Cancer treatments have advanced significantly in recent years, particularly with therapies targeting specific processes in cancer cells. One such strategy involves using CDK4/6 inhibitors, which are drugs that block a key part of the cell cycle, causing cancer cells to stop growing and enter a state called senescence. These therapies have become a cornerstone of breast cancer treatment and show promise for other types of cancer, including throat cancers. By halting cell division and forcing cells into senescence, CDK4/6 inhibitors not only suppress tumor growth but also make cancer cells more vulnerable to the immune system. However, not all patients respond to these therapies, and in some cases, cancer cells develop resistance over time, reducing the treatment's effectiveness.

Our research focuses on understanding how environmental toxins, specifically those found in food, might contribute to this resistance. One such toxin is Alternariol (AOH), a chemical produced by certain molds that can contaminate food such as grains, fruits, and vegetables. While strict regulations limit the levels of some toxins in our food, AOH is not yet fully regulated despite its potential harmful effects. Early studies suggest that AOH can interfere with important cellular processes, including those targeted by cancer therapies. For instance, AOH has been shown to cause oxidative stress, DNA damage, and disruptions in cellular pathways. These effects are particularly concerning because they may enable cancer cells to evade the effects of CDK4/6 inhibitors, continuing to grow despite treatment.

Our project investigates whether exposure to low levels of AOH could reduce the effectiveness of CDK4/6 inhibitors. This research is particularly relevant for patients with breast cancer. It is one of the most common cancers globally, and while CDK4/6 inhibitors have revolutionized its treatment, there are still gaps in understanding why some patients do not respond as expected. We aim to answer three key questions:

1. How does AOH disrupt the process of therapy-induced senescence?
2. Does AOH contribute to the acquisition of therapeutic resistance to CDK4/6 inhibitors?
3. Does AOH exposure make cancer treatments less effective in experimental models?

In our lab, we will conduct experiments on cancer cells grown in dishes and in specialized animal models. By exposing these cells to both CDK4/6 inhibitors and AOH, we aim to study how the toxin changes the cancer cells' response to treatment. We hypothesize that AOH might allow cancer cells to bypass senescence, enabling them to continue dividing and resisting the effects of the drugs. This process likely involves complex mechanisms, including changes in the cell cycle, stress responses, and interactions with the tumor environment.

We will also use animal models to better understand how AOH exposure impacts the overall effectiveness of CDK4/6 inhibitors in a living system. These studies will involve examining not just tumor growth, but also the broader tumor microenvironment, which includes immune cells and surrounding tissues. For example, we plan to investigate whether AOH affects immune cell infiltration into tumors or alters the levels of signaling molecules that influence tumor behavior.

Understanding the role of environmental toxins in cancer treatment resistance could lead to better outcomes for patients. If we find that AOH significantly weakens cancer therapies, it could prompt changes in food safety regulations or inspire new therapeutic approaches to counteract these effects. For example, identifying patients at higher risk of exposure to AOH could lead to personalized treatment strategies or dietary interventions to minimize risk. Additionally, our work could pave the way for developing drugs that block the harmful effects of AOH, ensuring that therapies like CDK4/6 inhibitors remain effective.

Ultimately, this research highlights the importance of considering environmental factors in cancer treatment. While much attention has been given to genetic and biological factors influencing therapy resistance, the role of diet and environmental toxins is an emerging field with significant implications. By addressing these hidden risks, we aim to improve cancer treatment outcomes and provide new insights into how to protect patients from unseen environmental challenges.