ABSTRACT
Asthma is a chronic airway disease that inflames and narrows the bronchi and bronchioles, thus making breathing very difficult. The absolute etiology of asthma is unknown but hereditary, food and environmental allergens seem to play significant roles in its onset. Unfortunately, there is no cure for asthma. Management focuses on treating symptoms in acute events and avoiding known triggers. The standard treatments are bronchodilators and steroids.1

CASE STUDY
Patient BC is a 7-year-old male who presents to the ER with severe respiratory distress symptoms consistent with a severe asthma exacerbation. Upon assessment, the patient has a fast heartbeat, is sweating, and has an E:T ratio of 1:4 inspirations to expiration. An X-ray shows inflamed and severely constricted lungs. When asked, the mother confirms that symptoms began the previous night and the patient’s symptoms have not responded to his albuterol metered dose inhaler. The patient is given high dose albuterol via a nebulizer treatment over 1 hour repeated twice. Staff worries that administration of albuterol may worsen the patient’s tachycardia, or fast heartbeat.

INTRODUCTION
Epinephrine is the body’s natural ligand and full agonist at the β2-receptor, which exists in an inactivated and activated state2. The inactivated state predominates3. The activated β2-receptor leads to a complex cell-signaling pathway resulting in an increase in cAMP and intracellular calcium levels. This reduction of calcium leads to relaxation of the bronchioles and subsequent inhibition of intracellular calcium release. This reduction of calcium leads to relaxation of the bronchioles and subsequent inhibition of intracellular calcium release.

MOLECULAR STORY
The β2-receptor is a G-protein coupled receptor (GPCR), which is a transmembrane receptor2. β2-receptors in the lungs. Research has shown statistically significant reductions in tachycardia with this enantiomeric3,5. Improvements to the albuterol structure should not alter the catechol ring structure, amine group, or hydroxyl group.

HOW ALBUTEROL BINDS3
Five critical amino acids on the binding site of the receptor appropriately align with the corresponding sites on the albuterol molecule.

HOW ALBUTEROL FUNCTIONS
• Reaches the β2-adrenergic receptors in the lungs through inhalation of the medication
• Sympathomimetic response of relaxing smooth muscles and relieving bronchospasm
• Side effects caused by stimulation of β2-adrenergic receptors in the heart include racing heart and jitters4

THE (R)-ALBUTEROL MOLECULE2
• Three domains that interact with amino acids in the binding site:
  - Secondary: amine: serves as a hydrogen bond donor with Asn329 and as a hydrogen bond acceptor with Asp121
  - Hydroxyl group: interacts with Asp121 as a hydrogen donor and with Asn329 as a hydrogen acceptor
  - Catechol ring: interacts with three different amino acids
• π-π interaction between the catechol ring and Phe307 of the receptor
• Van der Waals interactions with the catechol ring and the neighboring chains in the receptor
• Hydrogen bond between para-hydroxyl group on catechol ring and Ser211
• Hydrogen bond between meta-hydroxymethyl group on catechol ring and Asn310
• (R)-albuterol acting as the hydrogen donor in bothhydroxyl reactions

FURTHER RESEARCH
Albuterol causes off-target effects on β2-receptors in the heart leading to tachycardia. Future research should identify an antagonist to reduce or prevent tachycardia after albuterol administration. One study successfully utilized magnesium sulfate to prevent tachycardia after administration of salbutamol7. Another option is to utilize the R enantiomer, levalbuterol. Levalbuterol has higher affinity for the β2-receptors in the lungs. Research has shown statistically significant reductions in tachycardia with this enantiomeric3,5. Improvements to the albuterol structure should not alter the catechol ring structure, amine group, or hydroxyl group.

SUMMARY
β2-agonists dilate bronchioles resulting in increased air flow. Some adverse effects associated with albuterol are tachycardia, tremor and agitation5. However, the benefits far outweigh the adverse effects as an asthma attack can be life-threatening1.

The staff pharmacist recommended albuterol to the medical team because it causes bronchial dilation and airway relaxation, thus improving the patient’s ability to breathe. However, albuterol can exert off-target effects on other beta receptors at higher doses, so the minimum effective dose should be used3,10. Albuterol is not recommended as a daily asthma control agent. For this reason, the patient will need appropriate asthma control medications before being discharged from the hospital9.

Upon discharge the patient should be counseled on management of asthma. A long acting β2-agonist like salmeterol should be prescribed with a corticosteroid. Albuterol should be prescribed as a rescue inhaler. A leukotriene pathway inhibitor may also be prescribed11. If the patient is compliant and their asthma is well controlled, they should not have to use their albuterol rescue inhaler often. The patient should be educated about asthma attack triggers and the importance of medication compliance in order to prevent future attacks.

REFERENCES