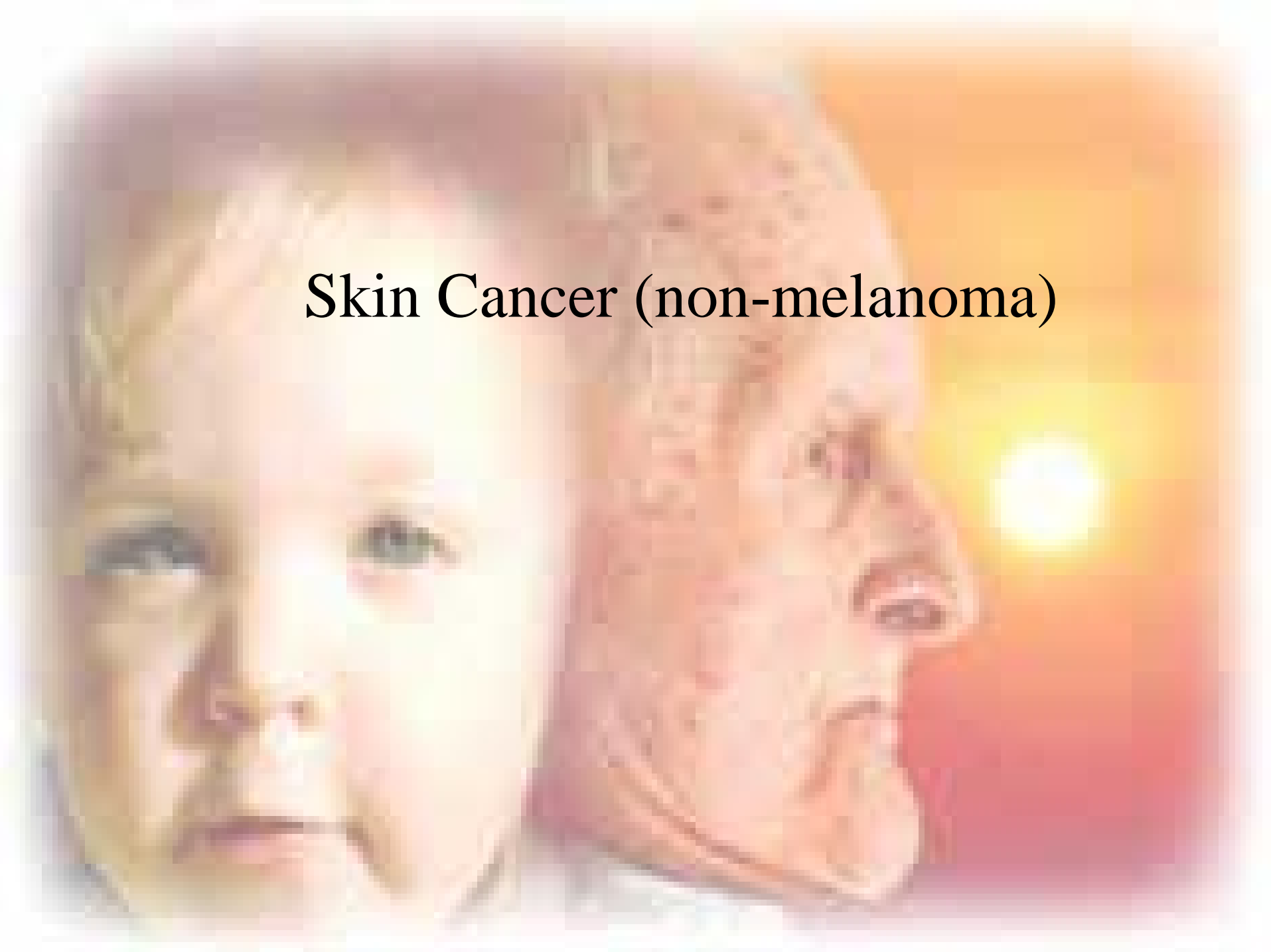
UVB	280-320
UVA	320-400
VISIBLE	400-700



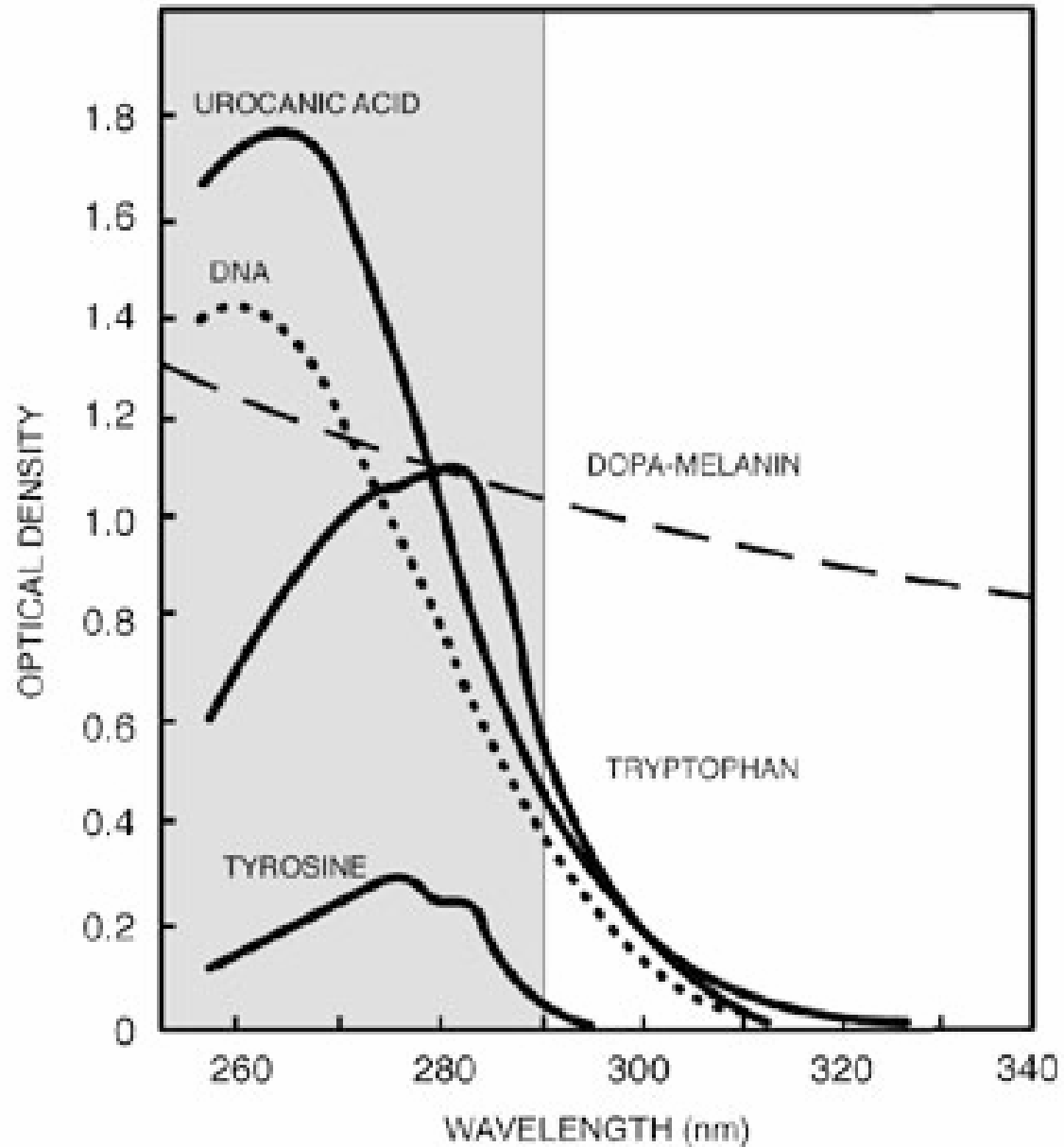
UVB Solar Radiation And Skin Cancer Risk

UVC - 100 to 290 nm
UVB - 290 to 320 nm
UVA - 320 to 400 nm

Skin Cancer (non-melanoma)



Absorption spectra for a few selected compounds



Examples of Non-melanoma Skin cancer





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American Academy of Dermatology Urges the Public to Practice Sun Safety-Long-Standing Studies Support UVB Radiation is a Leading Cause of Skin Cancer

SCHAUMBURG, IL (March 15, 2002) – Recent epidemiological studies indirectly linking ultraviolet (UV) exposure to a decrease in breast, colon and other internal cancers relied principally on geographic location as a basis for conjecture and do not firmly establish a link between sunlight per se and variations in cancer risk. Speculative theories that sun exposure somehow has a beneficial effect on internal cancer risk pose a potential threat to individuals who forgo sun protective behaviors in hopes that sunlight, the principal cause of skin cancer, may lower the risk for other forms of cancer.

"Many cancers vary in frequency from one region to another in ways that do not correlate with sun intensity - diet, lifestyle, racial variants, and chemical exposures are all variables," stated dermatologist Fred F. Castrow II, M.D., President of the American Academy of Dermatology (AAD). "It is dangerous to mislead the public that one carcinogen, such as UVB radiation, could prevent another form of cancer."

Sunlight consists of two types of harmful rays – UVA rays and UVB rays. The UVB rays are the sun's burning rays (which are blocked by window glass) and are the primary cause of sunburn and skin cancer. UVA rays (which pass through window glass) penetrate deeper into the dermis, or base layer of the skin. They also contribute to sunburns and skin cancer. Both UVA and UVB rays can cause suppression of the immune system which helps to protect you against the development and spread of skin cancer.

The AAD recommends that everyone practice a comprehensive sun protection program, including avoiding outdoor activities between 10 a.m. and 4 p.m. when the sun's rays are the strongest, seeking shade whenever possible, wearing a broad spectrum sunscreen with a Sun Protection Factor (SPF) of at least 15, and wearing sun-protective clothing.

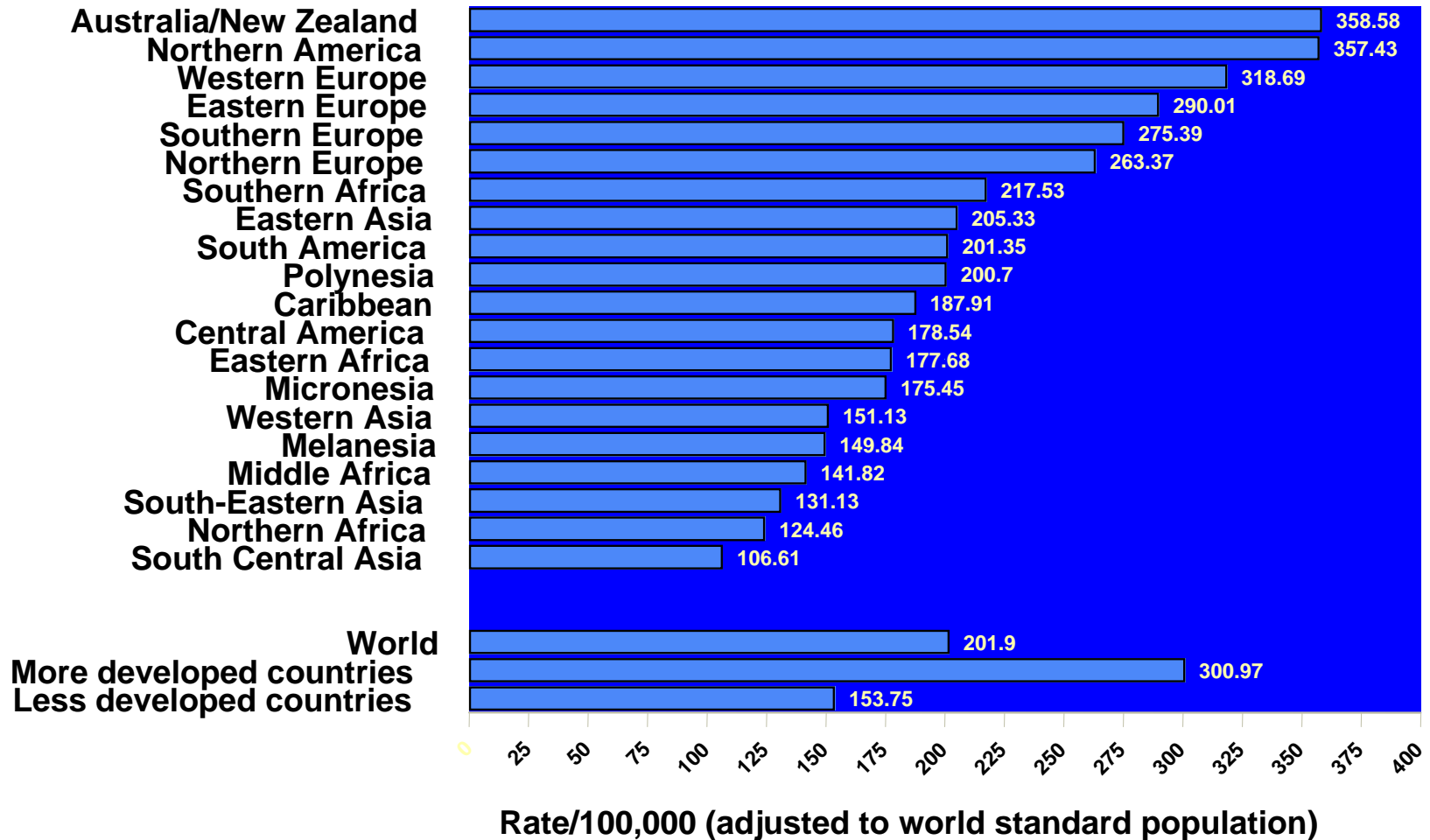
The American Academy of Dermatology, founded in 1938, is the largest, most influential, and most representative of all dermatologic associations. With a membership of over 14,000 dermatologists worldwide, the Academy is committed to: advancing the diagnosis and medical, surgical, and cosmetic treatment of the skin, hair and nails; advocating high standards in clinical practice, education, and research in dermatology; supporting and enhancing patient care for a lifetime of healthier skin. For more information, contact the AAD at 1-888-462-DERM or www.aad.org.

