UV Radiation

Figure 1
The Electromagnetic Radiation Spectrum with Expanded Scale for Ultraviolet Rays

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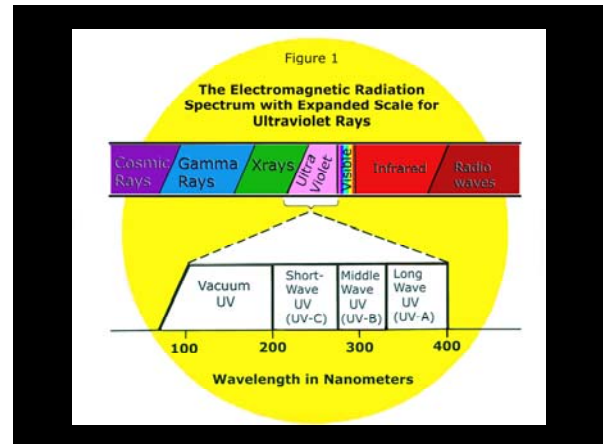
UV Radiation

- UVA 320-400 nm
- UVB 280-320 nm
- UVC <280 nm
- Major morbidities skin cancer, cataracts
- Sources
  - Solar
 - Artificial

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Dilemmas in UV Measurement

- Action spectrum not clear (UVB vs UVA vs both)
- Time and type of exposure
- Correlations between tumor location and exposure
- Potential long latency of tumors

UV Exposure in Populations

- Dominant source is sunlight
- For subpopulations, other exposures contribute substantially
- Primary endpoint usually skin dose
- Almost universal daily exposure
- Cannot separate UVA/UVB
- "Geographic" estimates
- Personal estimates

"Geographic" Measurements

- Latitude
- Altitude
- Day of year
- Time of day
- Cloud cover
- Ozone
- Particulates
- Smog
- Reflectance
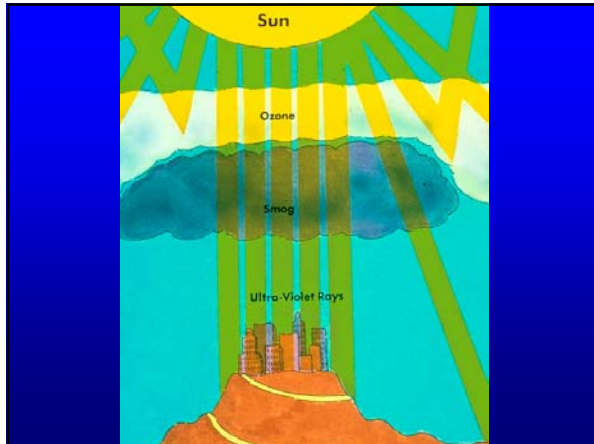
On Ground Measurements

- **Robertson-Berger meters-NOAA/NCI**
  - UBV only
  - Multiple sites in areas of cancer registries
  - In place for decades
  - Questions about QC
    - Instruments compared every year to standard
- **Multispectral meters**
  - EPA Brewer system-data available
  - NOAA 5 global monitoring observatories
  - USDA 34 stations in 29 states
    - Mostly rural
    - Started in mid 1990's

Satellite Measurements

- **NASA TOMS system**
- **Global coverage**
- **Theoretical estimate of ground UV**
- **Comparison with on ground measures**
  - Agreement within 12% overall
  - Better (8%) with clear skies
  - Aerosols contribute about 5% (based on measurements in Billings OK and Las Cruces NM)

Personal Measurements of Current Exposure

- **Polysulphone badges**
  - UVB
  - Calibrated to erythemal doses
  - Measures total dose over specified period
  - Relatively inexpensive
- **Dosimeters**
  - Vary in spectra
  - Continuous or intermittent monitoring
  - Small; handheld or attachable
  - Expensive

Personal Estimate of Historical UV Exposure

- **Complex to capture by questionnaire**
- **Average over long periods of time of routine activities**
  - Subject to recall bias
  - Imprecise
- **Varies by behavioral patterns**
- **Varies by host factors**
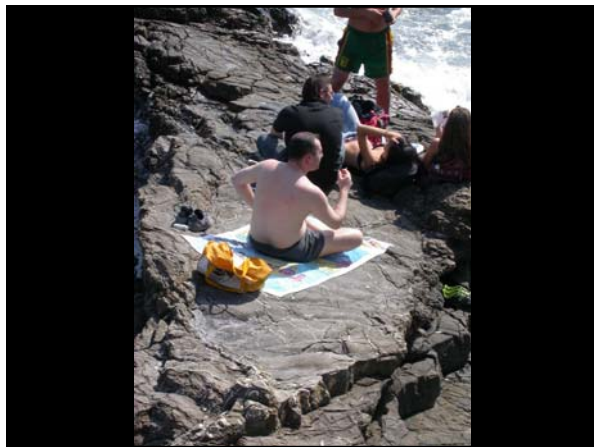
Frequently Assessed Personal Sun Exposure Variables

