

BREAST  
CANCER  
HUB<sup>SM</sup>

# (AM)<sup>2</sup> The Cure Malignant Melanoma

Age Group: 13-15

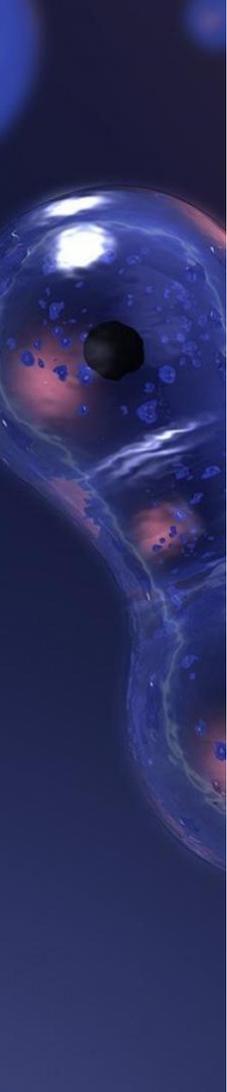
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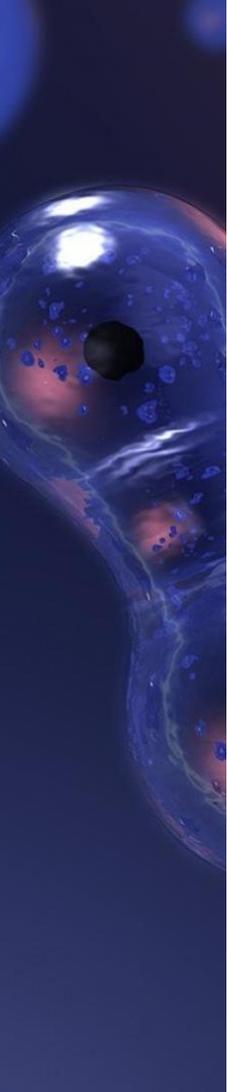
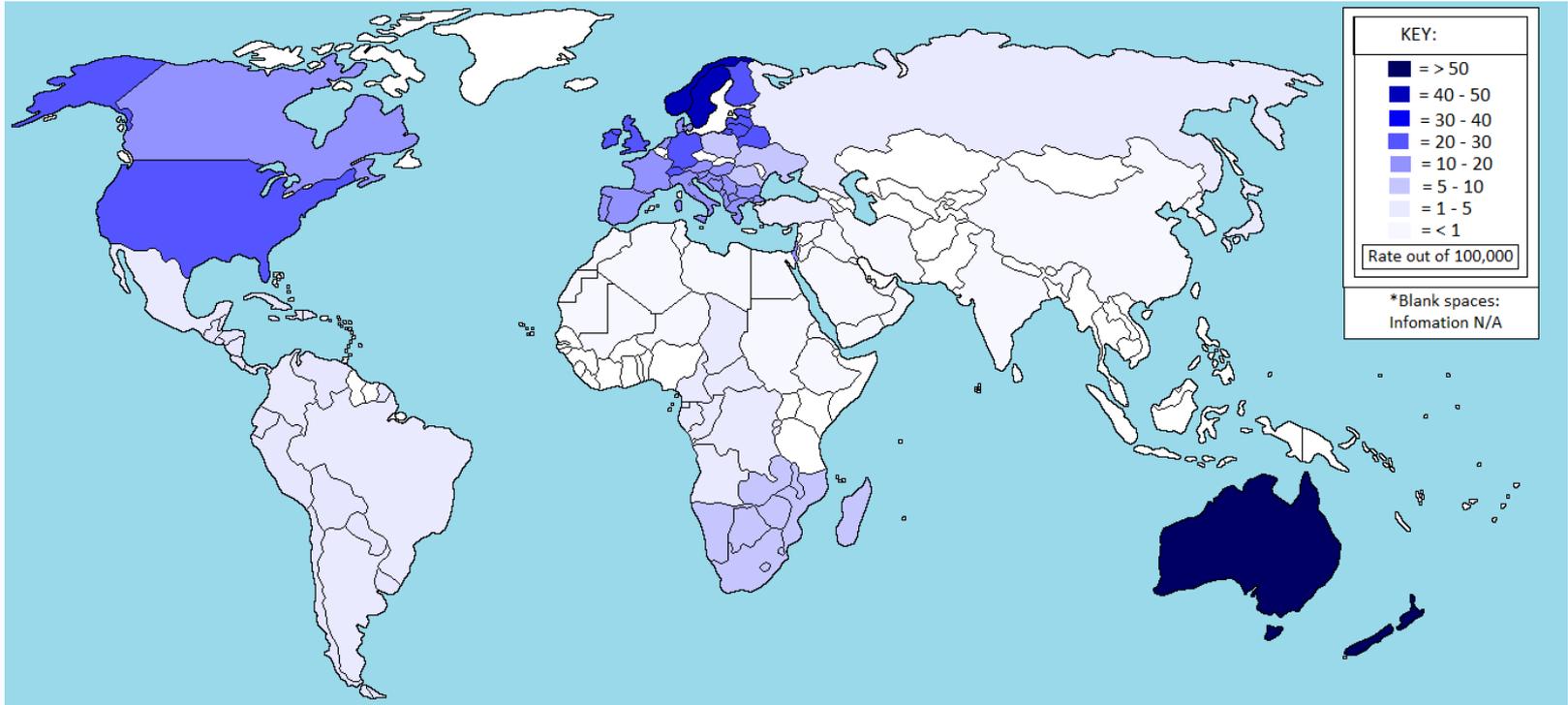
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# Abstract