Incidence of Skin Cancers

INCIDENCE

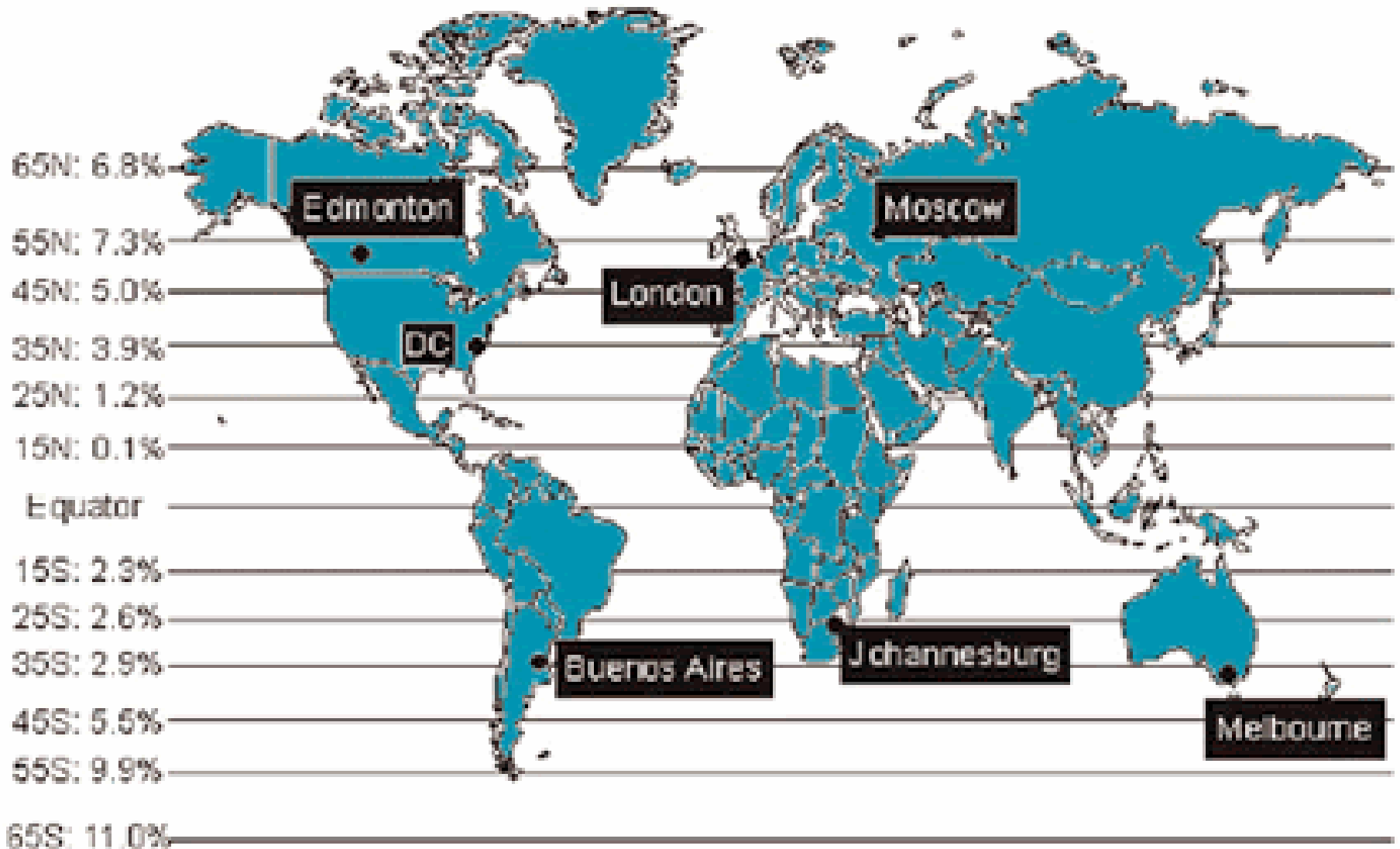
- Excluding carcinoma in situ (noninvasive cancer) of any site except urinary bladder or basal and squamous cell skin cancers
- In 2002 ~ 1,284,900 new cancer cases are expected
 - Men 637,500
 - Women 647,400
- More than 1 million cases of basal and squamous cell skin cancers are expected to be diagnosed this year
- Since 1990, nearly 16 million new cancer cases have been diagnosed

Age-Adjusted Incidence Rates from Cancer in Males by Geographic Region

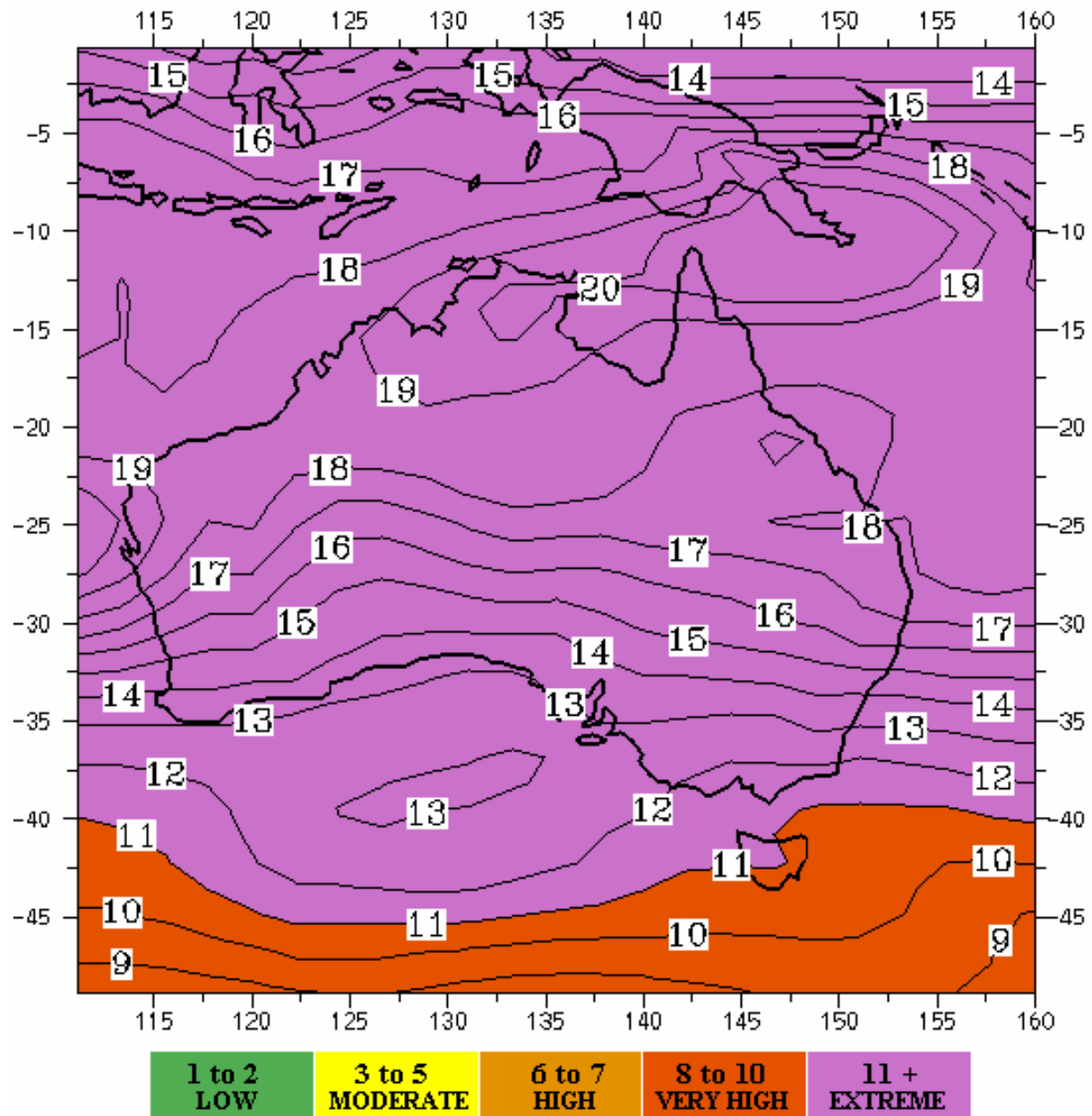


Epidemiology

UV-b Radiation Increases by Latitude



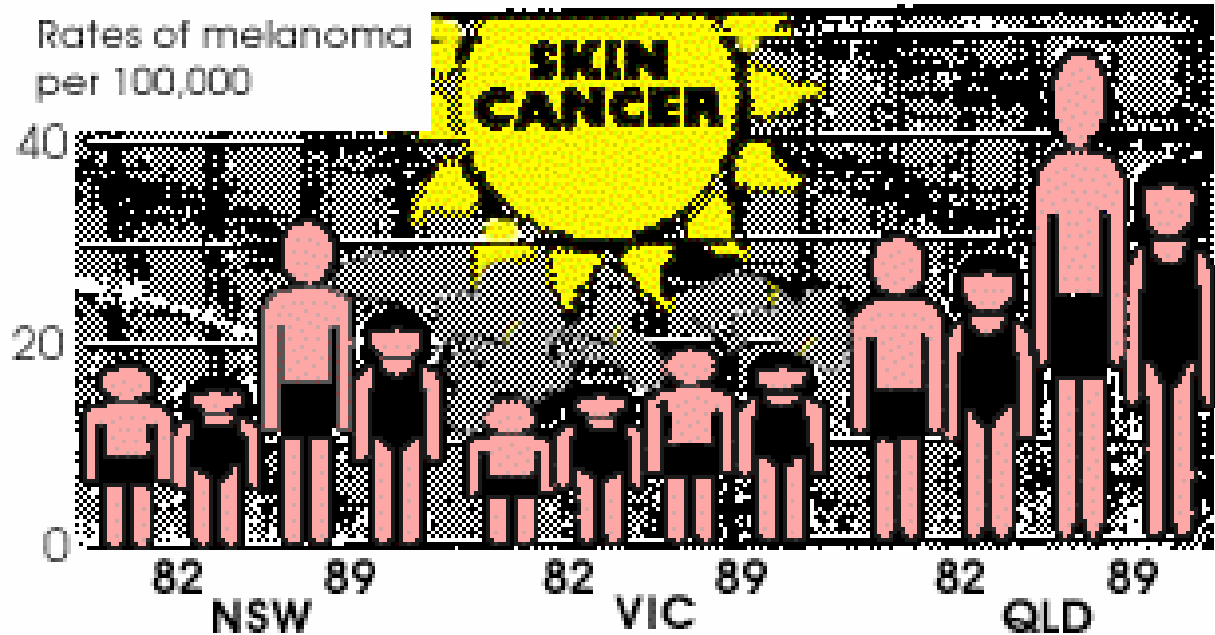
FORECAST CLEAR SKY UV INDEX FOR LOCAL NOON SAT 10 JAN 04