- **Number of sunburns**
- **Hours outdoors**
  - Time of day
  - Time of year
  - Age at exposure
  - Use of sun protective measures
  - Patterns of exposure
- **Occupational history**
- **Residence history**

Reproducibility of Exposure Measures

Variable	English et al. ICC/κ (95% CI)	Fears et al.
Time outdoors	0.77 (0.64-0.83)	Not good
Site –specific	0.65 (0.55-0.73)	N/A
Sunburn	0.53 (0.41-0.66)	Moderate
Vacation hours	0.30 (0.19-0.40)	N/A
Residence	N/A	Excellent

English DR et al. Ca Epi Biomarkers Prev 7:857-863, 1998

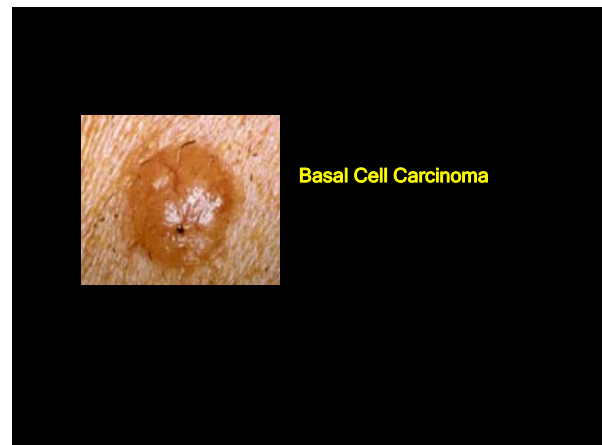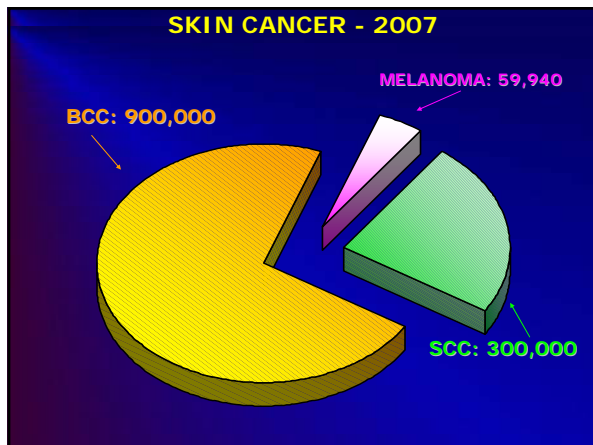## Layers of Skin

3
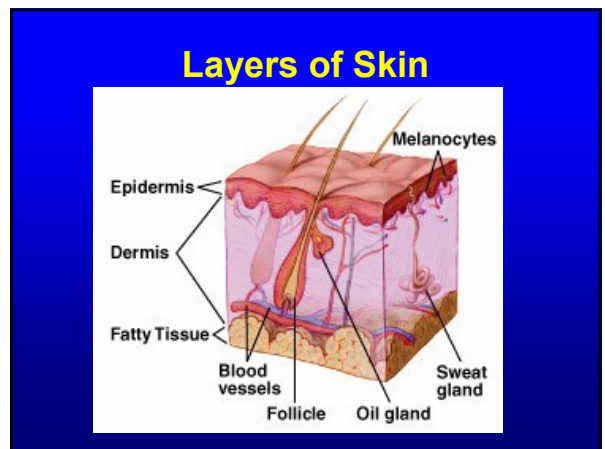
Acute UV Damage

- **Sunburn**
  - Cellular toxicity (ROS, induction p53)
  - DNA damage
    - Cyclobutane pyrimidine dimers
    - (6-4) pyrimidine-primidone photoproducts
    - C to T and CC to TT transitions
  - Release of cytokines and prostaglandins
  - Inflammatory response
- **Melanocyte stimulation**
  - Hyperplasia
  - Increased melanogenesis
- **Increased epidermal/dermal mitotic activity**