- Melanoma is the cancer caused by the malfunction of the melanocytes in the skin. It causes abnormal growth and evolution of surrounding skin. If left untreated the cancerous cells spread deeper, and eventually contaminate the blood stream and other organs
- This project aims to explain the signs and symptoms, types, stages, causes, demographics, incidence rates statistics, developing vs developed countries statistics, 2019 statistics, and history of melanoma, as well as the types of surgeries and therapies available for melanoma.
- Our sources range from documents in the United States National Library, PubMed, JSTOR, and other reliable Cancer researching institutes. We also used many desktop apps to create certain graphs and maps.
- We have researched the many types of melanoma, including hidden melanomas that effect Asian and African populations. We have also researched how different lifestyle aspects can effect melanoma and the variety of treatments, such as immunotherapy, that can be used to treat melanoma.
- Our conclusion is that melanoma is not a widely thought of cancer in countries without large Caucasian populations, but should be brought to the light, as melanoma can be fatal.

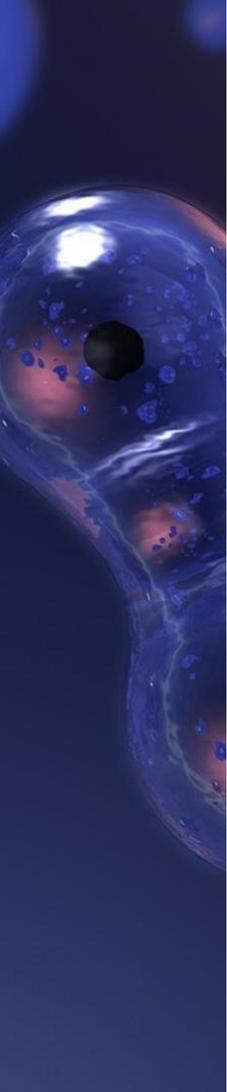


# Melanoma Around the World<sup>1</sup>



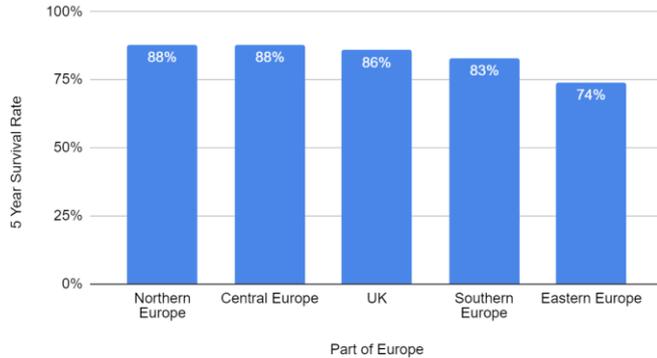
# 2019 Statistics for Melanoma<sup>2</sup>

- Superficial spreading melanoma is 65% of all cases
- Nodular melanoma is 20% of all cases
- In America, the incidence rate for all ethnicities is 2.3: Caucasians- 2.8%.
- There has been a 1.4% increase of incidence in Australian males, and a .7% increase incidence in Australian females.
- In 2019, 96,480 people are expected to be diagnosed with melanoma in the United States (men - 57,220, women - 39,260)
- More than 7,230 people are expected to die from melanoma in the United States