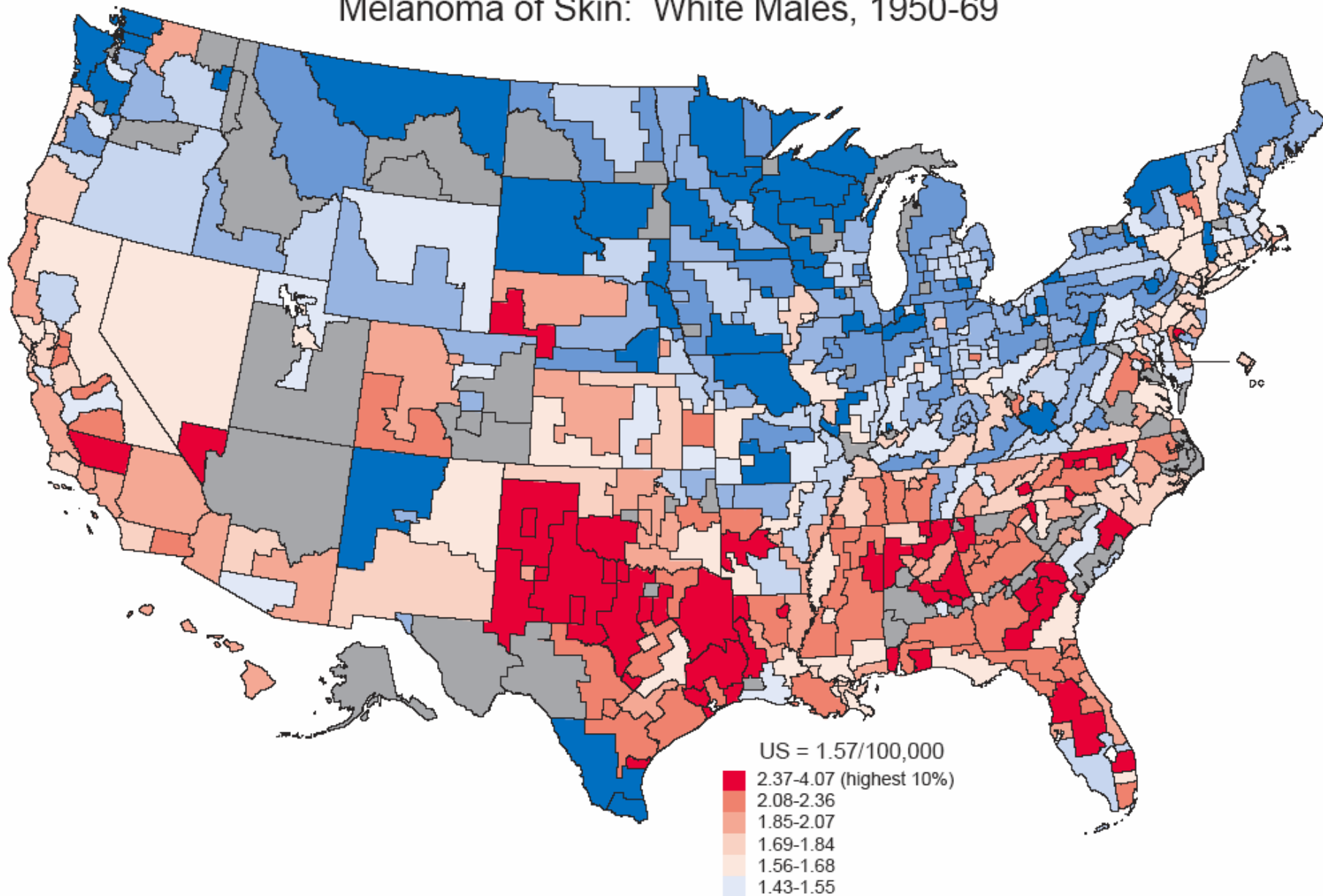
Geography and Skin Cancer

Rates of melanoma per 100,000

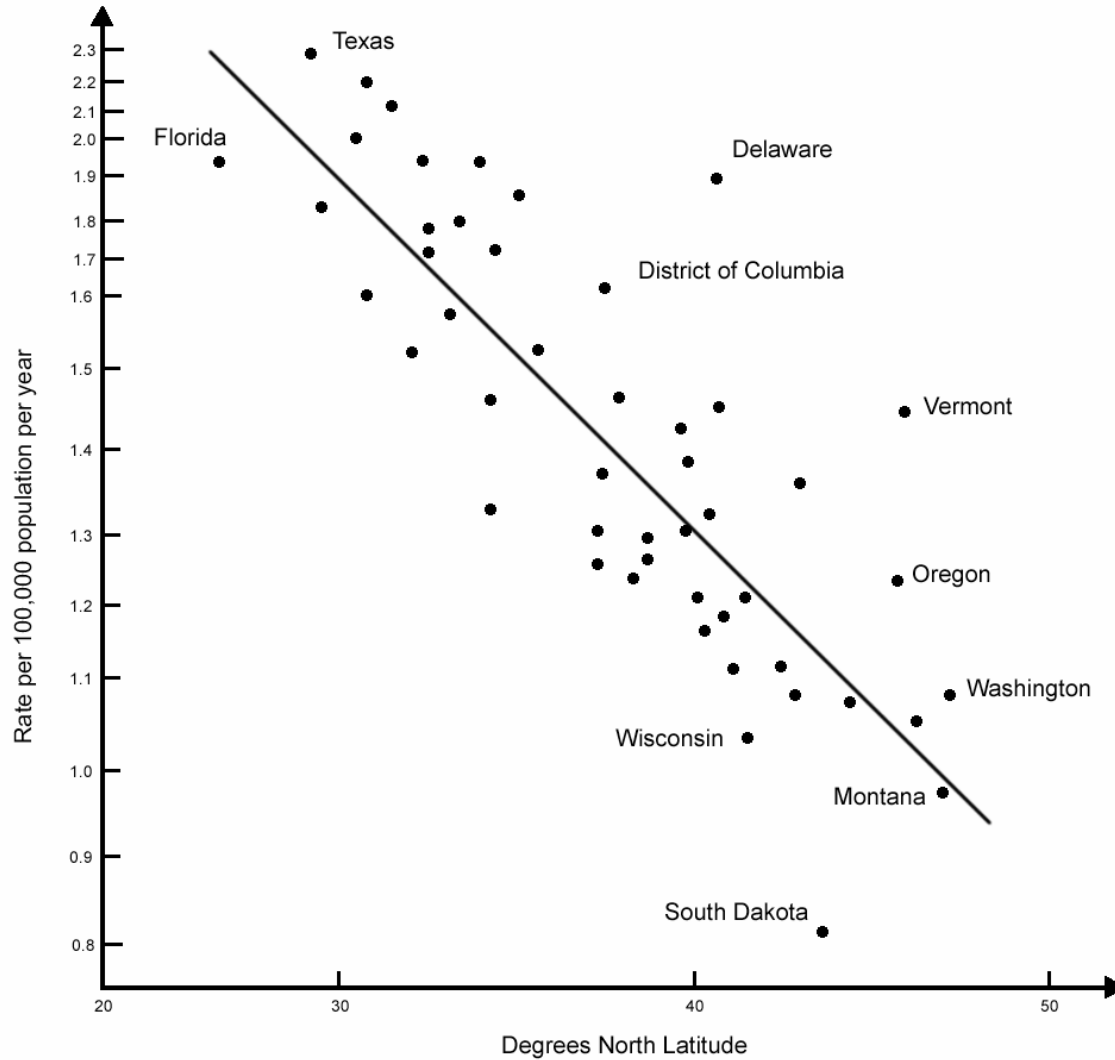


Cancer Mortality Rates by State Economic Area (Age-adjusted 1970 US Population)

Melanoma of Skin: White Males, 1950-69

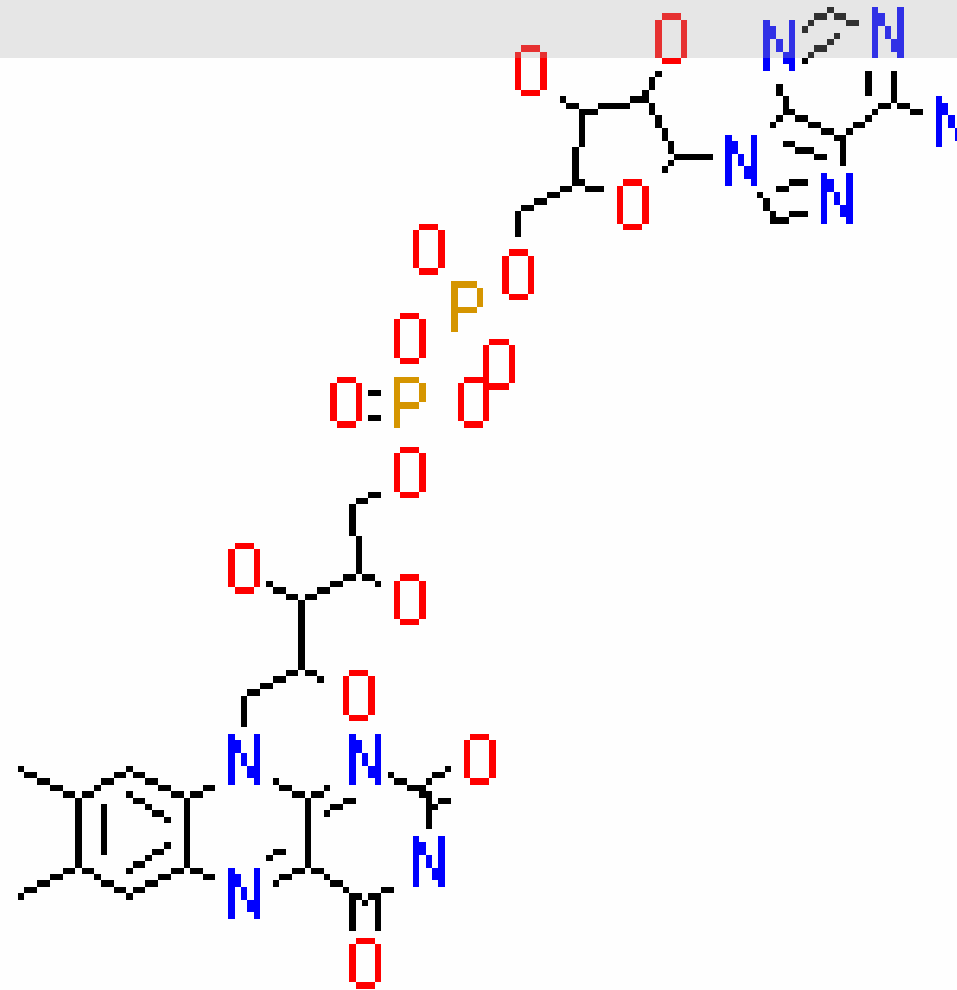


Latitude and Skin Cancer



Molecular Mechanisms

Photolyase substrate





Exposure-specific mutations

<http://www.iarc.fr/p53>

Some mutations have been linked (epidemiological and experimental evidence) to specific exposure and tumor sites:

Tumor	Mutation	Exposure
HCC	G > T (Arg > Ser) at codon 249	HBV, Aflatoxin
Skin cancer (non melanoma)	CC > TT	UV radiations
Lung cancer	G > T (codons 157, 158, 245, 248, 249, 273)	Tobacco smoke (benzo(a)pyrene)
Bladder cancer	G > C	Arylamines (tobacco smoke, chemical dye)

