

GINGERLY APPROACHING PAIN

A CASE STUDY ON THE MC1R PROTEIN AND HOW ITS MUTATION CHANGES MORE THAN JUST HAIR COLOR.

Introduction

In the past 10 years, there has been rising debate over whether or not individuals with red hair color (RHC) have increased tolerance to anesthetics and opioids.

Learning Objectives:

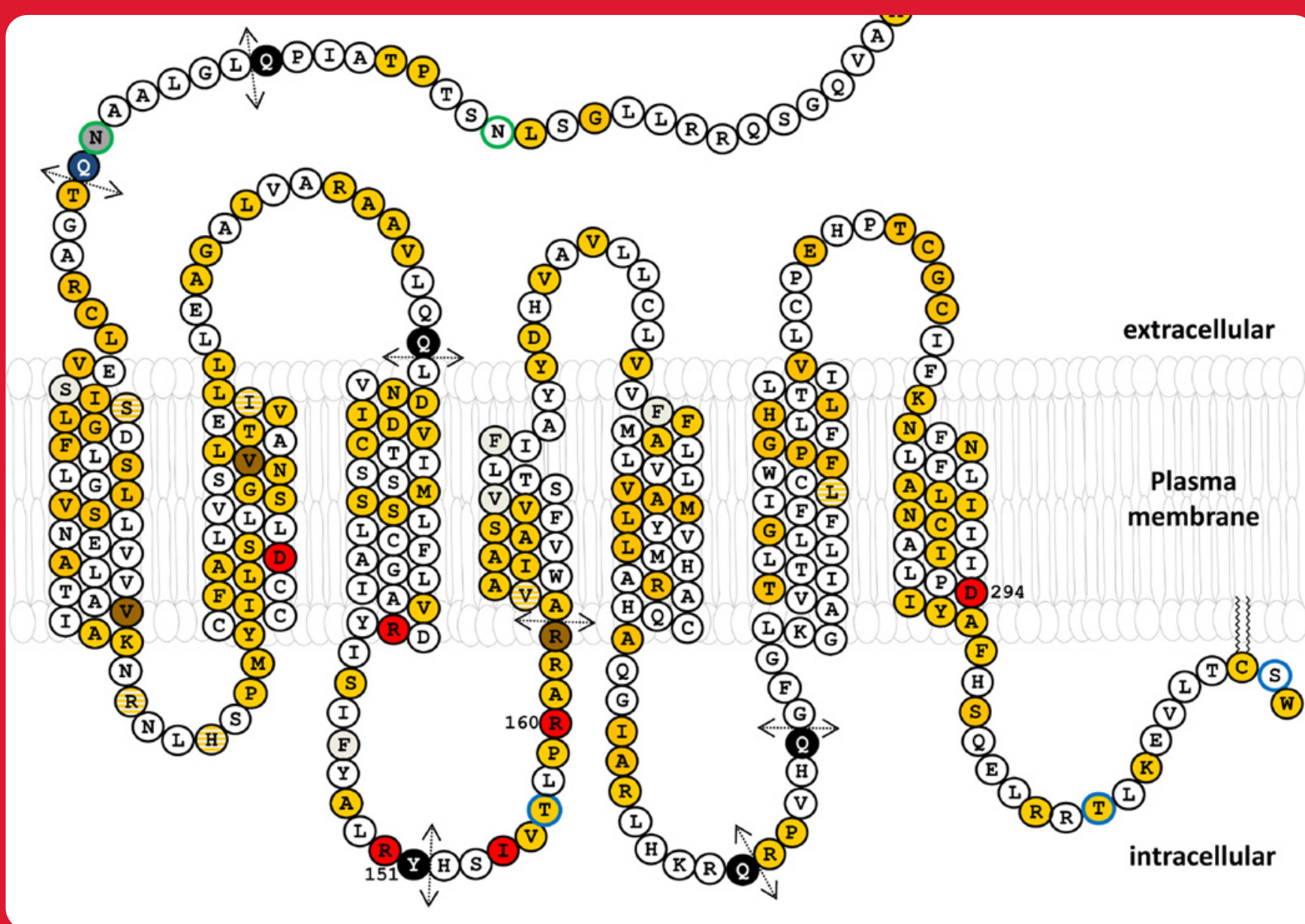
- Investigate the structure of wild type MC1R compared to RHC variant MC1R structures
- Study the mechanism of action for opioids and G-protein-coupled receptors (GPCRs)
- Analyze the downstream effects in the MC1R signaling and opioid receptor pathways
- Make connections between protein structure and function within a signaling pathway
- Critically analyze the available data
- Brainstorm future studies and research that should be done



During ballet rehearsal, Poppy developed a painful ingrown toenail. It had to be surgically removed, but when a single dose of local anaesthetic had no effect on Poppy's pain, the nurse had to administer a second dose. Poppy wonders if her increased tolerance to anesthetics has something to do with her red hair...

Background

Several studies in humans and mice have been conducted measuring the effects of RHC on opioid tone and anesthetic tolerance, and the results have been conflicting. Consequently, news articles and blog posts on this topic have differing opinions and recommendations being posted for the public. This debate stems from research surrounding the melanocortin-1 receptor (MC1R) which is responsible for producing eumelanin, dark pigment, in the skin. It is common for light-skinned and redheaded individuals to have polymorphisms in the MC1R gene, which reduces the activity of MC1R, leading to decreased levels of eumelanin production in the hair and skin as well as increased levels of pheomelanin production, red-yellow pigment, in the hair.



The most common amino acid substitutions for RHC individuals are colored in red and labelled with their corresponding position.

The Proteins

A study published in April 2021 has supported connections between RHC MC1R variants and disrupted downstream signaling in GPCR and opioid receptor pathways. A functional MC1R is required for effective synthesis of eumelanin whereas when an individual has a RHC variant, their MC1R is dysfunctional, showing decreased eumelanin in their skin and increased pheomelanin in the hair. Understanding the structure of MC1R is important to hypothesizing the downstream effects of RHC individuals with MC1R polymorphisms and their tolerance to analgesics and anesthetics. The secondary structure of MC1R, shown on the right, contains the most common amino acid mutations for RHC variants, colored in yellow.