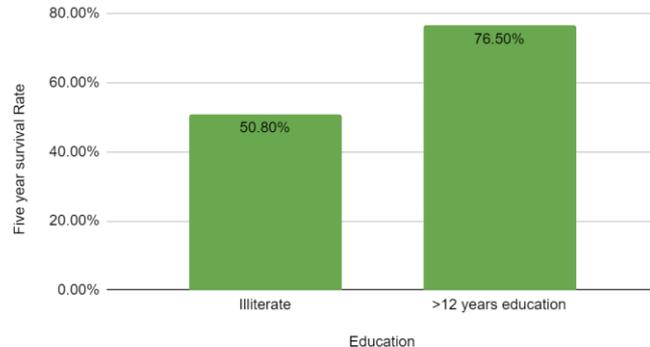
# Survival Around the World

5 Year Survival Rates in Europe



- Survival rates as drastically different based on whether the country is a developing or developed country
- Northern Europe, composed of only developed countries, despite having some of the highest melanoma rates, has a survival rate of 88%<sup>3</sup>
- Meanwhile Eastern Europe, which comprised only of developing countries only has a survival rate of 74%<sup>3</sup>

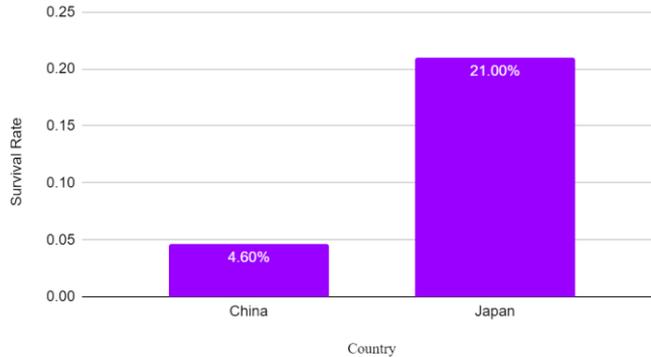
Five Year Survival Rate Based on Education in Brazil



- A study done in Brazil found that there was a large disparity based on gender, but more surprisingly, level of education<sup>4</sup>
- Brazil also found that a main reason that they might have such a low survival rate, 67%, was due to lack of awareness<sup>4</sup>
- Latin America actually has many risk factors including European decent, high UV radiation, tropical weather, high altitude, and a thinning ozone layers in some areas<sup>5</sup>

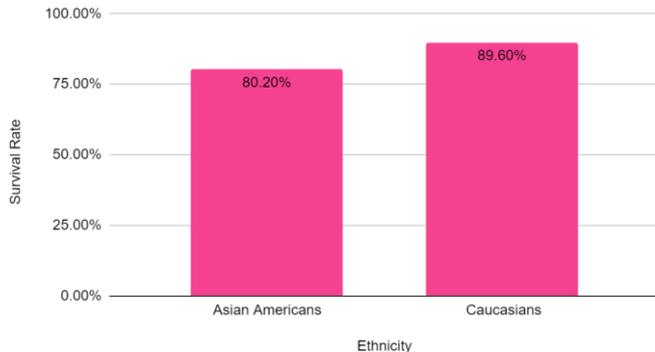
# Survival Around the World

5 Year Survival Rates for Stage 4 Melanoma in Japan vs. China



- The same difference between developing and developed countries in Europe can be seen in Europe
- Japan, considered a developed country, has survival rate for stage 4 melanoma, 21%, comparable to the US, 23%, and Canada, 15-20%<sup>(6,7,8)</sup>
- Meanwhile, China, which is considered a developing country has a survival rate for stage 4 melanoma of only 4.6 %<sup>9</sup>

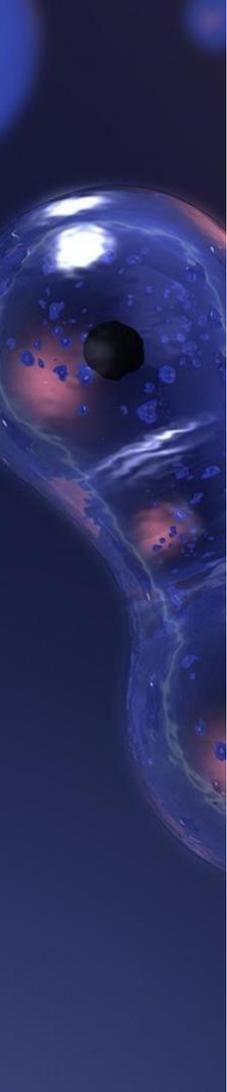
Survival Rate Based Ethnicity in America



