Development of a Curcumin-Based Pentraxin Conjugate for Targeted Cancer Therapy

Man, Athena (School: Central Bucks High School East)

In 2025, an estimated 2,041,910 new cases of cancer will be diagnosed in the United States, and 618,120 people will die from the disease (NIH, 2025). It is a leading cause of death worldwide, and the number is still on the rise. While current therapeutic options do exist, such as chemotherapy or radiation, they both cause severe side effects by damaging healthy cells in addition to cancerous cells. Consequently, a primary objective in immune-oncology research is to develop an anti-cancer therapeutic that is more selective for cancer cells, minimizing damage to healthy tissue, and reducing side effects. Curcumin, the active compound found in turmeric, has been discovered to induce apoptosis only in cancerous cells. To deliver the payload of curcumin to the phospholipid bilayer, a derivative was created by synthesizing an activated NHS ester, allowing it to bind to the surface lysines found on a pentraxin. A pentraxin is a 5-member protein ring that is part of the innate immune system, serving as a protein chassis. By utilizing a naturally occurring protein, the chances of the human body rejecting treatment will be reduced. Bound to the curcumin pentraxin conjugate is a VHH antibody engineered to bind the Kv10.1 ion-gated channel. This ion-gated channel is highly expressed in cancerous cells and is rarely expressed in regular cells, making it an effective target. The curcumin derivative was synthesized with a 27.6% yield, confirmed using analytical methods. Protein expression in mammalian cells was achieved but yielded low amounts, indicating a need for optimization. Preliminary conclusions support the proof of concept; however, further testing will be necessary. These factors, when combined, could potentially create an effective anti-cancer therapeutic.

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