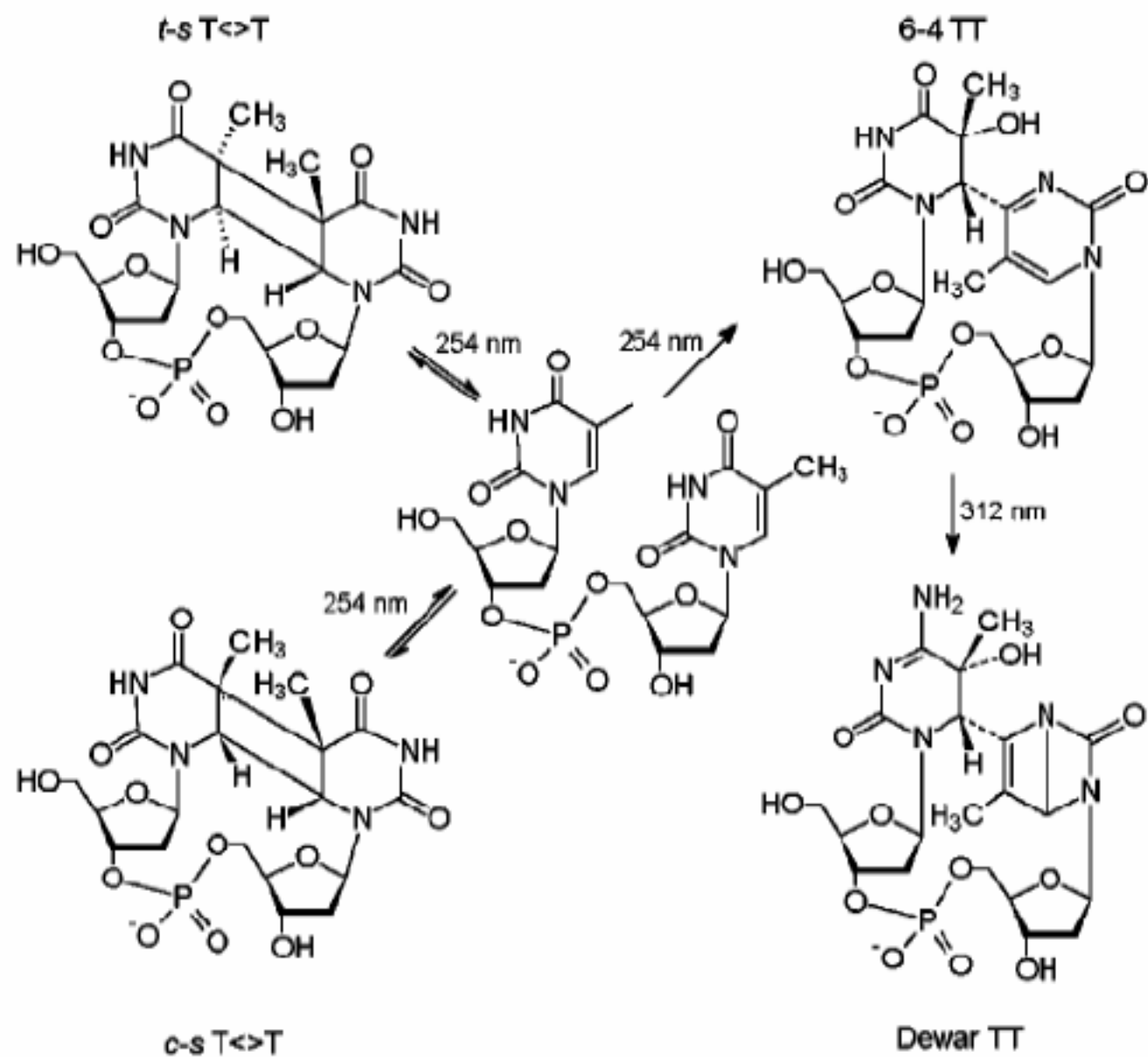
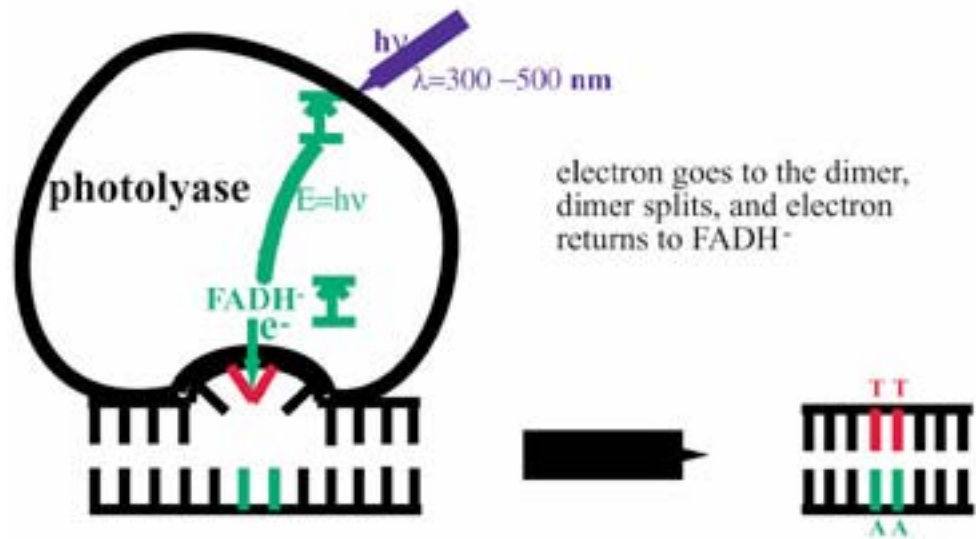
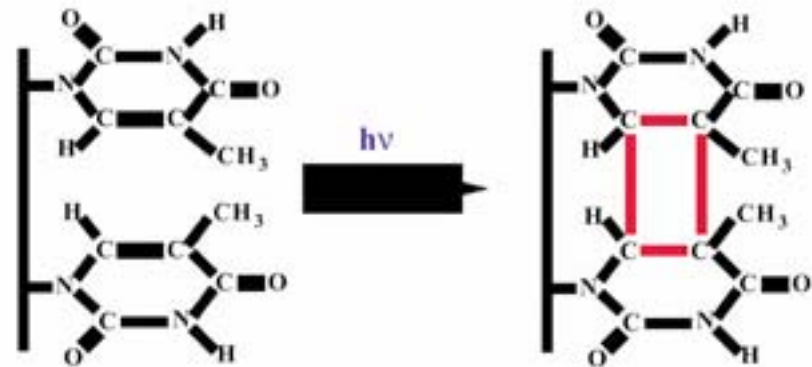
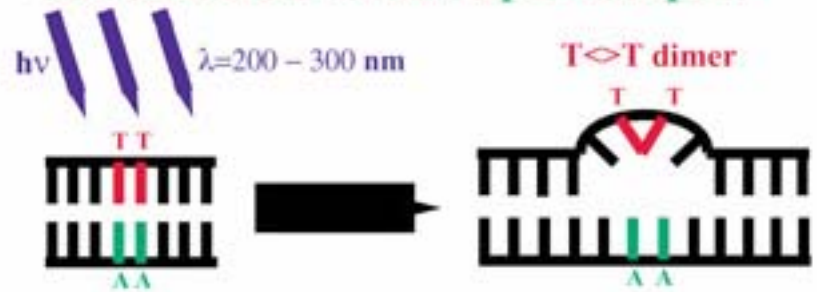
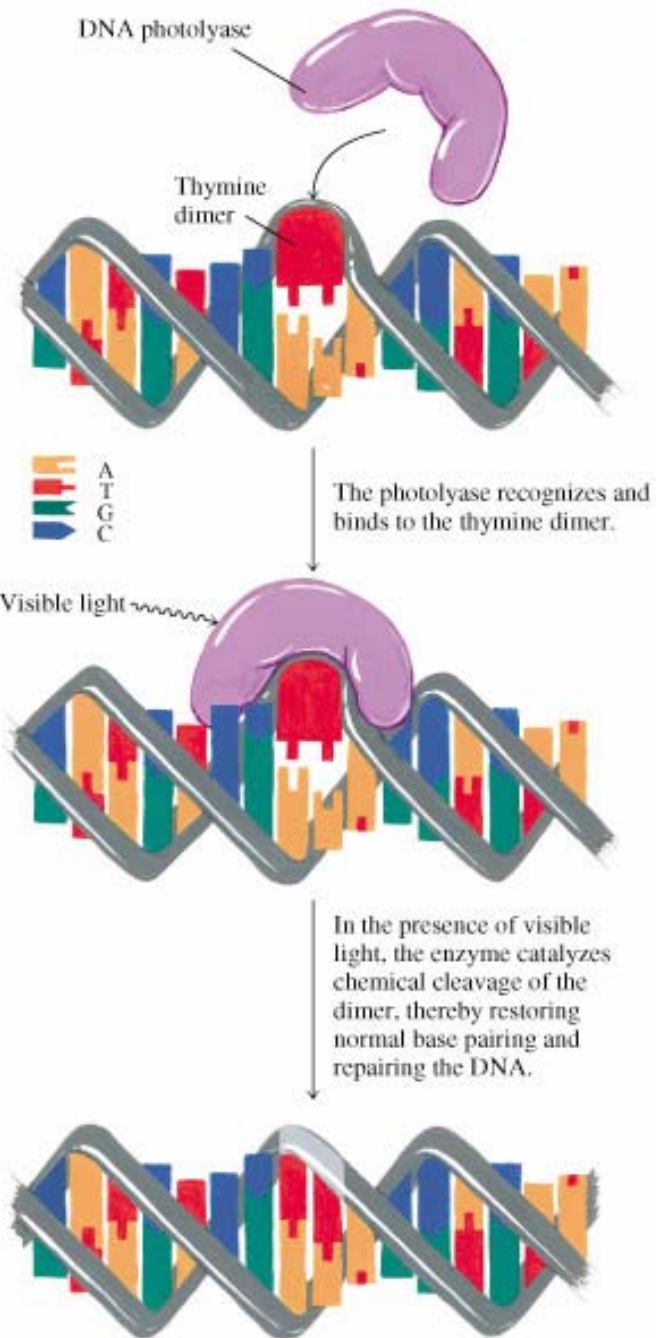


FIG. 1. Structure of the UV-induced thymine dimeric photoproducts.

Introduction to DNA photorepair





Proc Natl Acad Sci U S A. 2000 February 15; 97 (4): 1790–1795

Medical Sciences

Enzyme plus light therapy to repair DNA damage in ultraviolet-B-irradiated human skin

Helger Stege,^{*} Len Roza,[†] Arie A. Vink,[†] Markus Grewe,^{*} Thomas Ruzicka,^{*} Susanne Grether-Beck,^{*} and Jean Krutmann^{*‡}

Topical application of photolyase
reversed CBDs (thymine dimers) by 50 - 60%

Cellular functions of p53:

1. Suppresses progression through the **cell cycle** in response to **DNA damage**, thereby allowing **DNA repair** to occur before replicating the genome; hence, p53 prevents the transmission of damaged genetic information from one cell **generation** to the next
2. Initiates [apoptosis](#) if the damage to the cell is severe (this protects the organism from the *growth of damaged cells*, and so loss of p53 function is a key step in the *neoplastic* cascade).

Mediators of this effect: [bax](#) [[Ref.](#)]

3. Often as a **tumour suppressor**: Mutations in p53 can cause cells to become *oncogenically transformed* and transfection studies have shown that p53 acts as a potent [transdominant tumour suppressor](#), able to **restore** some level of **normal growth** to cancerous cells in vitro (!)