Chronic UV Damage

- **Skin cancer**
- **DNA damage**
  - Mutations in *p53, ras, PTCH*
  - Oxidative stress and activation transcription factors (prolif or apoptosis)
- **Photoaging**
- **Immune function**
  - Suppress immune function
  - Induce tolerance to antigens

SKIN CANCER - 2007

MELANOMA: 59,940

BCC: 900,000

SCC: 300,000

Basal Cell Carcinoma

Squamous Cell Carcinoma

Evidence of UV Association

- **Latitude gradient**
- **Migrant studies**
- **Analytic studies**
  - Type of exposure
  - Host factors

Migrant Studies

Age at Arrival	BCC	SCC	CMM
Birth	1.0	1.0	1.0
0-9	1.1 (0.4-2.5)	0.7 (0.1-2.8)	0.9 (0.4-1.8)
10-19	0.1 (0.0-0.5)	0.4 (0.1-1.6)	
20+	0.2 (0.1-0.4)	0.4 (0.2-0.7)	
10-29			0.3 (0.2-0.7)
30+			0.3 (0.1-1.1)

Armstrong and Kricker, 2001

Type of Exposure

Exposure	BCC	SCC	CMM
Total	1.0 (0.7-1.4)	1.5 (1.0-2.3)	1.2 (1.0-1.4)
Occup	1.2 (1.1-1.3)	1.6 (1.3-2.1)	0.9 (0.8-1.0)
Intermit	1.4 (1.2-1.5)	0.9 (0.7-1.2)	1.7 (1.5-1.9)
Sunburn	1.4 (1.3-1.5)	1.2 (0.9-1.7)	1.9 (1.7-2.2)

Armstrong and Kricker, 2001
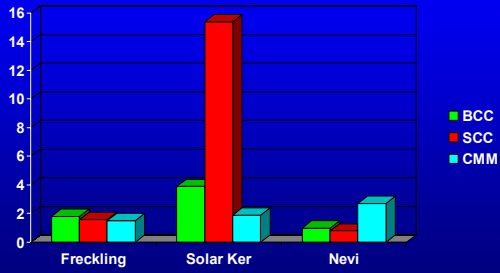

Male SEER Rates of Skin Cancer by Solar UV
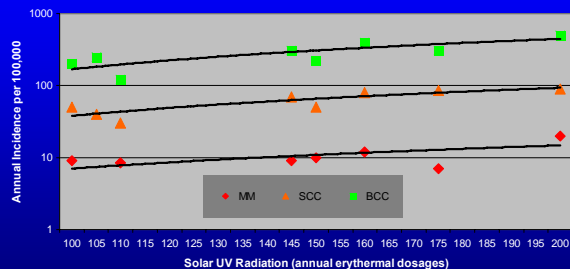
Scotto et al, 1983

Ability to Tan

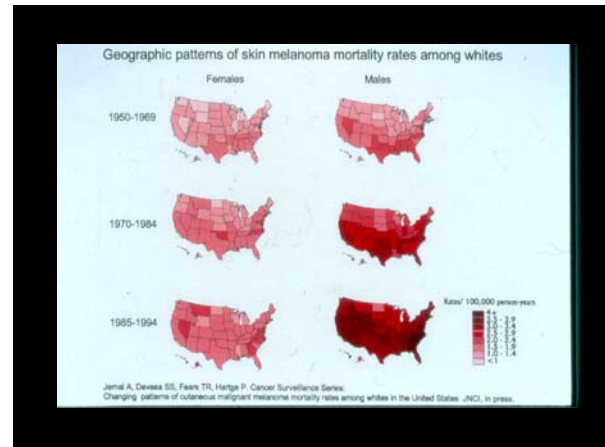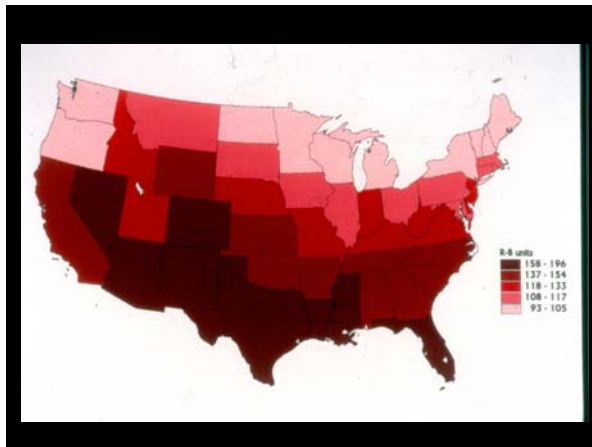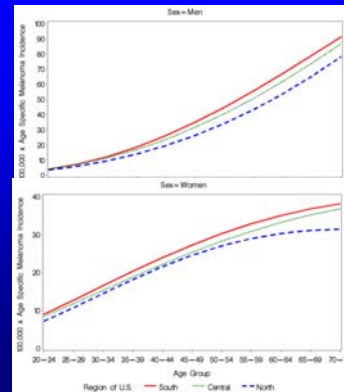| Tanning	BCC	SCC	CMM
Deep tan	1.0	1.0	1.0
Moderate	1.9 (1.3-2.8)	2.3 (1.3-4.0)	1.4 (1.1-1.9)
Light tan	3.2 (2.0-4.9)	4.6 (2.5-8.3)	2.3 (1.6-3.3)
No tan	3.7 (1.9-7.3)	6.9 (3.2-15)	3.5 (1.8-6.8)

