# Sending Mixed Signals:

A study of the Melanocortin-One-Receptor

By Whitney Wells, Savannah Simmons, and Bella Kloha

### Skin Pigmentation Variation

Skin pigmentation varies across ethnically diverse humans



#### Eumelanin VS Pheomelanin

Eumelanin

**Brown/Black** 



Protection from Ultraviolet Radiation (UVR)



Pheomelanin Red/Yellow

Mammalian Skin and Hair Color Arises from Melanin Pigments

# Tanning VS Burning







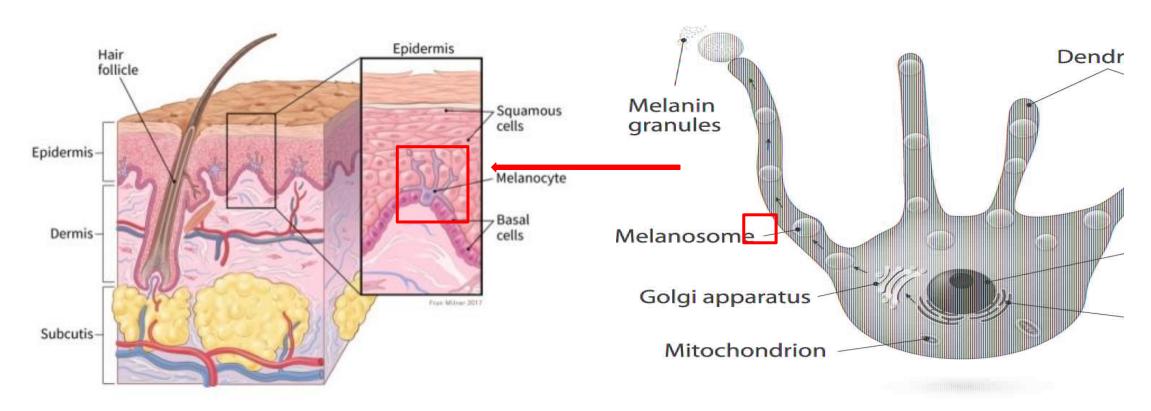
#### Skin Cancer





Skin cancer is the most common form of cancer according to World Health Organization (WHO).

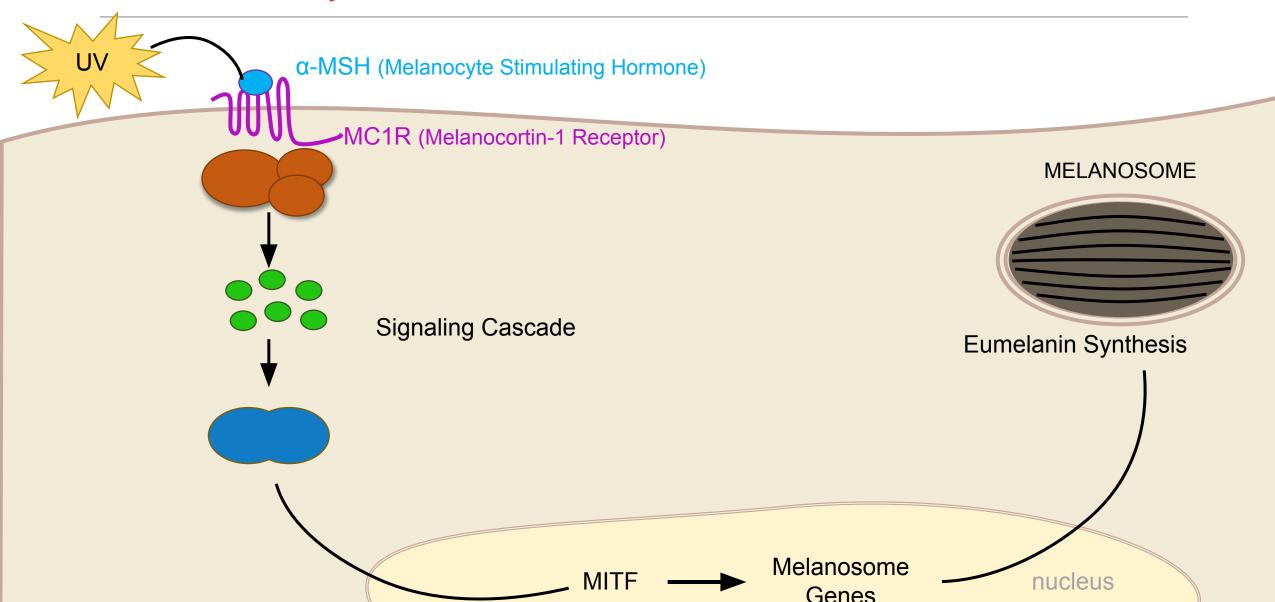
### Melanocytes, Melanosomes, and Melanin, Oh My!



