Prostate cancer is the most common cancer in men, after lung cancer and colorectal cancer. It is the second leading cause of death from cancer in men. It is a disease in which malignant cells form in the tissues of the prostate with symptoms such as frequent urination, trouble starting the flow of urine and emptying the bladder completely, pain or burning while urinating, blood in the urine or semen, a pain in the back, hips, or pelvis that doesn't go away. Aggressive prostate cancer is treated conventionally by chemical or surgical castration because cancer cells need hormones to grow. This slows down progression of the disease, but most hormone dependent cancers become resistant to treatment after a couple of years. It happens because cancer cells find a way to supply the flow of hormones on their own. They also become more efficient in utilizing the little hormones they have available. Nevertheless, they still show reliance upon hormones.

When cancer advances to metastasis stage, patients are faced with only ca. 50% one-year survival rate. Metastatic castration-resistant prostate cancer is especially difficult to treat due to resistance to conventional therapy. This is where CYP17A1 inhibitors come in. CYP17A1 is an enzyme that is responsible for production of androgen hormones. This enzyme operates in different cells whether they are cancer cells or not. By stopping this enzyme from functioning, a very efficient way of stopping hormone production can be achieved which in turn results in cancer starvation. So far there is only one approved drug capable of achieving this. This drug called abiraterone has been introduced in 2011 and so far, is the only drug that acts as the enzyme inhibitor. Unfortunately, this medicine is far from perfect. First, it prolongs a patient's life by only 4 months. Secondly, the recommended daily dose is 1000 mg which is rather high. And finally, it has many side effects, mainly associated with its steroidal structure, such as hypertension, hot flush, decreased potassium levels in serum, headache, and liver damage (due to high dose). No one seems to have found anything better so far. Another major problem associated with this drug is the resistance which greatly limits its sustained use. After some time, the drug loses its efficiency (hence its limited prolonged life period) and patients eventually succumb to the disease.

Researchers found that of the reasons why the drug becomes ineffective is another enzyme called AKR1C3. Now if only we could stop these enzymes from feeding cancer, we could have a potentially useful weapon in the battle against it. My project addresses this problem by trying to find new, better drugs. This will be achieved by means of designing molecules based on what we currently know about CYP17A1 and AKR1C3 enzymes using scientific computer programs. These programs are capable of simulating interactions of a drug with its targets (CYP17A1 and AKR1C3). Thus, this allows for understanding how to design a molecule with superior properties compared to the existing ones. Once the molecule is designed then comes the chemist who must make this molecule in a lab. This is the next step of this project and the process is called synthesis. It requires careful selection of chemical reactions to obtain the desired compound not only in sufficient quantity but also of satisfactory purity. Usually, many similar compounds are designed and synthesized to provide for the best chance of finding the one with the desired properties. Finally, the obtained compounds need to be tested to ascertain if they in fact exhibit the expected properties. There are many different levels of tests that can be applied but this project will explore the most relevant ones. The most important one is the ability to inhibit the enzymes activity. This test will be performed on the isolated enzymes and in the whole cells. Studying both these systems is important because it will broaden understanding of the compounds made. For instance, a compound can be active on an isolated enzyme yet in whole cells display diminished activity, possibly suggesting potential problems in reaching the cell's interior. This consequently sends a signal that design is on the right track, yet some modifications are needed to allow better cell permeability. Lastly, compounds will be tested for their physicochemical properties. These are also important because drugs do not magically teleport to the cancer site but need to be taken by patients (e.g., orally or by injection) and prior to that they need to be formulated. Tests like these will determine whether any modifications are needed to improve drug-likeness of the designed molecules. Ultimately, compounds with the best overall properties can be developed further to eventually help cancer patients. They can also prove to be useful as tool compounds to study prostate cancer contributing greatly to the scientific community focused on cancer research.