Armstrong and Kricker, 2001

UV-Related Conditions

Bar chart with categories Freckling, Solar Ker, Nevi. Legend: BCC (green), SCC (red), CMM (cyan). Y-axis from 0 to 16.

Risk Factors

- **Ethnicity**
- **Fair skin**
  - **Freckles**
  - **Sunburns**
- **Older age**
- **Gender**
- **UV exposure**
- **Nevi (for melanoma)**

R-B units
158 - 196
137 - 154
118 - 133
108 - 117
93 - 105

Geographic patterns of skin melanoma mortality rates among whites

Females   Males

1950-1969

1970-1984

1985-1994

Rates/ 100,000 person-years

Jemal A, Devesa SS, Fears TR, Hartge P. Cancer Surveillance Series:
Changing patterns of cutaneous malignant melanoma mortality rates among whites in the United States. JNCI, in press.

Continental United States categorized by estimated annual UVB.

region North Central South

Estimated five year melanoma incidence rates by region of the U.S.

Sex=Men

Sex=Women

Age Group

Region of U.S.   South   Central   North

## Melanoma Case-Control Study

- **Hospital-based; U Penn and UCSF**
  - **738 newly diagnosed invasive melanoma**
  - **1024 outpatient clinic controls**
    - **clinics with same triage area**
    - **matched on age, gender, race, geography**
- **Data collection**
  - **In-person interview**
  - **Full skin exam with nevus characterization**
  - **Photography of back and 3 most atypical nevi; optional nevus biopsy**
  - **Self-administered diet questionnaire**

Residence History

- **History of residence locations reconstructed in 6 month intervals**

- **Each residence location assigned estimate of incident UVB at ground level (UVB flux)**

- **13% of subjects had stable residence**

Fears TR et al., Cancer Res 2002;62:3992-6

Average interval UVB flux in both sexes by age, case-control status for San Francisco
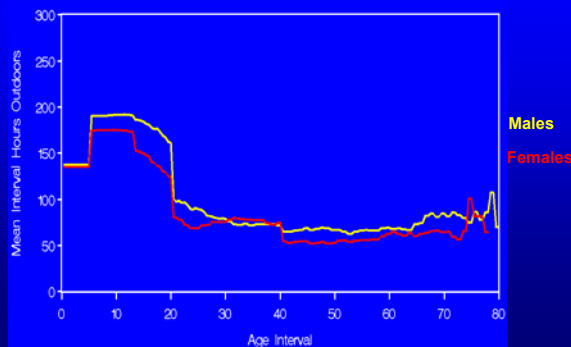

cases   **controls**
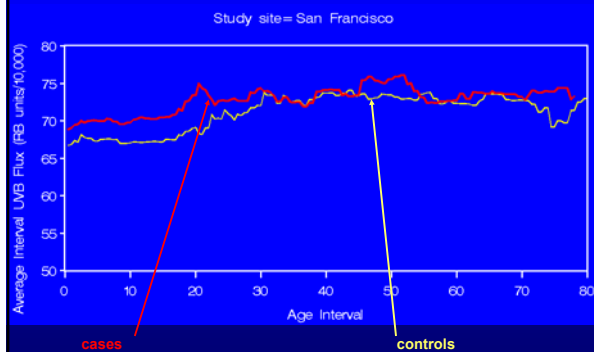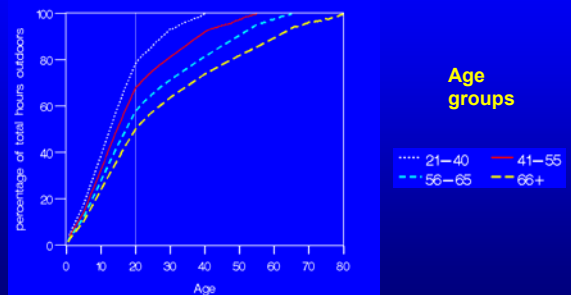