4. p53 is a potent **transcription factor** and once activated, it represses transcription of one set of genes (several of which are involved in stimulating cell growth) while stimulating expression of other genes involved in cell cycle control

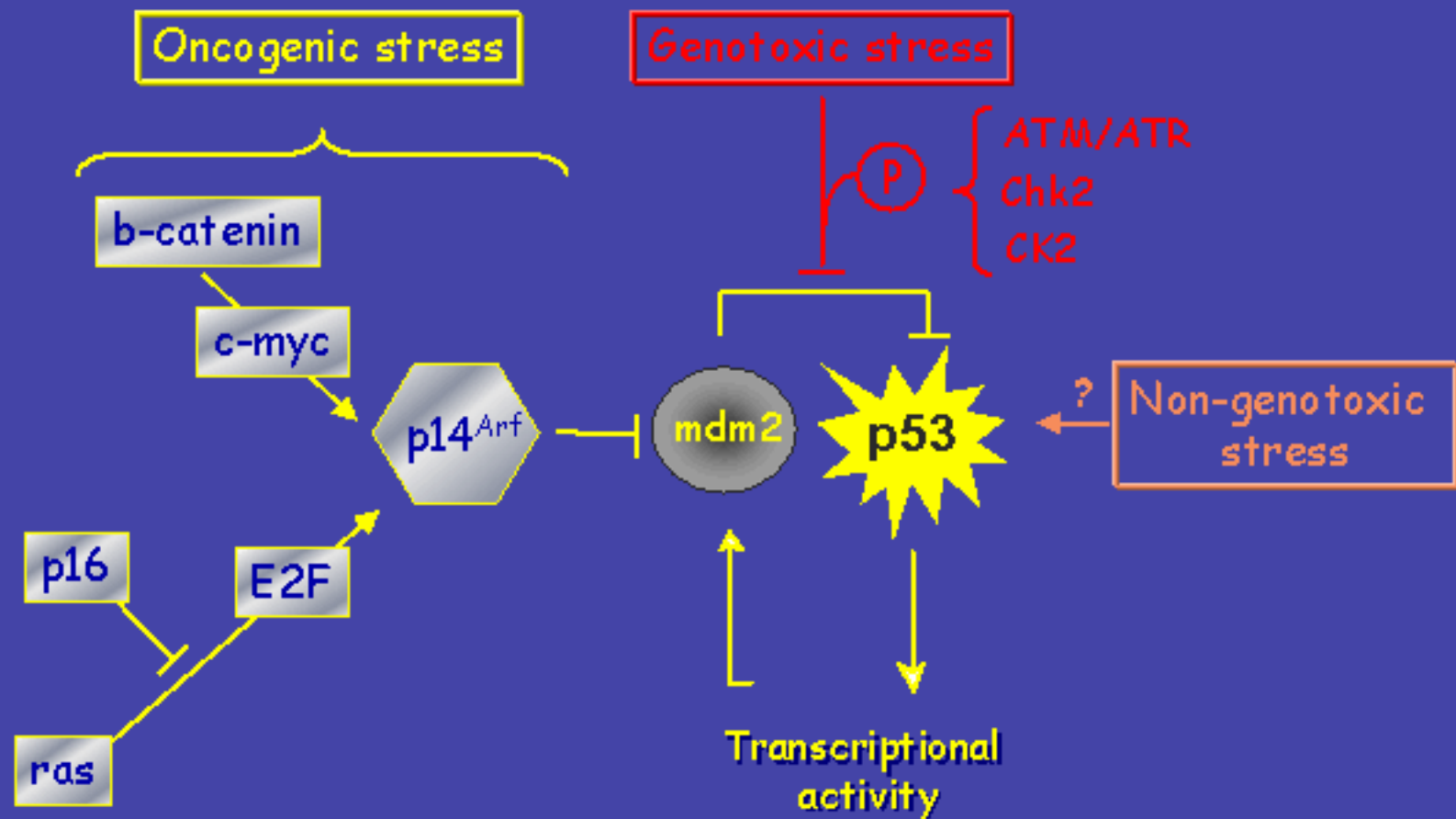
5. [the p53 pathway](#) (picture summarizing the *cellular functions* of p53, 996, by [Hall PA](#) et al.)

<http://bioinformatics.weizmann.ac.il/hotmolecbase/entries/p53.htm>

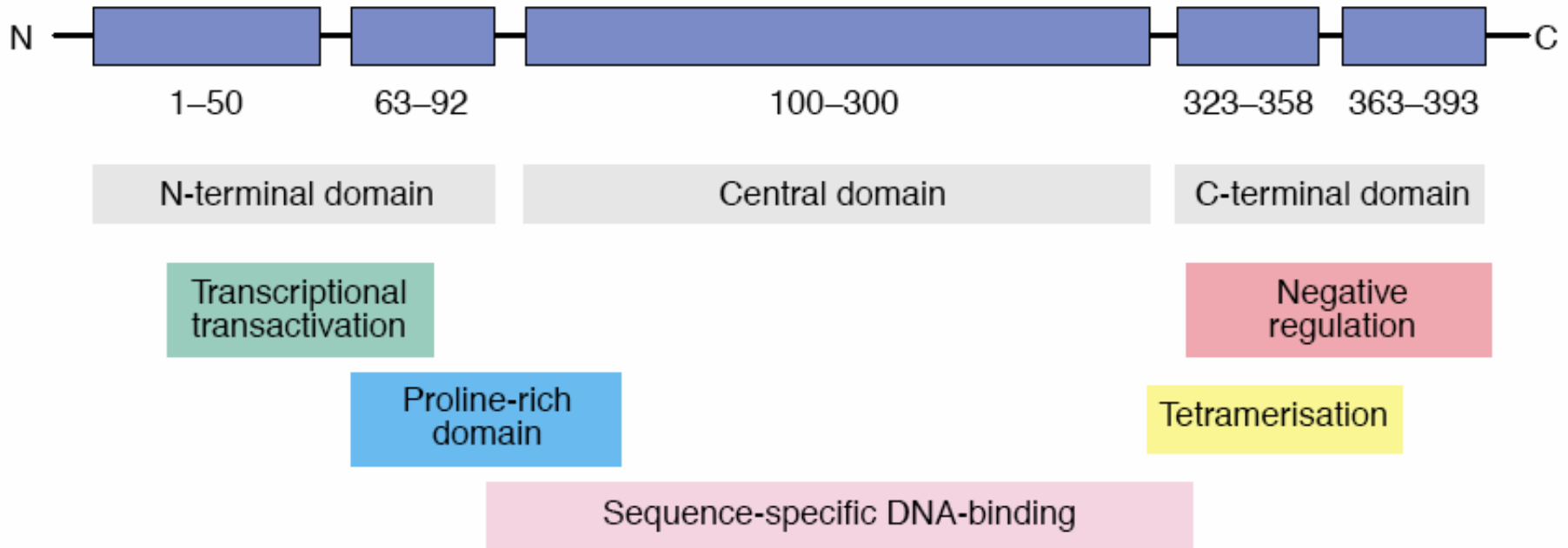


P53 activation pathway

<http://www.iarc.fr/p53>



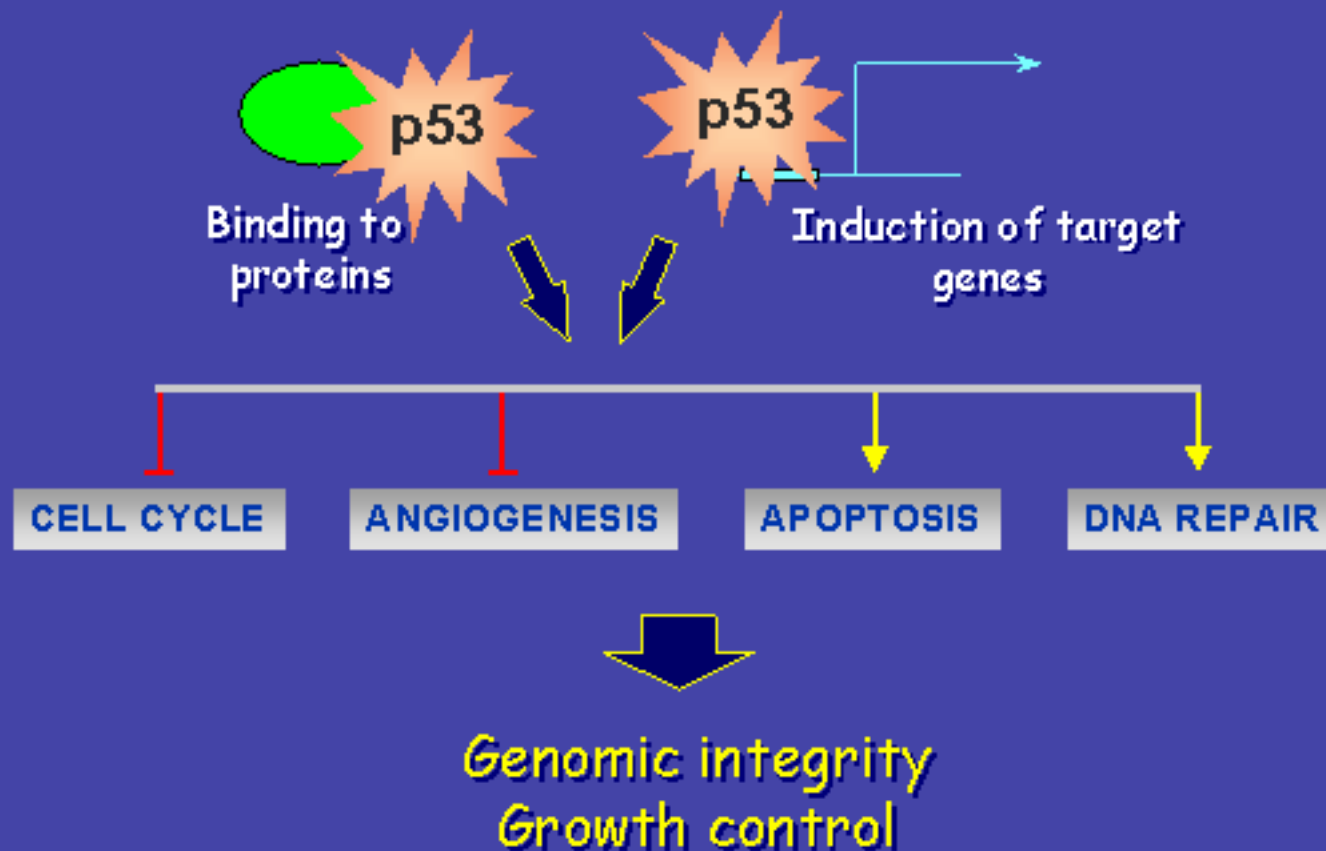
Structure of p53 Protein





P53 acts on several pathways that control cell life and death

<http://www.iarc.fr/p53>



Oncogene. 1999 Jul 22;18(29):4247-53.



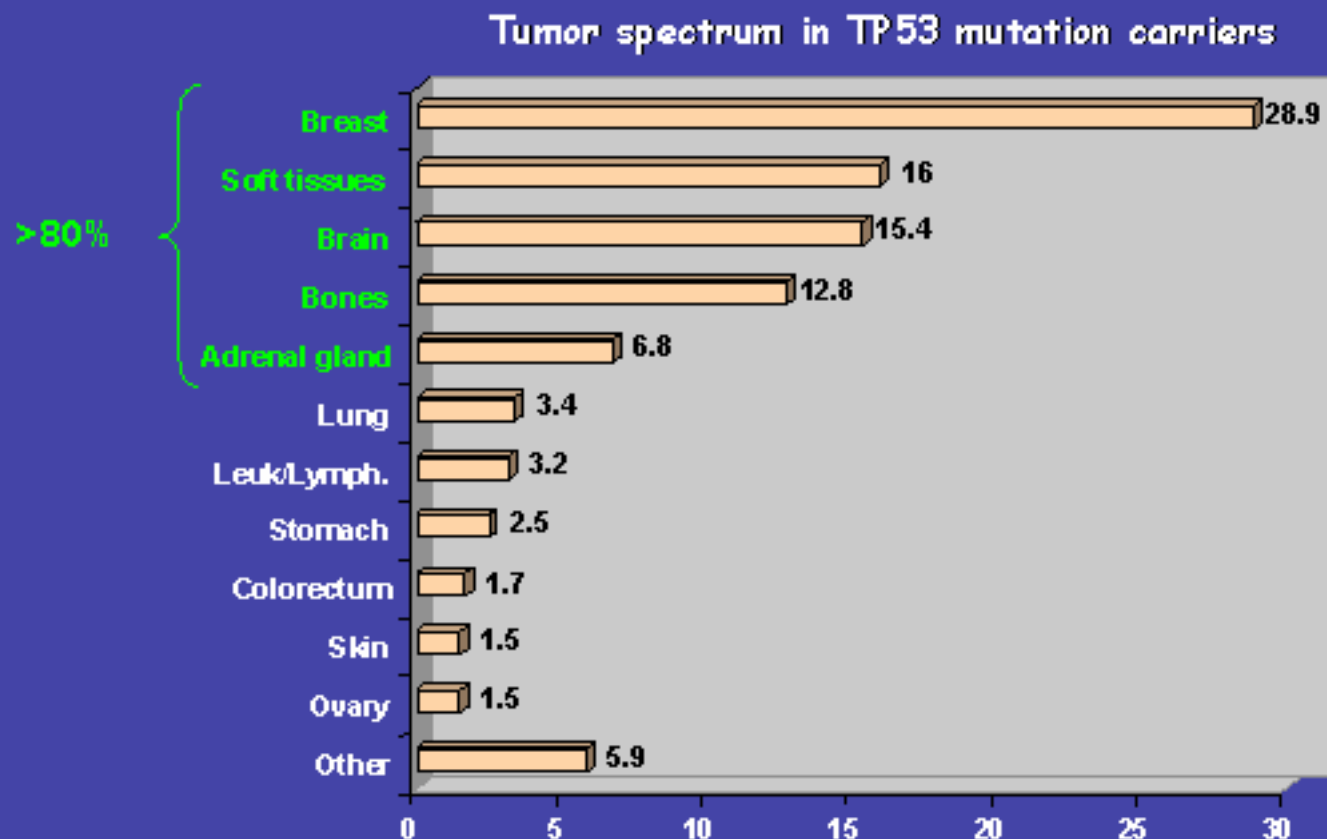
p53 protects against skin cancer induction by UV-B radiation.