- Lower survival rates could be because of the type of melanoma that effects Asians.
- In Asia, countries have reported that acral lentiginous melanoma makes up for about 41.8-65% of cases, unlike majority of countries that have 70% of cases of cutaneous melanoma<sup>6</sup>
- Acral Lentiginous melanoma has a lower survival rate, and as it effects Asians more, it is reflected in statics for Asians and Asian Americans<sup>6</sup>

# Types of Melanoma

- Superficial spreading melanoma<sup>10</sup>
  - Most common type of Melanoma - 70% of melanoma cases
  - The survival rate: 95% and rising
- Nodular melanoma<sup>11</sup>
  - It accounts for 15% of all cases
  - Normally occurs around the age of 50.
- Lentigo maligna melanoma<sup>12</sup>
  - Increases with age and often found in areas that are exposed to the sun
  - Occurs in 13% of cases



# Types of Melanoma

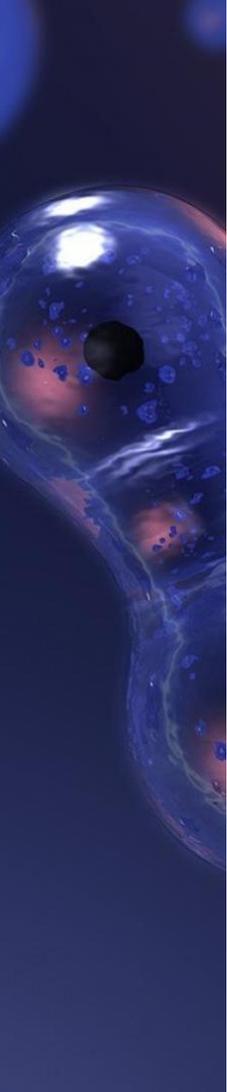
- Hidden Melanomas:
  - Acral-lentiginous<sup>13</sup>
    - More common in those with darker skin: 70% -African Americans and 46% -Asians
    - Mainly occurs in the nail beds, palms, and soles
    - 2-3% of cases
  - Mucosal melanoma<sup>14</sup>
    - 1.4% of all melanoma and 14 percent for 5 year survival rate
    - Can occur anywhere: respiratory system, genitals, urinary system, or GI tract
  - Ocular melanoma<sup>15</sup>
    - Mainly occurs in the Uvea
    - 3% of cases.

<i>Superficial spreading melanoma</i>	<i>Nodular melanoma</i>	<i>Lentigo maligna melanoma</i>	<i>Acral lentiginous melanoma</i>
			
<ul style="list-style-type: none"><li>- Most Common</li><li>- Flat and irregular in shape &amp; color</li><li>- Shades of black and brown</li></ul>	<ul style="list-style-type: none"><li>- Usually starts as a raised area</li><li>- Dark black/blue or bluish/red</li><li>- Some are not colored</li></ul>	<ul style="list-style-type: none"><li>- Usually occurs in older skin types</li><li>- Commonly on face, neck, arms, etc</li><li>- Abnormal skin areas usually large, flat, and tan with areas of brown</li></ul>	<ul style="list-style-type: none"><li>- Least common</li><li>- Usually found on palms, soles, and even under fingernails</li></ul>

Different types of melanomas<sup>16</sup>

# Signs and Symptoms

- Melanoma : unusual growth on skin<sup>17</sup>
- Nevi or moles can be a predictor of melanoma
- Look for changes in existing moles and new ones<sup>18</sup>
  - A- Asymmetrical moles<sup>18</sup>
  - B- Irregular Bordering for moles<sup>18</sup>
  - C- Changes in color of moles<sup>18</sup>
  - D- The Diameter of the mole<sup>18</sup>
  - E- The “Evolution” of the mole<sup>18</sup>