Hours Outdoors

Estimate of hours outdoors for each six month interval of each residence using:

- **Occupational sunlight exposure history**

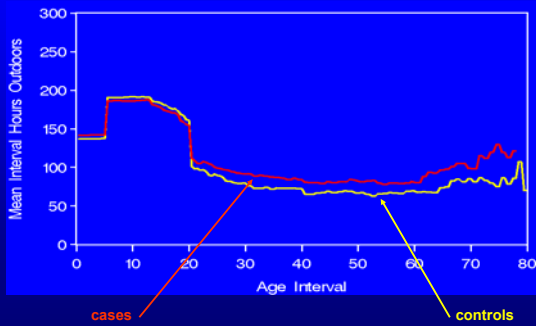- **Non-occupational sunlight exposure for specified ages**

Mean interval hours outdoors plotted against age level for controls by gender

Males

Females

Percentage of total hours outdoors at interview by age for male controls

Age groups

····· 21–40   —— 41–55
— — 56–65   – – 66+

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Mean interval hours outdoors against age level by case-control status for men

Melanoma Risk Associated with 10% Increase in Exposure

Exposure	Men	Women
UVB Flux	1.19	1.16
Hrs out age 0-19	0.99	0.99
Hrs out age 20+	1.03	Tan 1.06

Estimated Relative Risk of Melanoma for Men Age 50

light tan		RR
Atlanta	10 hrs/week	1.00
New Orleans	10 hrs/week	1.19
Atlanta 0-25		
New Orleans 25+	10 hrs/week	1.09
dark tan		
Atlanta	10 hrs/week	0.47
	13 hrs/week	0.51
	25 hrs/week	0.62

Average Annual Hours Outdoors by Gender and Tan Type in Controls
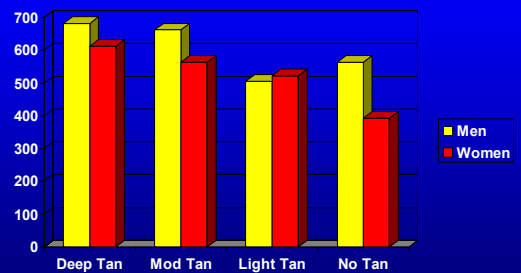
Sunbed

Tanning Bed Exposure

- **Estimated 25,000,000 persons use commercial facilities per year in U.S.**
  - 8% age 16-19
  - 42% age 20-29
  - 71% female
- **Approximately $6 billion/year industry**

Use of Sunbeds

- **Studies varied in design**
- **Use varies by gender in adolescence**
  - Higher at older ages
  - Males 1-35%
  - Females 14-75%
- **Most robust studies**
  - Sweden 19% males; 40% females
  - US 11% males; 37% females

Lazovich D, Forster J. Eur J Cancer 2005; 41:20-27

Risk of Melanoma With Artificial UV

| Exposure	# Studies	Summary OR	95% CI
Ever/Never	10	1.25	1.05-1.49
Young adult 1st expos	5	1.69	1.32-2.18
Highest freq exposure	6	1.61	1.21-2.12