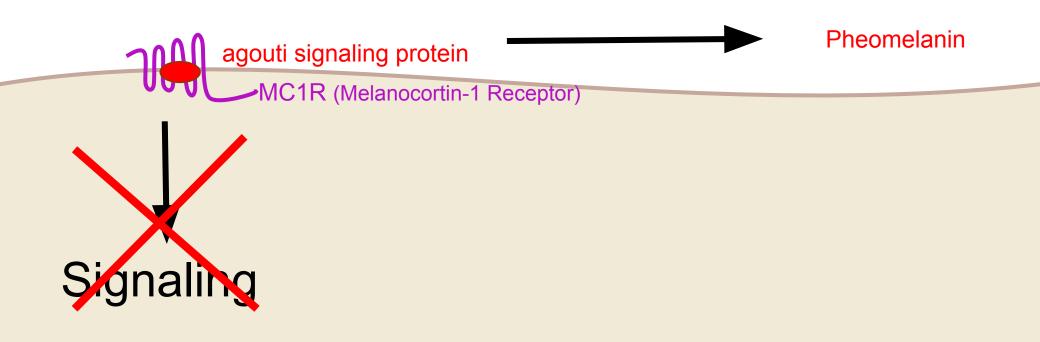
https://www.cancer.org/cancer/melanoma-skin-cancer/about/what-is-melanoma.html

http://www.thecosmeticchemist.com/education/skin\_science/know\_your\_skin\_cells\_iii\_the\_melanocytes.htm