Jiang W, Ananthaswamy HN, Muller HK, Kripke ML.



Inherited TP53 mutation and cancer susceptibility

<http://www.iarc.fr/p53>



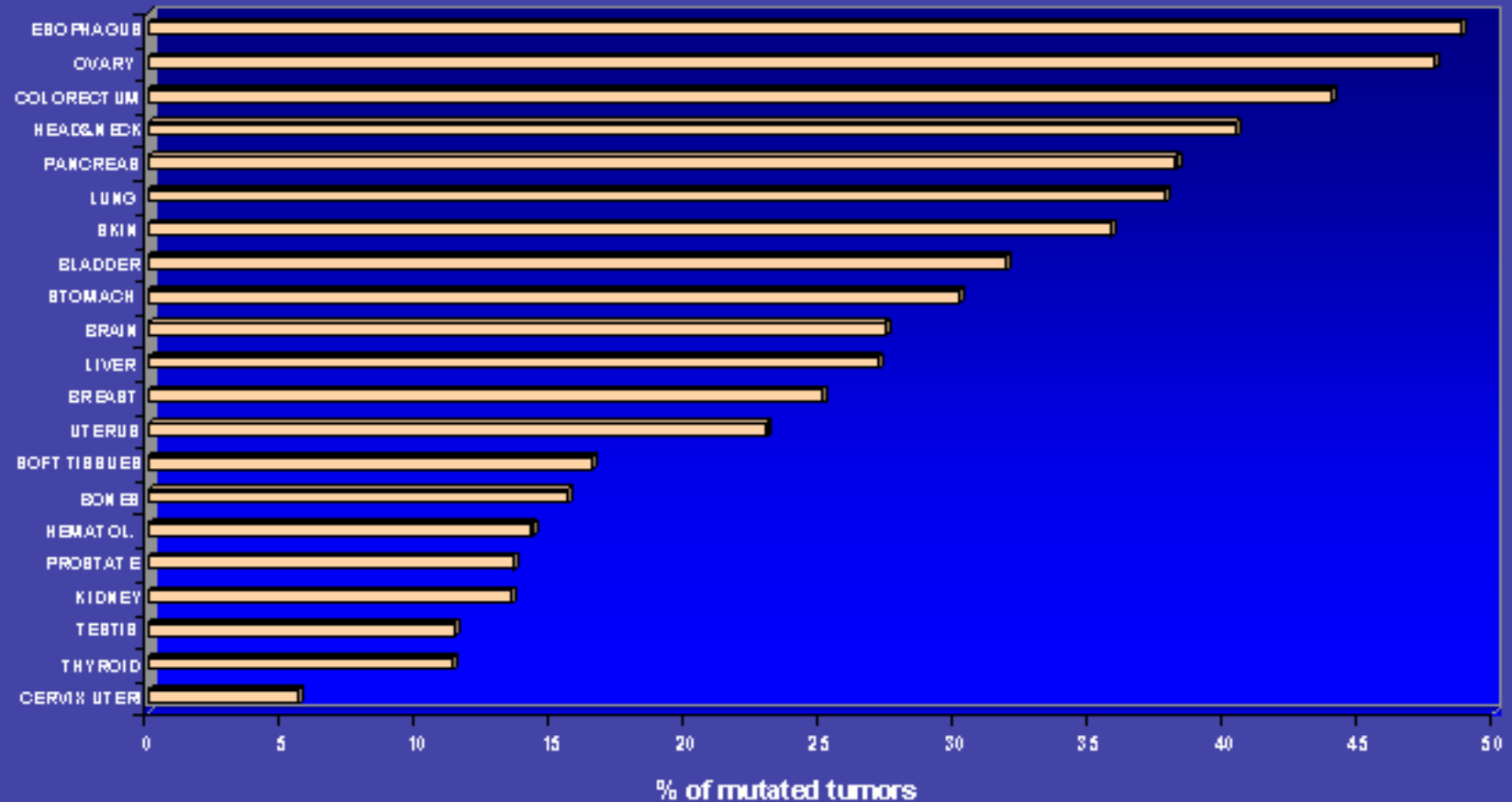
Data from the IARC TP53 germline database (R8, 2003)



TP53 mutation prevalence in sporadic cancers

<http://www.iarc.fr/p53>

IARC TP53 Database, R8



May 2003

Magali Olivier, Pierre Hainaut, IARC



The most frequent mutated codons in p53

<http://www.iarc.fr/p53>



Codon: 175 > 248 > 273 > 282 > 249 > 245 > 220 > 176

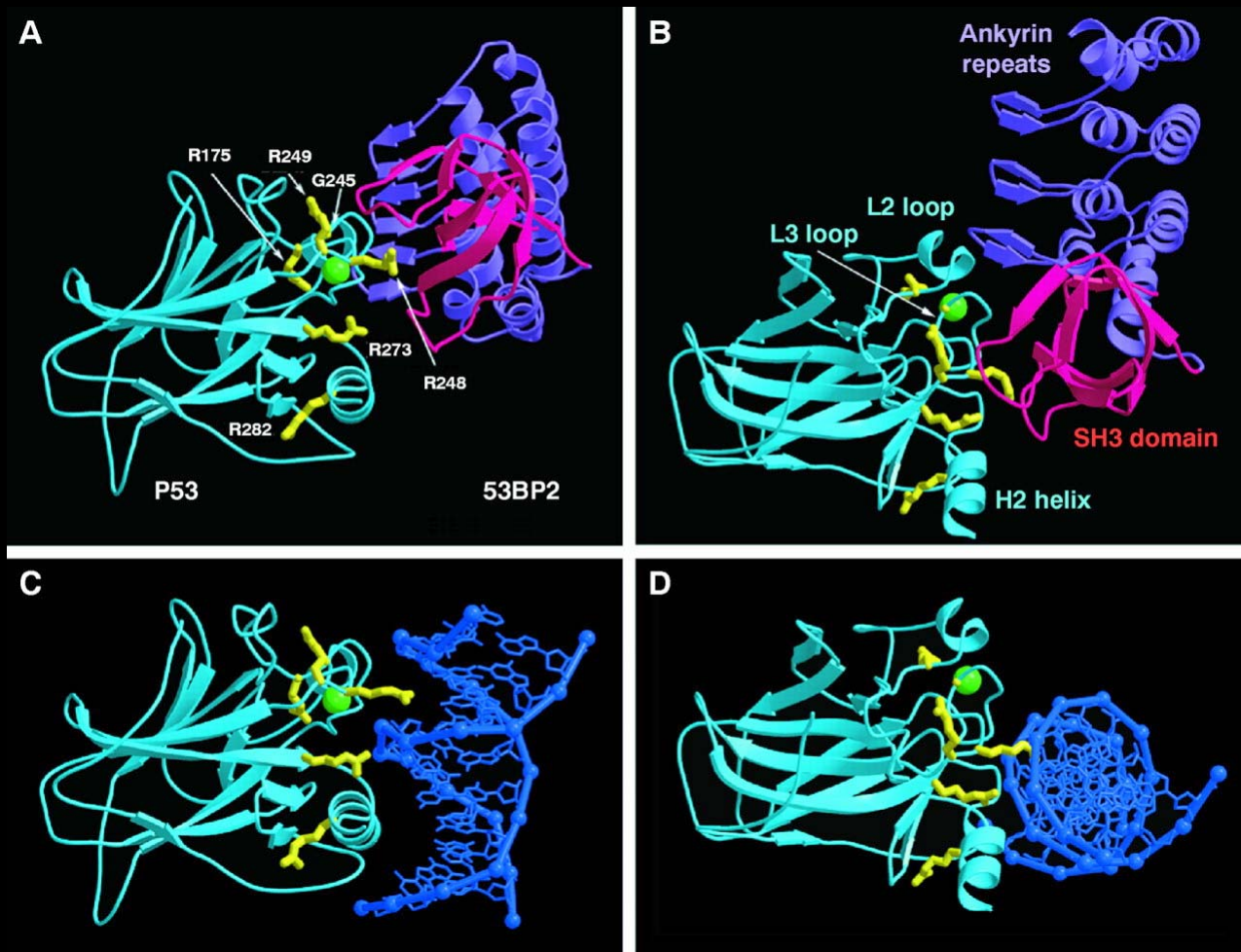
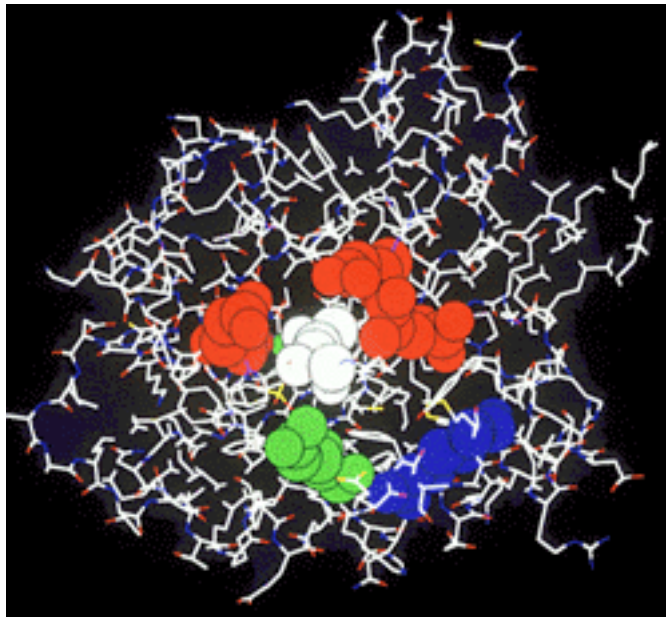


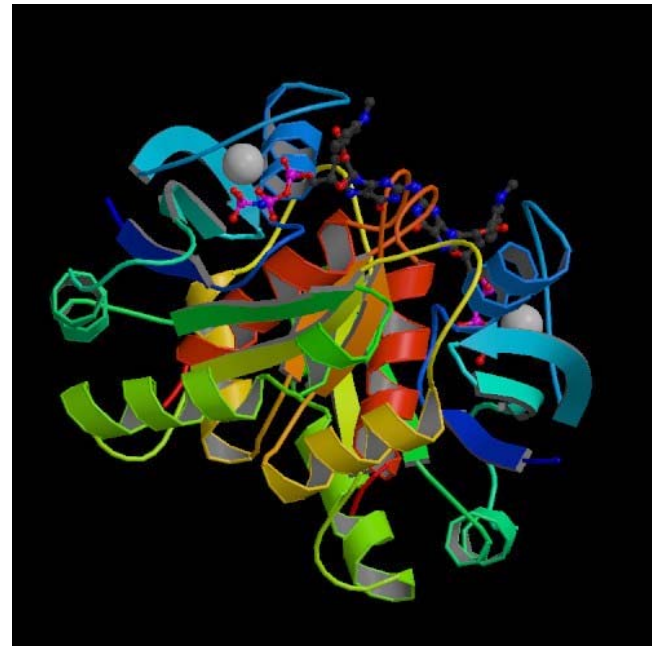
Figure 2. Comparison of the p53-53BP2 and p53-DNA (15) complexes in two orthogonal views (rotated by 90° about the x -axis). The six most frequently mutated amino acids of p53, highlighted in yellow, are at or near both the 53BP2 and DNA interfaces. (A and B) The 53BP2 SH3 domain (red) binds the L3 loop, while the fourth ankyrin repeat (magenta) binds the L2 loop of the p53 core domain (cyan). The zinc atom of p53 is shown as a green sphere. (C and D) Comparison with the p53-DNA (blue) complex (15) in the same p53 orientations as (A and B). Abbreviations for the amino acid residues are: A, Ala; C, Cys; D, Asp; E, Glu; F, Phe; G, Gly; H, His; I, Ile; K, Lys; L, Leu; M, Met; N, Asn; P, Pro; Q, Gln; R, Arg; S, Ser; T, Thr; V, Val; W, Trp; Y, Tyr.

The Ras (Rause-associated sarcoma) Oncogene

In about 30% of human cancers, Ras is mutated so that it is permanently switched on, telling the cell to grow regardless of whether receptors on the cell surface are activated or not



The three-dimensional structure of Ras protein. Many of the mutations of Ras observed in human cancers have been pin-pointed and mapped onto this structure. [Image credit: Mark Boguski, NCBI, NIH, Bethesda, USA.]