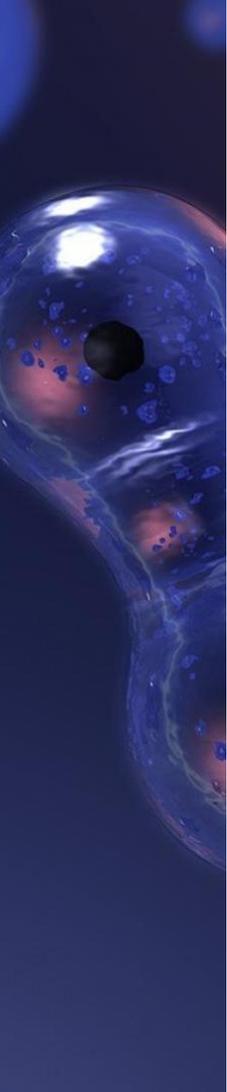
# Causes<sup>19</sup>

- The exact cause of melanoma isn't known.
- Because melanoma is a malfunction of the melanocytes in the skin, scientists suspect a mix of factors.
  - Environment
  - Genetics
  - UV ray exposure



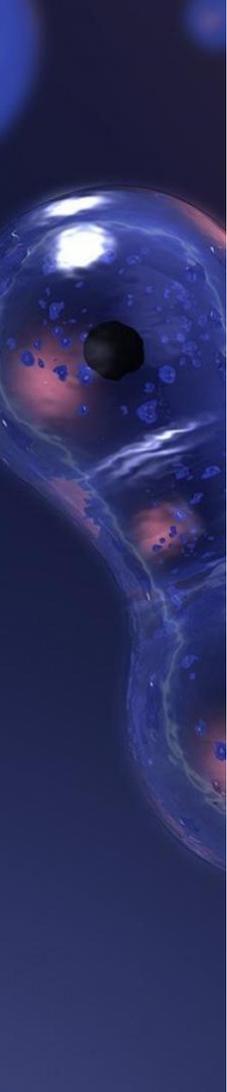
# Genetics

- MC1R gene<sup>20</sup>:
  - Eumelanin: brown or black hair and dark skin that tans easily
  - Pheomelanin: red or blond hair, freckles, light-colored skin, and tan poorly
- V600E mutation or BRAF mutation<sup>21</sup>
  - Protein that signals cell growth
  - Mutation can cause growth of noncancerous mole - can mutate
- CDKN2A gene mutations<sup>22</sup>
  - In 40% of melanoma cases
  - Protein affected is a tumor suppressor
- Familial Melanoma<sup>23</sup>
  - More likely similar environmental factors or melanin type
  - Chromosome 9p13-p22 – possible locus for familial melanoma



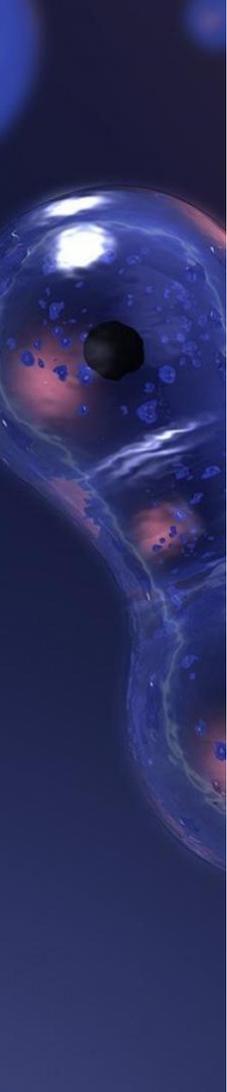
# Risk Factors - Prevention<sup>24</sup>

- Lot of exposure to UV rays
- A history with severe sunburn
- A family history of melanoma
- Those with a weakened immune system whether it be from AIDS or from an organ transplant.
- Benzoyl peroxide, a commonly used chemical to prevent acne, has been shown to increase cases of melanoma within mice populations
- Tanning Salons-BIG NO!(increases the risk of all types of skin cancer)



