**Opioid Oppression**
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**ABSTRACT**
Opioid abuse is now a leading cause of accidental death in North America, yet opioids remain the most prescribed drugs in the United States. Opioid drugs are powerful painkillers, but their adverse side effects—addiction, tolerance, and extreme constipation—severely limit their medical use. Chris Cunningham, Ph.D., is working to create a drug or drugs that will bind to μOR without causing tolerance. μ-opioid receptor (μOR) is one of the G protein-coupled receptors (GPCR) traversing the cell membranes of primarily neuronal cells in the brain and spinal cord. μOR is found on the outside of presynaptic cells in the brain. Normally, endorphins (such as beta-endorphins, which are classified as opiates) bind to the receptor, which results in a release of ions and a cascade to effecter proteins (such as ion channels), ultimately leading to various reward circuit oriented behaviors and analgesic effects. Other opioids (natural derivatives, e.g. morphine), opioids (synthetic derivatives), and similar compounds instead bind to μOR, which prevents normal endorphin binding activity. μOR is a single chain protein with 8 helices. Its active site is on the inside of the protein, binding involves 14 residues. Interactions between the other helices, disulphide bond (Cy510-Cys217), and salt bridge (Arg165-Asp164) stabilize the protein structure. Polar binding between Thr279-Ile226 maintains the protein in the inactive state. Lys123 covalently binds to both morphine (agonist) and beta-FNA-fentanylamine hydrochloride (antagonist). Currently, Chris Cunningham Ph.D., has investigated naltrexone which partially excites the μ-active site while also binding to a σ-OR receptor slightly reducing tolerance. Other chemicals need to be investigated that will provide an effective analgesic while eliminating all side effects. The Wauwatosa West SMART (Students Modeling a Research Topic) Team used 3D printing technology to study EPTF OF OPIOIDE DRUGS IN THE U.S.
Opioids are the most prescribed drugs in the United States. While they are highly effective painkillers, they are also extremely addictive. The CDC calls the addiction to prescription pain medications in America an epidemic. Every year, over 11,000 people die from opioid-related poisonings. In addition, the impact of addiction cost the U.S. society $53 billion per year.

**MODEL INFORMATION**
- Sheets: Dodgerblue
- Helices 1, 2, 3, 4, 7, 8: Darkblue
- Helix 5 (contain the active binding site): Turquoise
- Helix 6 (contain the active binding site): Chartreuse
- Hydrogen Bonds: Skyblue
- Strips: White
- Cy510-Cys217 (Disulphide bridge): Limegreen
- Thr279 (stability for inactive protein): Yellow
- Ile226 (stability for inactive protein): Yellow
- Arg165 (salt bridge): Darkgold
- Asp164 (salt bridge): Darkgold
- Lys123 (termed covalent bonds to ligands like opioids): Red
- His257 (interacts exclusively with morphine): Orange

**CONCLUSION**
Opioid abuse is one today’s most pressing issues, costing billions of dollars and thousands of lives each year. Along with painkilling properties, opioids have serious side effects that can lead to death yet remain one of the most prescribed drugs in the U.S. Already in use, Narcan, or naloxone, acts as an antagonist to block the action of opioids following an overdose. In the future, scientists such Chris Cunningham Ph.D. are working to create a drug or drugs that can activate the μ-receptor to provide pain relief, while deactivating the σ-receptor to eliminate the building of tolerance.