

2024 NJABR High School Essay Contest
3rd Place

Cecelia E.

The Pennington School
Pennington, NJ

Zoladex: Mimicking the Body's Natural Signaling to Eradicate Cancer

In April of 2016, my family lost my paternal grandfather to prostate cancer. And while the loss of his presence in our lives was devastating and pains us still to this day, I can now, eight years later, fondly reflect on the years I was able to spend with him. When I reached high school, I began to learn from my parents about the nature of my grandfather's cancer. Contrary to my beliefs, it was not sudden—in fact, he had been diagnosed with prostate cancer before I was born—yet, due to the innovations of biotechnology, he was able to keep his cancer at bay for fifteen years. Knowing this, I can now see how significantly biomedical research extended his life, and fully appreciate the precious moments it allowed me to share with him.

My grandfather was diagnosed with low grade and androgen hormone dependent prostate cancer in 2000, eight years before I was born. He was then prescribed Zoladex, a polymeric controlled release system for the delivery of goserelin, a luteinizing hormone blocker, to manage the cancer's progression. Over the past few years, I was led by an interest in biomedical technology to explore the mechanisms by which Zoladex acts to limit the progression of prostate cancer, as well as its preclinical development.

Goserelin was initially developed as a systemic peptide analogue to gonadotropin releasing hormone (GnRH) which binds to GnRH receptors on the pituitary gland¹. This results in internalization of the GnRH receptors, which initially causes an increase in luteinizing hormones (which can stimulate hormone dependent prostate cancer). However, prolonged exposure to GnRH or goserelin can result in desensitization of the GnRH-dependent production of luteinizing hormones, suppressing the release of pro-cancer hormones².

To enable the controlled release of goserelin over time, thereby inducing the desensitization of GnRH receptors, the goserelin is incorporated into a polymer matrix, composed of poly(lactic-co-glycolic acid) (PLGA)³. PLGA contains a series of ester bonds that are naturally biodegradable, resulting in water soluble byproducts including carboxylic acids and alcohols.

Researchers used healthy male and female Sprague-Dawley rats to determine the release kinetics of this PLGA-goserelin matrix and the resulting impacts on testosterone and other hormones involved in endocrine signaling⁴. Using this animal model, which adhered to the ethical requirements established by the the Institutional Animal Care and Use Committee (IACUC), researchers found that the release of the drug can be extended to approximately twenty-one days. Using this model, they further evaluated the toxicity of PLGA, its byproducts, and goserelin at various doses to establish safe and effective doses for human clinical trials.

The advancement and approval of Zoladex might have slowed considerably without the use of animal testing. Due to genetic similarities between mammals, such as rats, and humans, their place in testing can be indispensable. However, this use of animals as test subjects is also greatly controversial—especially with respect to moral and ethical codes—which is why it is vital that all animal tests are completed in accordance with the IACUC ethical requirements⁵.

Once these animal studies were conducted and demonstrated that Zoladex was safe and effective at affecting endocrine signaling, the therapy advanced to human clinical trials in healthy and diseased populations. One of the key findings of the Phase III trials was that Zoladex produced survivorship and safety profiles similar to that of the standard of care, an invasive resection surgery. These extensive studies eventually resulted in the approval of Zoladex for the treatment of hormone-dependent cancers, including breast and advanced stage prostate cancer.

For fifteen years following his initiation of Zoladex, my grandfather was able to fend off his cancer. During those fifteen years, he was able to attend my parents' wedding, see the birth of each of his grandchildren, and make irreplaceable memories with all of us. The benefit that this treatment brought to his life was truly priceless. I am endlessly grateful for the advances of biomedical research in the treatment of cancer through Zoladex. Without those advances, I may not have been able to experience my childhood with my grandfather.

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