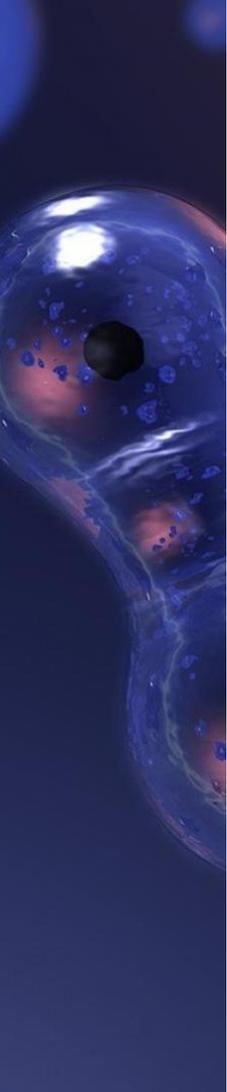
# Demographics

- Lighter skin, eye colors, and hair colors more at risk for melanoma<sup>25</sup>
- Hidden melanomas occurs more in populations with darker pigmentation<sup>25</sup>
- Superficially spreading melanoma more common in younger individuals<sup>26</sup>
- Nodular and lentigo more common in older individuals.<sup>26</sup>
- Mean age of melanoma - 55 years old <sup>25</sup>
- The most common location:
  - Women – legs<sup>25</sup>
  - Men - trunk<sup>25</sup>



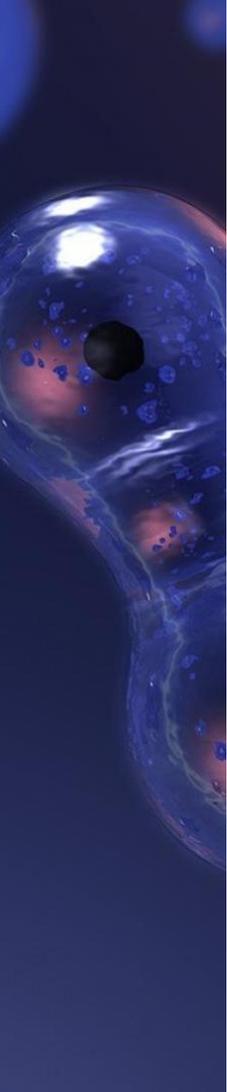
# Diet

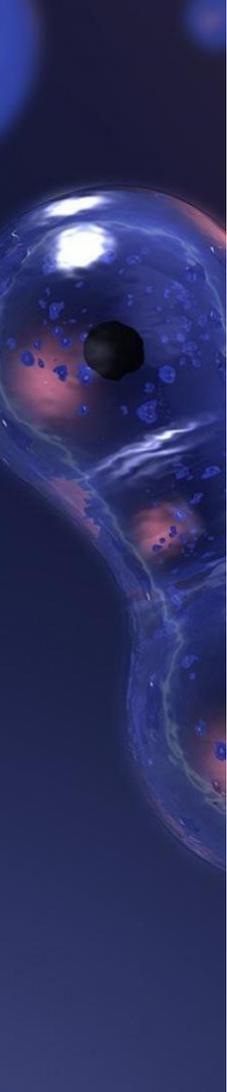
- Diet is an unknown factor in melanoma<sup>27</sup>
- Vitamin D and carotenoids could reduce risk for melanoma<sup>28</sup>
- Anti-oxidant foods leads to 20% reduced risk for melanoma<sup>28</sup>
- Selenium high foods also reduce risk<sup>28</sup>
- Low levels of alcohol also reduces risk<sup>28</sup>
- Overweight men carry a 31% increased chance for melanoma<sup>28</sup>



# Stages of Melanoma<sup>29</sup>

- Localized Melanoma:
  - Stage 0: Abnormal/ brownish cells in the epidermis of skin
  - Stage 1: Spread to at most 2mm of the skin( removable)
  - Stage 2: Spreads deeper into the skin
- Regional Melanoma:
  - Stage 3: Spread to the lymph nodes
- Metastatic Melanoma:
  - Stage 4: Spread to the other organs
    - Lymph nodes (59%), Lungs (36%), Liver (20%), Bones (17%), and Brain (20%)



