

Genomics and Medicine

Malignant Melanoma

What is Malignant Melanoma?

- Most fierce form of skin cancer
- Cancer to melanocytes
 - Melanocytes – skin, eye, meninges, digestive tract, lymph nodes
- About 8-12% of cases due to heritage¹
- Malignant melanoma may start on its own or from preexisting mole
- Caused by intense sporadic exposure to the sun

Characteristics

- Asymmetric, ragged, weirdly colored, and large



Classical Diagnosis

- Excisional Biopsy
- Check lymph nodes
- If tumor is thick:
 - X-rays
 - Blood tests
 - Scans

Classical Treatment

- Surgery
- Chemotherapy
- Radiation Therapy
- Preventive Measures:
 - Protective clothing
 - Sunscreen
 - Avoid midday sun

Genetic Mechanism

- Autosomal Dominant and Polygenic
 - Polygenic possibly if affecting:
 - Only a generation of siblings
 - 2nd or 3rd degree relatives
 - Autosomal Dominant if occurring within a large family

CDKN2A and CDK4

- CDKN2A [9p21]
 - Codes for p16
 - Control checkpoint at G1-S
 - Binds to complex that contains CDK4 (prevents transcription)
- CDK4 (Cyclin-dependent kinase-4) [12q14]
 - Involved in control of cell growth at G1 phase
 - Inhibited by p16

Another Gene?

- CDKN2A and CDK4 give increased risk of MM. Only account for 20-25% of families with multiple cases of MM
 - 2003 Gilanders located 1p22
 - Identified by deletion mapping as tumor suppressor gene

Biotech Treatment

- Do not prevent melanoma
- Interferons (interferon alpha 2b)
 - “Negative growth factor”
 - Interferon helps body respond to disease
- Interleukins
 - Activates WBCs
 - IL-2 (T-cell growth)

Recruiting the Body to Fight Cancer

- Researchers found destroying normal skin cells can trigger the body to kill cancerous versions of those cells (2004)

- 1. Gave tumors to mice

2. Antiviral Drug (ganciclovir) + 2 types of DNA [boosts immune reactions or code viral enzyme]



3. Melanocytes take up DNA and start manufacturing proteins

4. Viral enzyme + antiviral drug = Apoptosis

Released Immune-boosting proteins set off response by immune cells

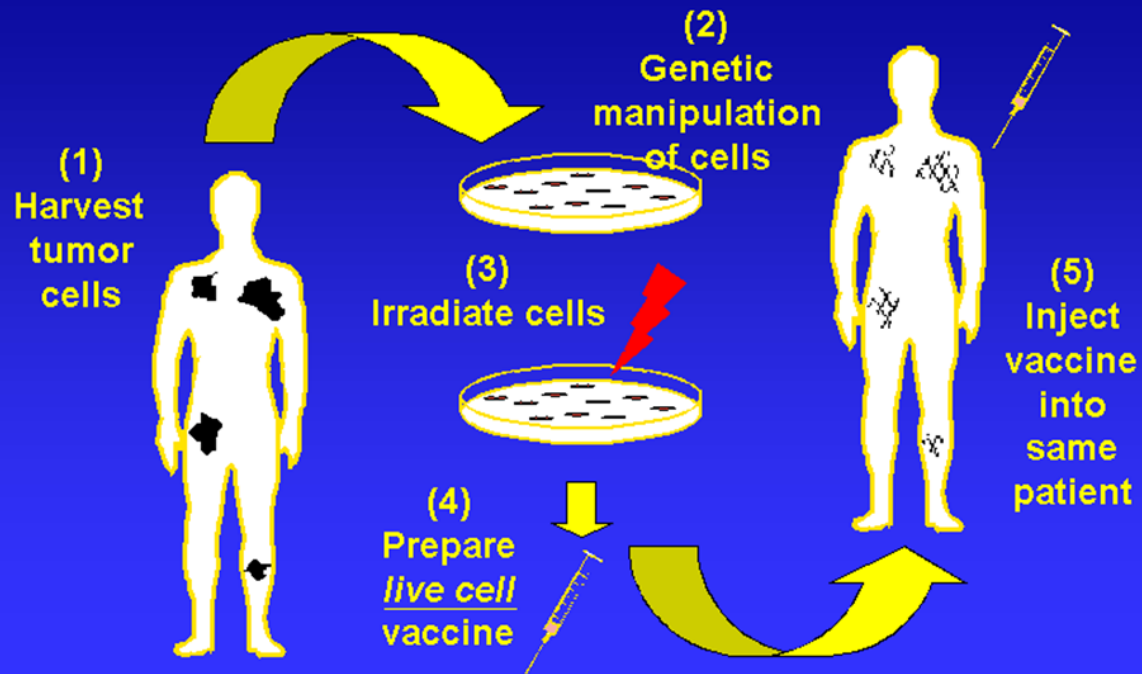
Genetic Diagnosis

- Genetic Tests not recommended:
 - Incomplete understanding of mechanisms (CDKN2A and CDK4)
 - Variations in penetrance
- Melaris® - test for CDKN2A

Sources

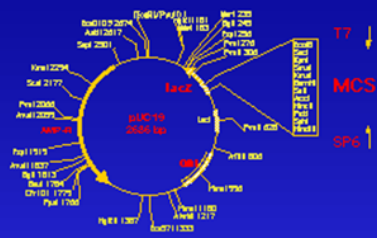
- <http://atlasgeneticsoncology.org/Kprones/DysplNevusID10013.html>
- <http://www.asco.org/patient/Learning+About+Cancer/Genetics/The+Genetics+of+Melanoma>
- <http://www.ncbi.nlm.nih.gov/entrez/dispmim.cgi?id=155600>
- <http://www.ncbi.nlm.nih.gov/books/bv.fcgi?call=bv.View..ShowSection&rid=gnd.section.104>
- <http://www.asco.org/patient/Cancer+Types/Familial+Malignant+Melanoma>
- <http://dermatology.cdlib.org/DOJvol6num1/transactions/melanoma/naylor.html>
- http://gdziesieleczyc.pl/magazine.php?magazine_id=14&article_id=2559&magazine_subpage=ABSTRACT
- <http://www.springerlink.com/content/58g4943runkm94y1/fulltext.pdf>
- <http://www.cancer.gov/cancertopics/wyntk/melanoma/>
- http://www.healthatoz.com/healthatoz/Atoz/common/standard/transform.jsp?requestURI=/healthatoz/Atoz/ency/malignant_melanoma.jsp
- <http://www.mpip.org/topframeset.shtml?http://newscenter.cancer.gov/pressreleases/melanomavaccine.html>
- <http://www.bmj.com/cgi/content/full/324/7351/1412/a>
- <http://www.ncbi.nlm.nih.gov/pubmed/18025917>
- <http://blue.regence.com/trgmedpol/lab/lab49.html>

Recombinant (DNA) Cell Vaccines



<http://dermatology.cdlib.org/DOJvol6num1/transactions/melanoma/fig009.gif>

DNA Vaccines



(1)
Insert genes to be expressed (peptide antigen genes, GM-CSF gene, IL2 gene, etc.) into plasmid vector(s)

(2)
Prepare vaccine (usually an adjuvant of some type plus naked plasmid DNA)



(3)
Genes are expressed in skeletal muscle cells or adipocytes where they facilitate an immunologic response

<http://dermatology.cdlib.org/DOJvol6num1/transactions/melanoma/fig009.gif>

MC1R, gene for melanocortin 1 receptor -
associated with skin and hair color.

Controls type of melanin produced by
melanocytes

Alterations harming function

