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Prostate Cancer: Abstracts

Nanocell Application to Prostate Cancer

Over 234,000 men in the United States will be diagnosed with prostate cancer this year. It is the second leading cause of cancer-related deaths in men. Current treatments of prostate cancer such as chemotherapy show drastic side effects including hair loss, nausea, vomiting, infertility, and liver damage. Despite these violent symptoms, the chemotherapy drugs do not cure the cancer, but merely prolong or improve the quality of life.

Docetaxel is one of two common chemotherapy drugs discovered in 2004. Docetaxel inhibits cell growth by inducing apoptotic cell death through the cleavage of caspase-3. However, docetaxel also affects normal body cells, which is a cause of side effects. This study proposes a new treatment for prostate cancer using the novel technology of nanocells. They will allow for targeted drug delivery, bringing docetaxel only to the prostate cancer cells which will prevent damage to the normal body cells and thus prevent many of the violent side effects.

The docetaxel can be bound to the polymer core of the nanocell and held inactive until the polymer degrades and releases the drug, thus activating it. For time-mediated drug release, polylactide-coglycolide (PLGA) polymer will be tested. It degrades at a slow rate with doxorubicin, but should be tested with docetaxel. Different amounts of the drug can be combined with PLGA to produce an oligomer which can be tested and compared to free docetaxel to create a concentration-effect curve to figure out the best combination for the ideal release rate. The patent for the composition of Docetaxel will expire in 2007 in Europe and in 2010 in the United States which will allow a generic form to be created for a more cost-efficient treatment.

Prostate specific membrane antigens (PSMA) are created by all prostate cells and are up-regulated in prostate cancer cells. PSMA-specific antibodies target and bind to these antigens. MLN591 or a different PSMA-specific antibody will be attached to the outer shell of the nanocell (a lipid bilayer envelope composed of 2,000-Da poly-(ethylene glycol) distearoylphosphatidylethanolamine, phosphatidylcholine and cholesterol with combretastatin to allow optimal loading), making it exclusively target prostate cancer cells.

Prostate Cancer Cell Apoptosis via MK886 Delivered Specifically with EDVs

Over 234,000 men in the United States will be diagnosed with prostate cancer this year. It is the second leading cause of cancer-related deaths in men. Current treatments of prostate cancer such as hormone therapy and chemotherapy have many disadvantages. Hormone therapy for prostate cancer does not cure the cancer and the cancer may develop into an advanced state in which chemotherapeutic drugs are necessary. However, these chemotherapeutic drugs have many side effects including hair loss, nausea, vomiting, infertility, and liver damage. Despite this, they still have very little effect on the survival of people with hormone-prostate cancer. Our proposed method is to localize the release of an agent that causes apoptosis in prostate cancer cells. It is effective against all types of prostate cancer.

MK886 is a specific inhibitor of arachidonate 5-lipoxygenase, preventing its activation and thus, depriving a cell of 5-lipoxygenase metabolites. These metabolites normally suppress phosphorylation of c-Jun N-terminal kinase (JNK), keeping it in an inactive state. Inhibiting arachidonate 5-lipoxygenase thus induces activation of JNK, which then phosphorylates c-Jun, a transcription factor that regulates a cell apoptosis pathway.

To localize the release of MK886 only around prostate cancer tumor cells, we propose the use of an EnGeneIC Delivery Vehicle (EDV) or a similar delivery mechanism. EDV is a non-living nanoparticle surrounded by a rigid and stable biological membrane that will not break down in the extracellular environment. We would like to fuse prostate specific antibodies to the membrane of the EDV to recognize and bind to prostate specific antigens, which are only found on the surface of prostate cells and is upregulated in prostate cancer cells. Once the EDV reaches the prostate cancer and binds, the MK886 will be released and taken up by the local prostate cancer cells. Apoptosis is known to begin as early as 1-2 hours after exposure to MK886 and commence 6-8 hours after treatment.