Gallager RP et al. Cancer Epidemiol Biomarkers Prev 2005;14:562-6

Xeroderma Pigmentosum

- **Autosomal recessive disorder**
- **Risk of skin cancer >1000 fold increased**
- **Impaired ability to repair UV-induced DNA damage**
- **7 nucleotide excision repair complementation groups (A-G)**
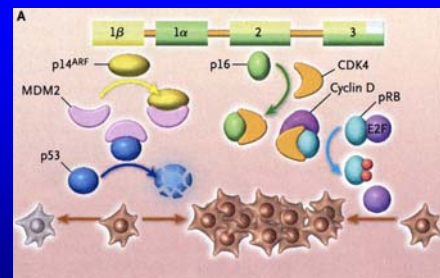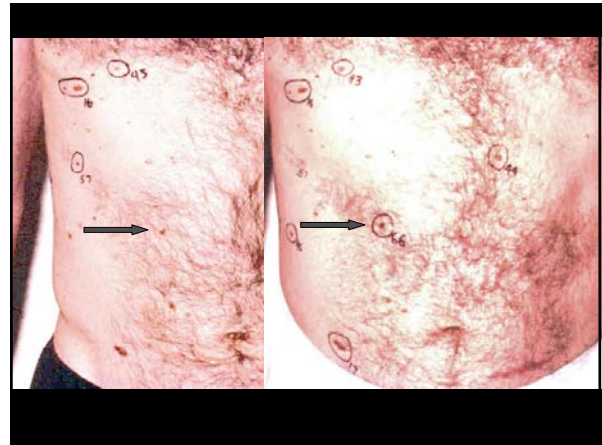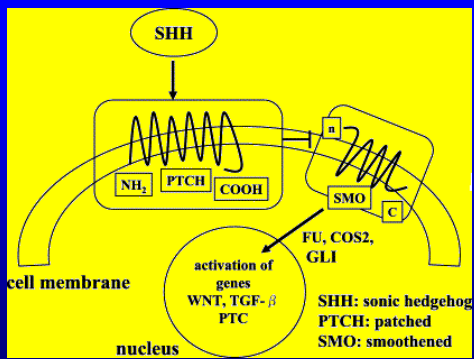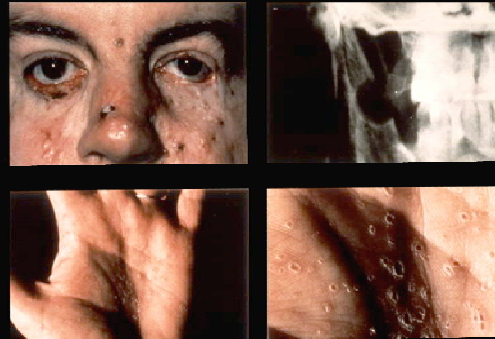- **1 nucleotide excision repair proficient with deficient post replicational repair**

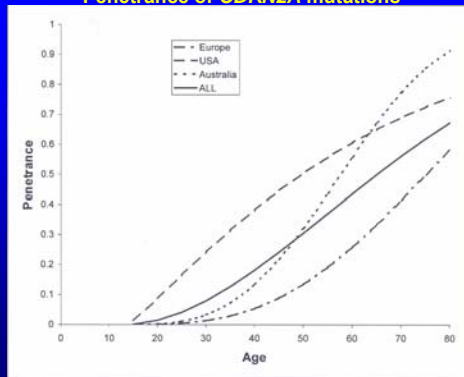XP Back
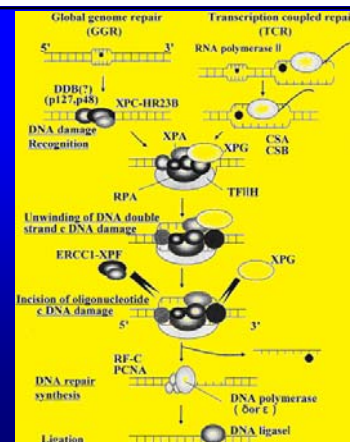
Nevoid Basal Cell Carcinoma

- **Autosomal dominant disorder**
- **Very high risk of basal cell carcinoma**
  - In sun-exposed
  - In radiation fields
- **Other findings**
  - Odontogenic keratocysts of jaw
  - Palmar/plantar pits
  - Skeletal anomalies/extra osseous calcifications
  - Medulloblastoma
  - Ovarian fibromas

Nevoid Basal Cell Carcinoma Syndrome

SHH

NH₂ PTCH COOH

SMO C

FU, COS2, GLI

activation of genes
WNT, TGF-β
PTC

cell membrane

nucleus

SHH: sonic hedgehog
PTCH: patched
SMO: smoothened

Tsao et al., NEJM 2004;350:924-32

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Penetrance of *CDKN2A* mutations

JNCI, 2002

Conclusions

- **UV exposure, either sun or artificial, is important in melanoma risk**
- **Cannot establish action spectrum for humans; exposures always mixed**
- **Patterns of behavior vary by gender, skin type, age, and other factors**
- **Age at exposure is not a simple metric; adult exposure contributes to risk**
- **Need to have very clear public health messages about UV exposure**

Collaborators

- **Thomas Fears**
- **Alisa Goldstein**
- **Mary Fraser**
- **DuPont Guerry IV**
- **David Elder**
- **Allan Halpern**
- **Richard Sagebiel**
- **Wallace Clark**
- **Elizabeth Holly**
- **Patricia Hartge**
- **Ken Kraemer**