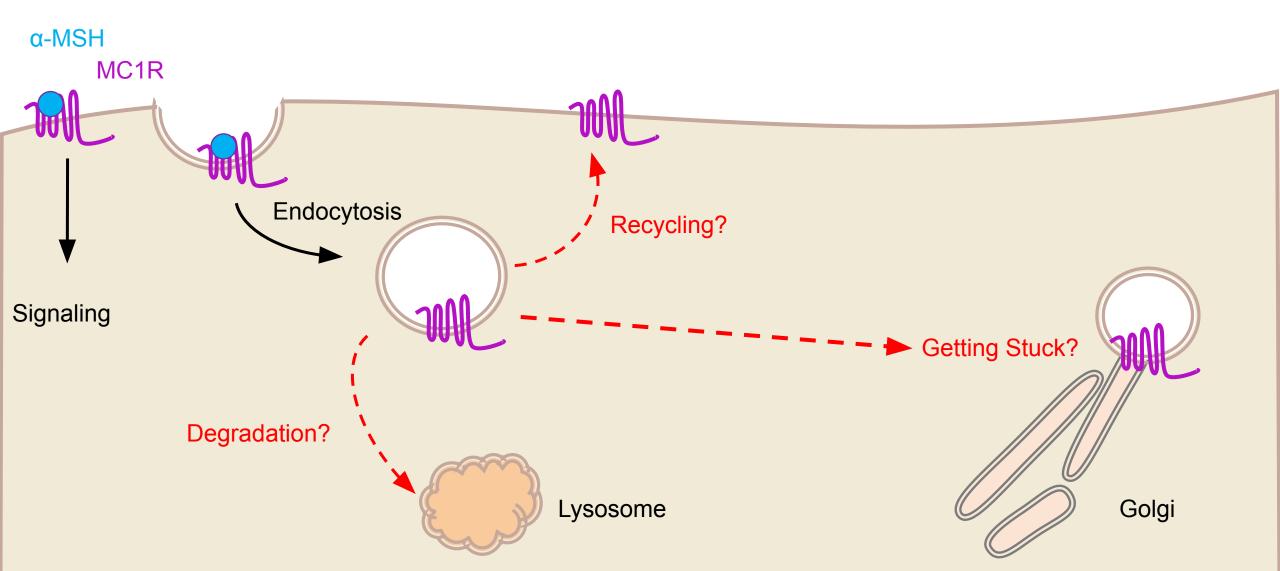
### **Eumelanin Synthesis**



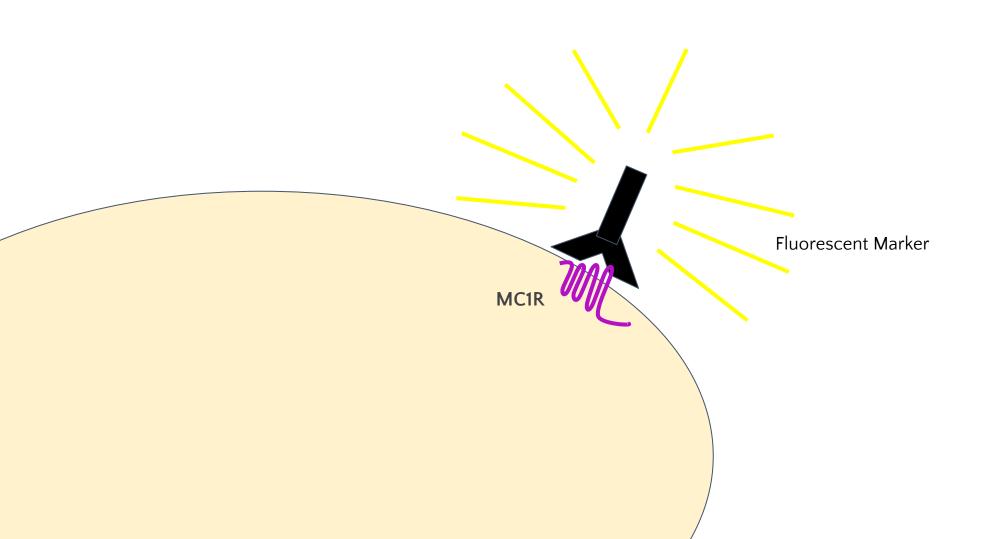
# Pheomelanin Synthesis



## What happens to MC1R?

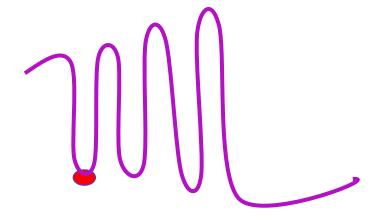


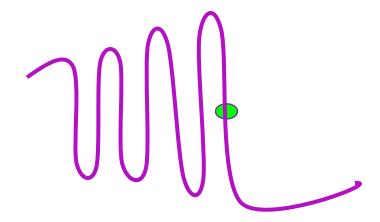
# How does MC1R Trafficking Affect Surface Signals?