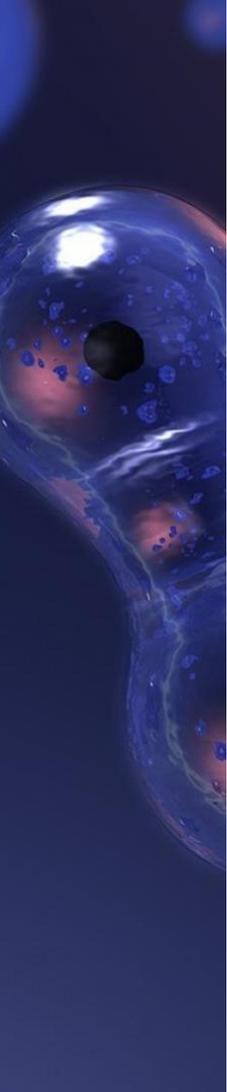


# Treatment History<sup>30</sup>

- **5th century B.C:** Hippocrates writes about melanoma
- **1787:** A Scottish surgeon named John Hunter is the first to remove a melanoma tumor.
- **1844:** Samuel Cooper suggests that benefit is determined by the early removal of the disease.
- **1956:** Henry Lancaster, an Australian Mathematician, makes the first connection between sunlight and the presence of melanoma.
- **1957:** Early forms of Immunotherapy.
- **1966:** Wallace Clark created a standard scale to assess the prognosis of melanoma . Upon previous examination. Also leads to the five year survival rate.
- **1975:** Dacarbazine is approved for stage IV melanoma.
- **1992:** Interleukin-2 is FDA approved.
- **2011: BRAF inhibitors** is FDA approved.

# Surgery

- Varies depending on current stage of melanoma<sup>31</sup>
- Removal of affected area is the main part in all stages<sup>31</sup>
- Surgery is usually used for stage two, to remove the cancerous tumor<sup>32</sup>
- Stage 3 can be difficult to perform surgery but is possible in most cases<sup>32</sup>
- Metastatic melanoma is inoperable<sup>33</sup>
- Types of Surgeries<sup>34</sup>:
  - Wide Excision: For thin melanomas – small operation
  - Amputation: Melanoma is on finger/toe (uncommon)
  - Lymph Node Dissection: Removal of all lymph nodes near area of melanoma



# Chemotherapy<sup>35</sup>

- Not the main source of treatment for melanoma
- Drugs used for melanoma chemotherapy:
  - Dacarbazine
  - Temozolomide
  - Cisplatin
  - Paclitaxel
  - Carboplatin
- Isolated Limb Perfusion: a way of giving chemotherapy at an advanced stage of melanoma constricted to an arm or leg



# Radiation Therapy<sup>35</sup>

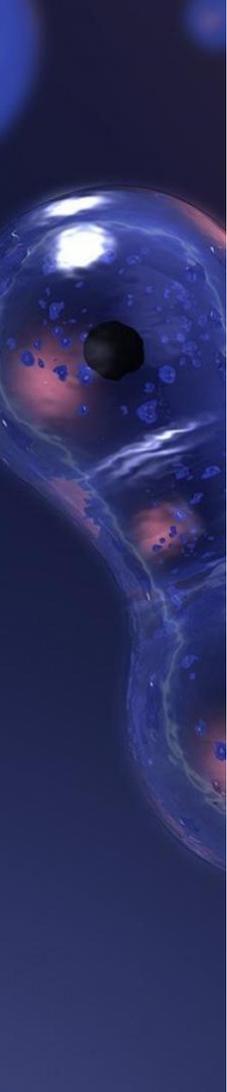
Radiation is used to kill cancer cells

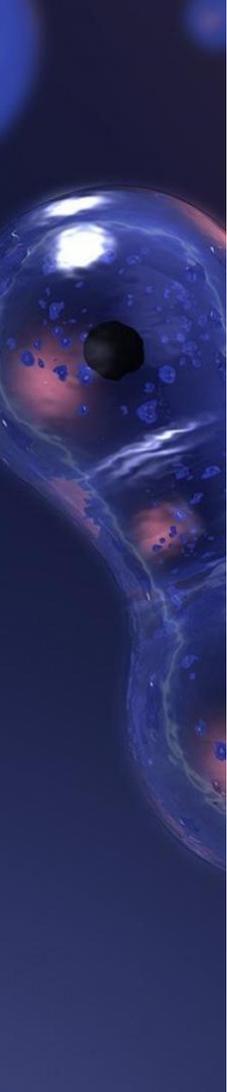
- Radiation therapy is only useful in the early stage of Melanoma
- Used for types of melanoma where surgery is not an option.
- Even if it can't be cured, radiation therapy relieves pain
- Radiation is used to denature the cancer cell's DNA
- It uses as many as three to four beams to target one point with tremendous accuracy at different angles
- It leaves the normal tissue almost unharmed, but destroys the tumor
- Symptoms: higher level of fatigue and pain in the area of the target.
- Radiation therapy and immunotherapy are often combined to treat patients with metastatic melanoma.