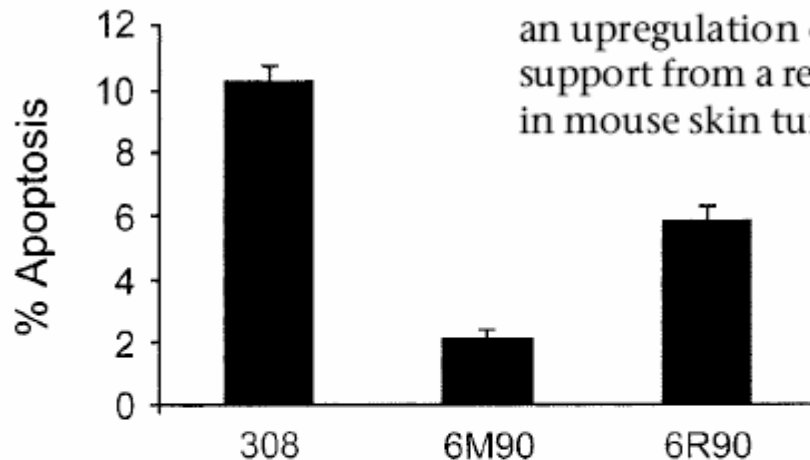




Elevated basal reactive oxygen species and phospho-Akt in murine keratinocytes resistant to ultraviolet B-induced apoptosis.

Butts BD, Kwei KA, Bowden GT, Briehl MM.

Our model, which suggests that steady-state levels of increased ROS contribute to malignancy through an upregulation of Akt activity, has some correlative support from a recent report by Segrelles et al. on Akt in mouse skin tumorigenesis [42]. This in vivo study



(Akt = serine-threonine kinase)

Figure 1. Decreased ultraviolet (UV) B-induced apoptosis in the two malignant variants, 6M90 and 6R90, compared to the parental 308 keratinocyte cell line. Cells were exposed to a 300 J/m² dose of UV-B and harvested 13 h later. Percent apoptosis was determined by morphological assessment of 200 cells per slide (see Materials and Methods). All values are the mean \pm the standard error of the mean (SEM) from six independent experiments.



Beyond the pale. Sunscreen has come a long way since early creams, but blocking UVB rays prevents the skin from making vitamin D.

Selected References

Sitailo, LA, Tibudan, SS, and Denning, MF. Activation of caspase-9 is required for UV-induced apoptosis of human keratinocytes. *J Biol Chem.* 2002;277:19346-19352.

Denning MF, Dlugosz AA, Threadgill DW, Magnuson T, Yuspa SH. Activation of the epidermal growth factor receptor signal transduction pathway stimulates tyrosine phosphorylation of protein kinase C ©. *J Biol Chem.* 1996;271:5325-5331.

Kowalczyk AP, Bornslaeger EA, Borgwardt JE, Palka HL, Dhaliwal AS, Corcoran CM, Denning MF, Green KJ. The amino-terminal domain of desmoplakin associates with and clusters desmosomal cadherin-plakoglobin complexes: Reconstituting the desmosomal plaque. *J Cell Biol.* 1997;139:773-784.

Denning MF, Guy SG, Ellerbroek SM, Norvell SM, Kowalczyk AP, Green KJ. The expression of desmoglein isoforms in cultured human keratinocytes is regulated by calcium, serum, and protein kinase C. *Exp Cell Res.* 1998;239:50-59.

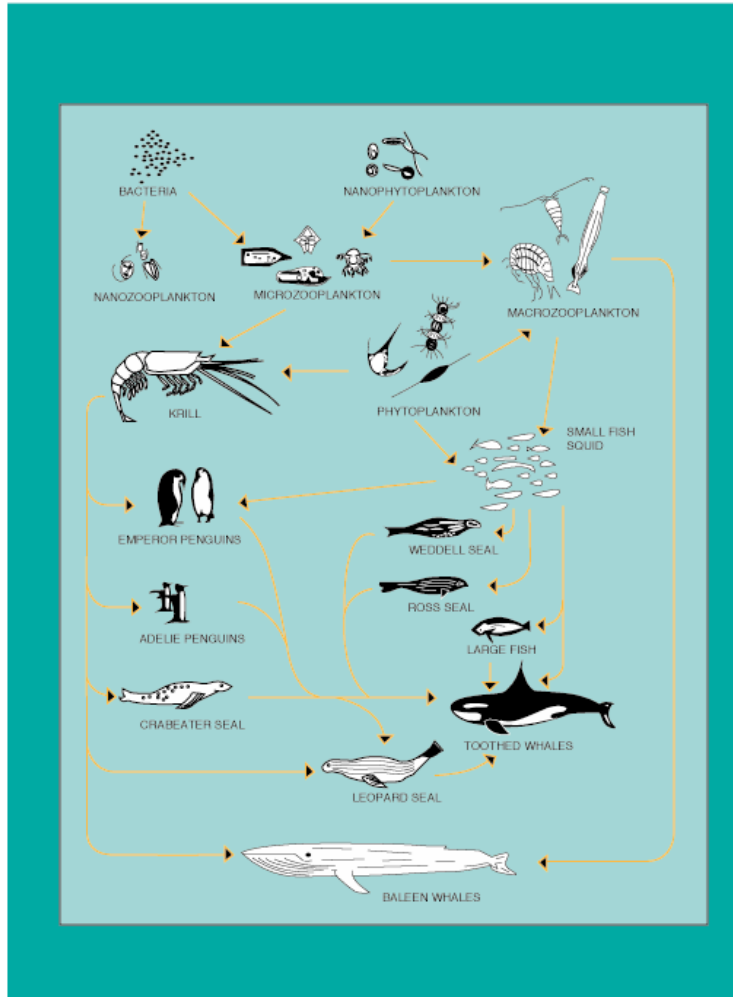
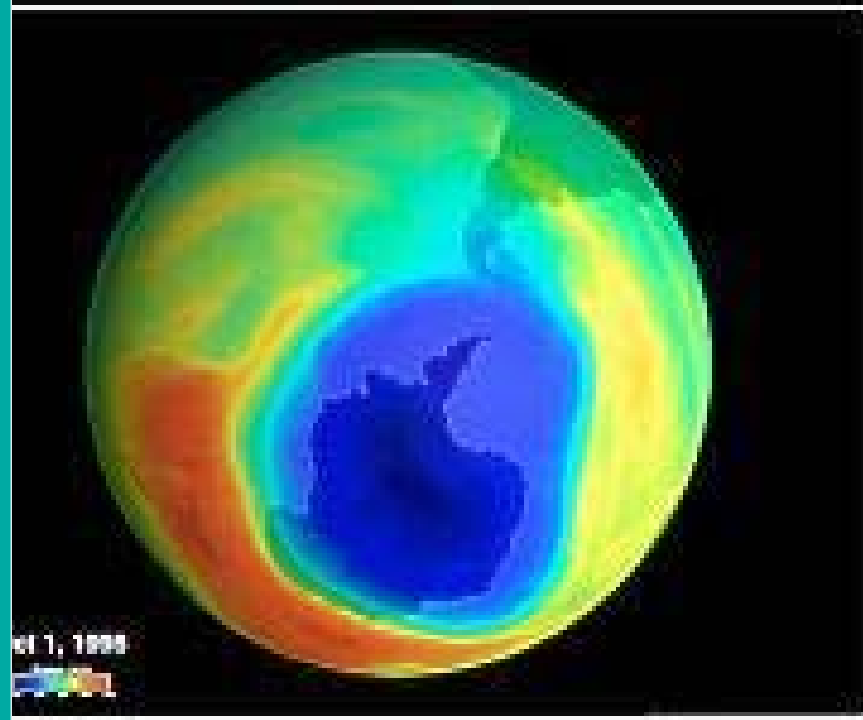
Medical Ecology Of Stratospheric Ozone Depletion:

The Rest of Life on Earth

Large losses of total ozone in Antarctica reveal seasonal ClO_x/NO_x interaction

Nature 315: 207-10.

J. C. Farman, B. G. Gardiner & J. D. Shanklin*



* First article to document ozone hole over Antarctica

Keystone species



Krill



Species: Antarctic krill (*Euphausia superba*)

Classification:

- Phylum: Arthropoda
- Class: Crustacea
- Order: Euphausiacea
- Genus: Euphausia

Solar UVB-induced DNA damage and photoenzymatic DNA repair in antarctic zooplankton

(ozone depletion/DNA damage and repair/photolyase/marine ecosystems)