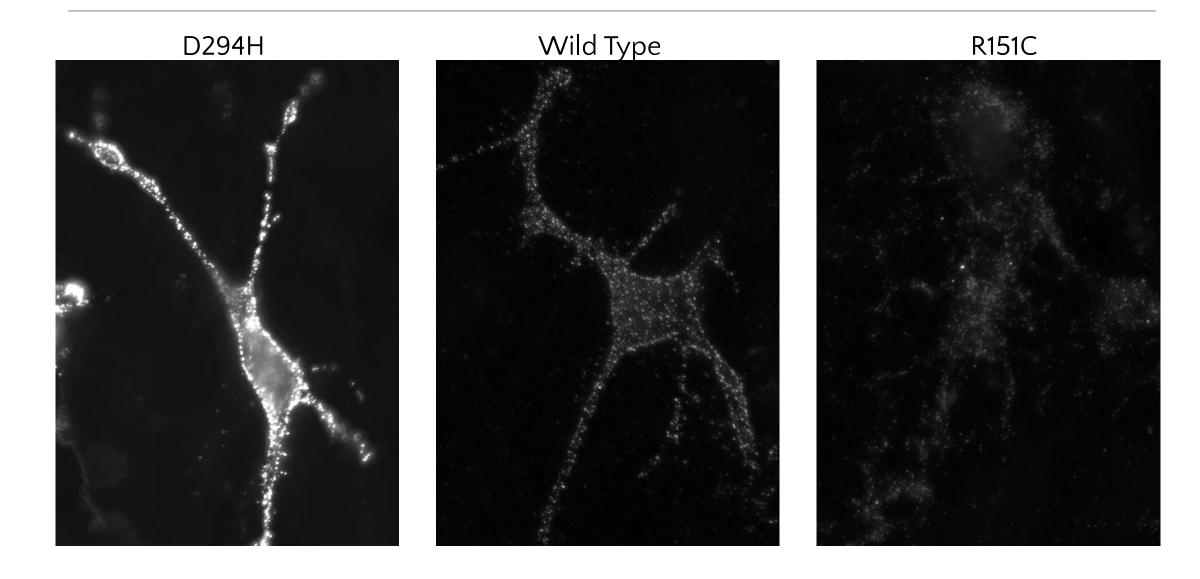
#### MC1R Mutations in HEK Cells

- Both mutants are associated with red hair, fair skin, and an increased risk of skin cancer (melanoma)
- R151C shows lower surface levels
- D294H shows higher surface levels

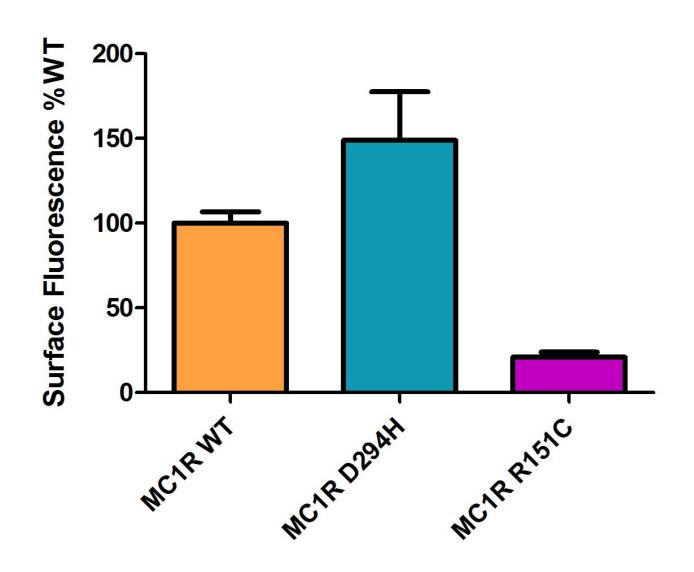




### How do Mutations in MC1R affect Surface Levels?



### How do Mutations in MC1R affect Surface Levels?



#### **Future Directions**

- Is endocytosis required for MC1R signaling to increase expression of pigment genes?
- How do these mutations affect receptor localization within the cell and how does this impact signaling?
- Could MC1R signaling occur in other locations in the cell besides the cell membrane?

### POP QUIZ!!!

### Which of the following should you be doing this summer?

- A. Sun-burning
- B. Sun-bathing
- C. Sun-tanning
- D. None of the above- WEAR SUNSCREEN!!!!





Nawrat, Allie. Skin Cancer Awareness Month: Overcoming Drug

Resistance in Skin Cancer. 8 May 2019, www.pharmaceutical-technology.com/features/skin-cancerprevention-treatments-drug-resistance/.

"Skin Cancer Facts & Statistics." The Skin Cancer

Foundation, The Skin Cancer Foundation, 10 July 2020, <a href="https://www.skincancer.org/skin-cancer-information/skin-cancer-facts/">www.skincancer.org/skin-cancer-information/skin-cancer-facts/</a>.

Dr. Shanna Bowman

Murdock Charitable Trust

Professors Dorothy Bennett and Elena Sviderskaya at St George's University in London

Professor Gregory Barsh at Hudson Alpha Institute and Stanford University

Professor Michael Marks at The University of Pennsylvania