# Targeted Therapy<sup>36</sup>

- Hinders the abnormalities of molecules within cancer cells that maintain their growth
- Purpose: Slows down the growth of melanoma cells
- Blocks the function of the MEK protein and mutation of the BRAF protein.
- Drugs used in targeted therapy:
  - Encorafenib (Braftovi) + Binimetinib (Mektovi)
  - Dabrafenib (Tafinlar) + Trametinib (Mekinist)
  - Vemurafenib (Zelboraf) + Cobimetinib (Cotellic)





# Immunotherapy<sup>37</sup>

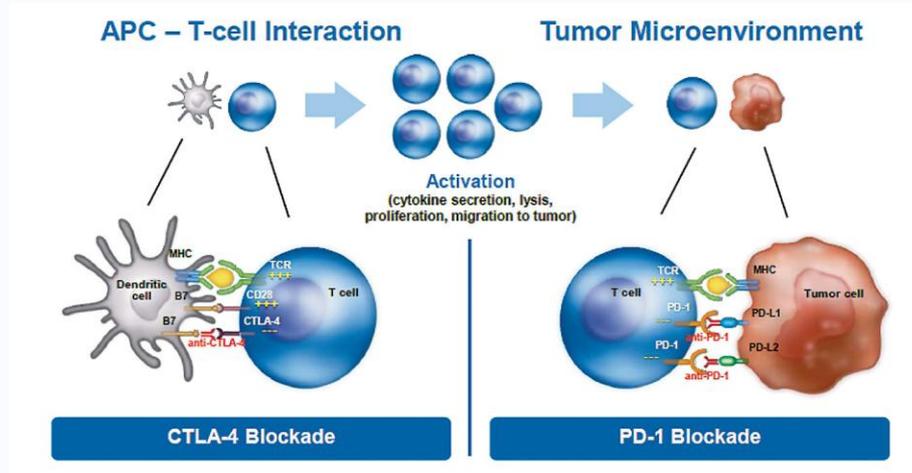
- Immunotherapy is a cancer treatment that assists the immune system fight cancer
- New drugs have been introduced to help the immune cells recognize cancer cells and eradicate them by stopping/slowing down the growth of cancer cells and prevent the spread to other parts of the body
- You can stimulate your immune system to help fight against cancer

**Immunotherapy Vaccines:** vaccines that utilize specific protein allowing the body to stimulate the immune system. In the recent decades, we have found certain vaccines that contain protein very specific for cancer cells.

# Immunotherapy<sup>38</sup>

## Checkpoint blockade Inhibitors:

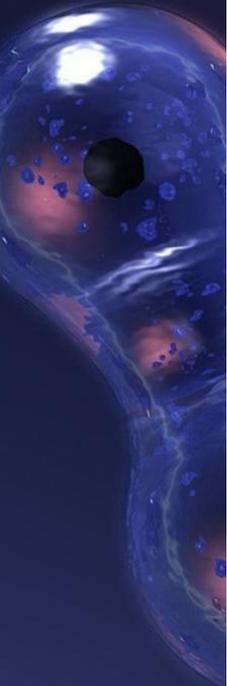
- Cancer cells have checkpoints in the immune system which works as signals.
- The mechanism of action of checkpoint blockade inhibitors is to disrupt cancer cell's "signals" allowing the immune system to attack



Checkpoint Blockade inhibitors help the T-cells identify the cancerous cells.<sup>40</sup>

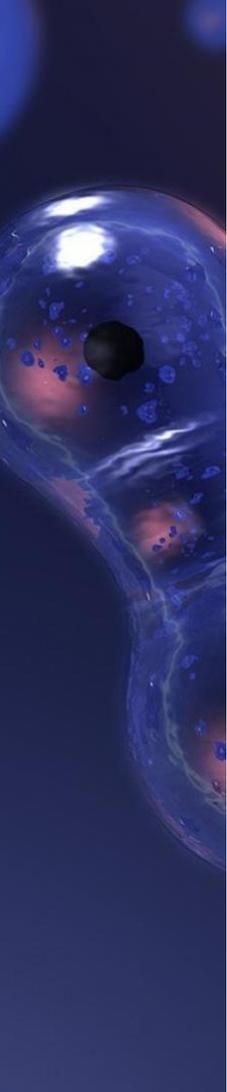
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