KIRK D. MALLOY*, MOLLY A. HOLMAN*, DAVID MITCHELL†, AND H. WILLIAM DETRICH III*‡

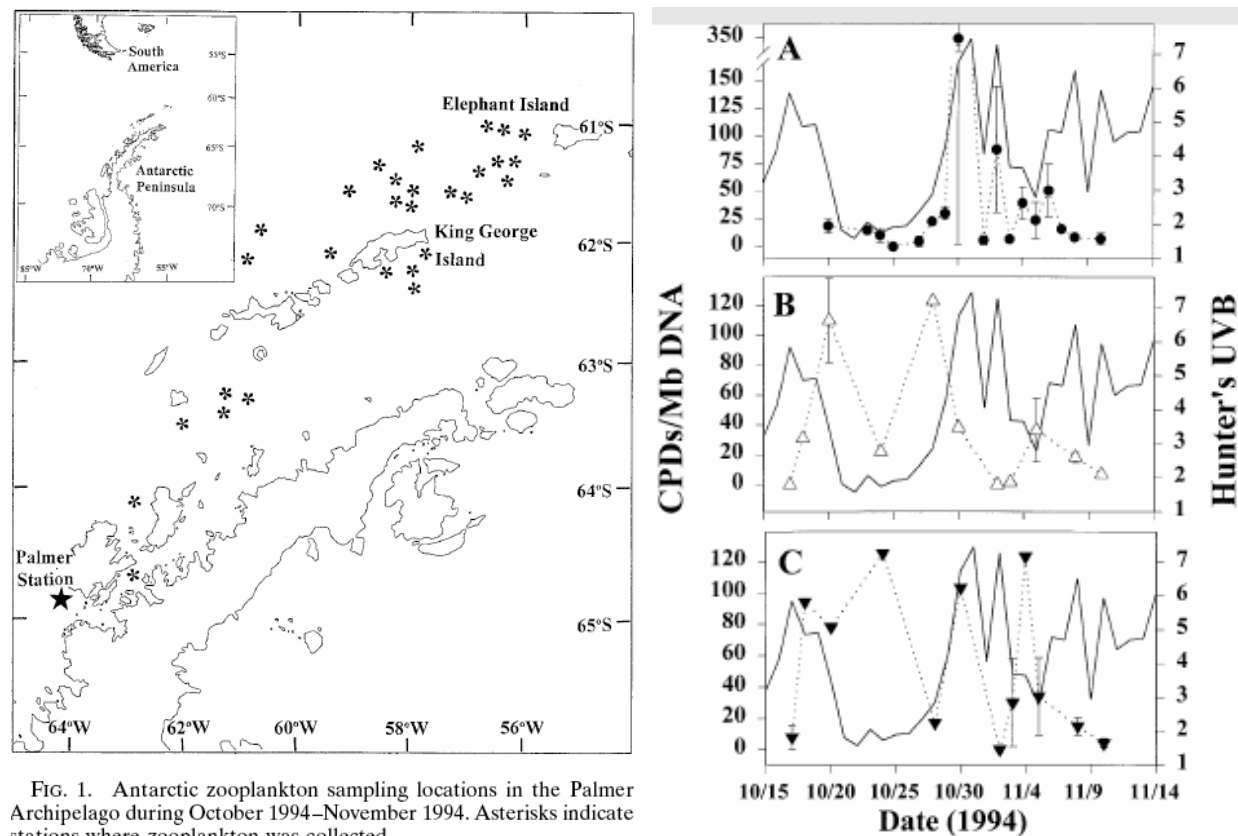


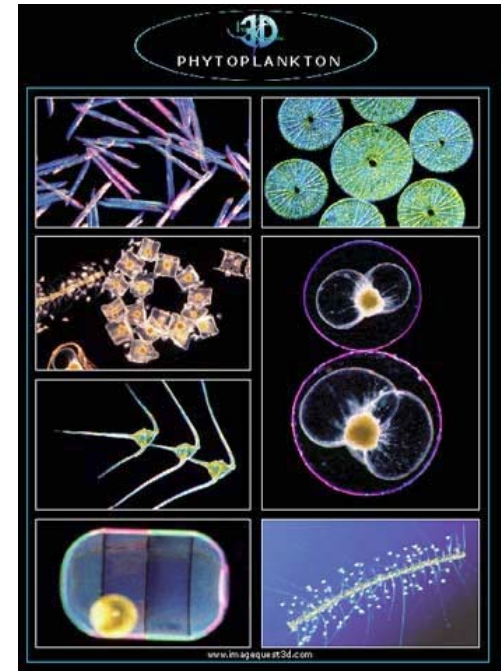
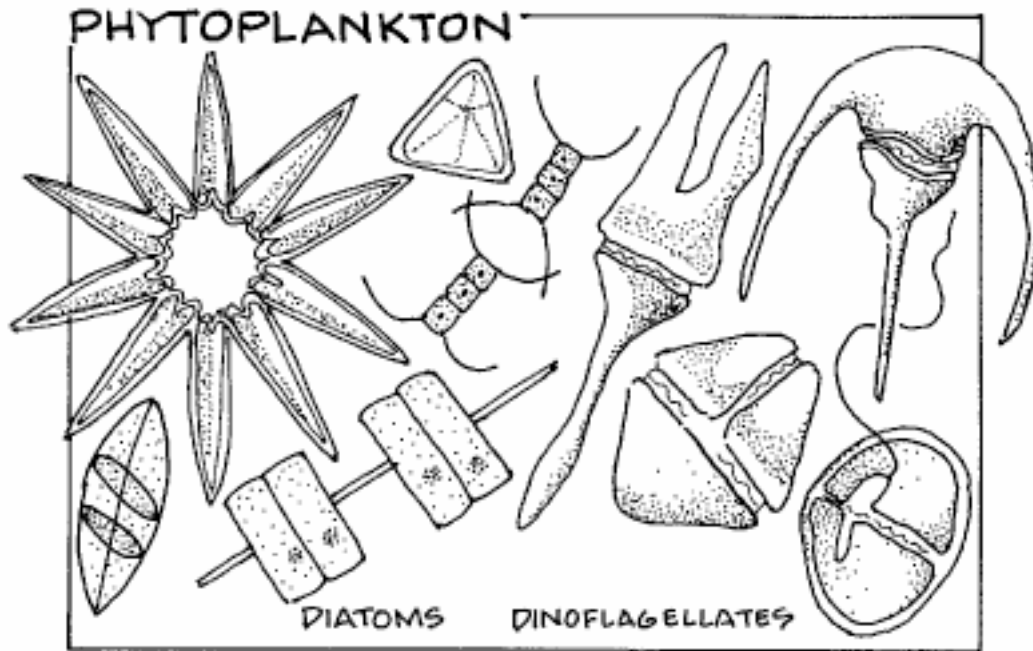
FIG. 1. Antarctic zooplankton sampling locations in the Palmer Archipelago during October 1994–November 1994. Asterisks indicate stations where zooplankton was collected.

Thus, elevated solar UVB flux during the austral spring may have a substantial impact on populations of both primary producers and heterotrophs of the Antarctic marine ecosystem.



Photoinhibition in Antarctic phytoplankton by ultraviolet-B radiation in relation to column ozone values

Osmund Holm-Hansen, Virginia E. Villafaña, and E. Walter Helbling,
*Polar Research Program, Scripps Institution of Oceanography,
University of California, San Diego, La Jolla, California 92093-0202*



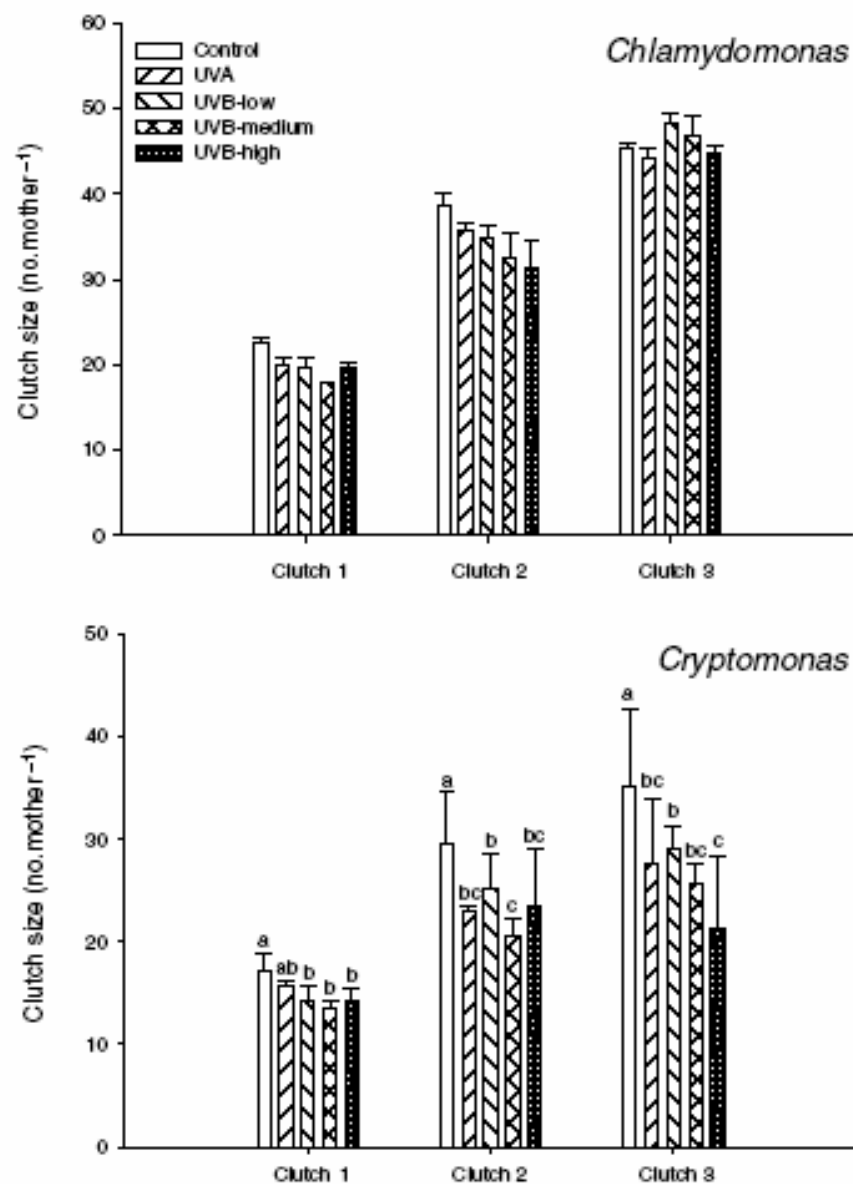


Fig. 3 Clutch sizes ± 1 SE of *Daphnia* in the different treatments: upper panel = *Chlamydomonas* experiment, lower panel = *Cryptomonas* experiment. Differences were tested with ANOVA and Tukey test, homogeneous groups are indicated with lower case letters.

Negative effects of UVB-irradiated phytoplankton on life history traits and fitness of *Daphnia magna*

HENDRIKA J. DE LANGE AND PAUL L. VAN REEUWIJK

Aquatic Ecology and Water Quality Management Group, Department of Environmental Sciences, Wageningen University, Wageningen, The Netherlands

SUMMARY

1. We tested the effect of ultraviolet-B (UVB)-irradiated phytoplankton on life history characteristics of *Daphnia magna*. Two phytoplankton species were used, *Chlamydomonas reinhardtii* and *Cryptomonas pyrenoidifera*. The phytoplankton species were cultured under photosynthetically active radiation (PAR) conditions, and under PAR supplemented with ultraviolet-A and ultraviolet-B radiation, and fed to *Daphnia*.
2. Life history traits of *Daphnia* were negatively affected when fed on UVB-irradiated *Cryptomonas*. Size at maturity was depressed and fewer juveniles with lower fitness were produced in the UVB treatments. In the *Chlamydomonas* experiment, no significant effects were found.
3. The cause of the observed UVB effects is likely to be constraints in food quality. Ultraviolet-B radiation thus has the potential of inhibiting energy transfer from the first to the second trophic level.



Smithsonian Environmental
Research Center

Ecological effects of ultraviolet solar radiation

Thompson, A., E. A. Early, J. Deluisi, P. Disterhoft, W. D., J. Kerr, J. Rives, Y. Sun, T. Lucas, M. Duhig and P. J. Neale. 1997. The 1994 North American interagency intercomparison of Ultraviolet monitoring spectroradiometers. National Institutes of Standards and Technology Journal of Research. 102: 270-322.

Neale, P. J., R. A. Davis & J. J. Cullen. 1998. Interactive effects of ozone depletion and vertical mixing on photosynthesis of Antarctic phytoplankton. *Nature* 392: 585-589.

Neale, P. J., J. J. Cullen and R. F. Davis. 1998. Inhibition of marine photosynthesis by ultraviolet radiation: Variable sensitivity of phytoplankton in the Weddell-Scotia Sea during the austral spring. *Limnol. Oceanogr.* 43: 433-448.

Minimal effects of UVB radiation on Antarctic diatoms over the past 20 years

A. McMinn^{*}, H. Heijnis[†] & D. Hodgson[‡]

Minimal compositional changes in 20-year sequences of diatom assemblages from the Vestfold Hills suggest that the enhanced UVB levels resulting from the 'ozone hole' has had little effect on the diatom component of the phytoplankton community. In coastal areas such as this one, the presence of an

NATURE · VOL 370 · 18 AUGUST 1994

Blaustein, A.R., J.M. Kiesecker, D.P. Chivers, and R.G. Anthony. 1997. Ambient UV-B radiation causes deformities in amphibian embryos. *Proc. Natl. Acad. Sci. USA* 94:13735-13737.

BioScience: Vol. 53, No. 11, pp. 1028–1029.

Amphibians in a Very Bad Light

ANDREW R. BLAUSTEIN,^a and LEE B. Kats^b

^a*Department of Zoology, Oregon State University, Corvallis, OR 97331*

^b*Frank R. Seaver Chair, in Natural Science, Natural Science Division, Pepperdine University, Malibu, CA 90263*

Evolution & Development

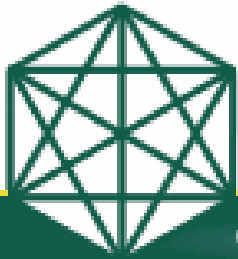
Volume 5 Issue 1 Page 89 - January 2003

doi:10.1046/j.1525-142X.2003.03014.x

Amphibian defenses against ultraviolet-B radiation

Andrew R. Blaustein^{a,} and Lisa K. Belden^b*





INTEGRATED RESEARCH CHALLENGES IN ENVIRONMENTAL BIOLOGY

The Global Decline of Amphibians

OVERVIEW OBJECTIVES MEMBERS PUBLICATIONS PROTOCOLS LINKS NEWS

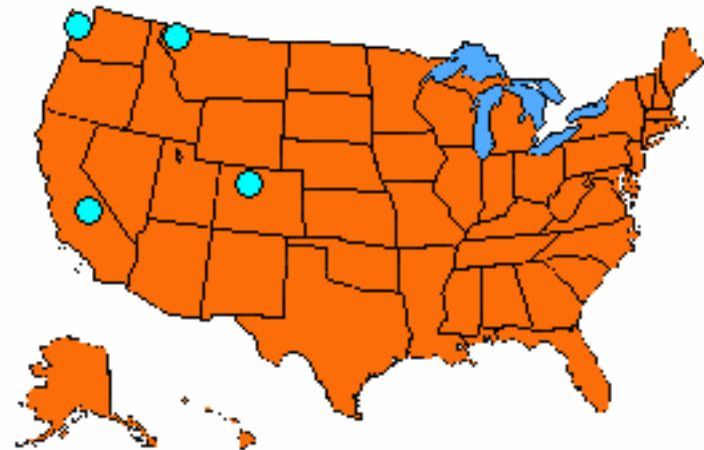
HOST-PATHOGEN BIOLOGY AND THE GLOBAL DECLINE OF AMPHIBIANS





science for a changing world

Biological Resources



**Evaluation of Solar Ultraviolet Radiation
as a Factor in Amphibian Decline in Montane Habitats**

Duration: February 1999 - September 2003

**Principal Contact: Dr. Edward E. Little, USGS
Columbia Environmental Research Center**

