Small Molecular Weight Inhibitors of the DNA - KU70/80 Association to Sensitize Cells for Radiation or Chemotherapy

UA ID Technology #ua14-189

Title: Small Molecular Weight Inhibitors of the DNA - KU70/80 Association to sensitize cells for radiation or chemotherapy

Background: Each year over 700,000 American patients with common epithelial malignancies (i.e., prostate, breast, colon, and lung cancers) are likely to receive radiation as either their sole or primary treatment in combination with other modalities to target and destroy cancer cells. For all tumors, there is a dose-response curve that indicates better control with higher doses of radiation. Radiation therapy, however, can damage normal cells as well. As a result, researchers are searching for drugs that make tumor cells more sensitive to radiation therapy without the negative side effects of treatment. These compounds, also called radiosensitizers, makes tumor cells easier to kill when combined with radiation therapy. Since an increase in radiation dosage is limited by the tolerance level of the healthy organs, sensitizing the malignant cells by specific radiosensitizers has long been a goal of cancer research.

Invention: The present invention provides methods and compositions for inhibiting cancer cell survival and/or promoting cell death following radiation or chemotherapy applied in cancer treatment. This invention can be used to treat cancer alone as well. UA investigators found compounds that may disrupt the Ku70/80 - DNA repair association. The Ku70/80 dimer protein is involved in the repair of radiation-induced DNA double strand breaks (DSBs) in human and mammalian cells. These Ku70/80-DNA association inhibitors synergistically sensitized human cancer cells to radiation treatment at sub-cytotoxic concentrations.

Applications:

- Potential to develop an effective therapy to treat various cancers by combining this compound with radiotherapy to make cancer cells more susceptible to death by radiation than the surrounding, healthy cells
- Novel class of radiation-sensitizing drugs for use alongside radiation therapy of solid cancers
- Potential to be used in cancer therapies alone.

Advantages:

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The University of Arizona, Tucson, Arizona
• Reduces negative side effects of radiation treatment including damage to normal cells.
• Increased probability of destroying targeted tumor cells.
• Potential novel tumor drugs.

Publications:

*A novel small molecule inhibitor of the DNA repair protein Ku70/80. DNA repair, Volume 43, July 2016, Pages 98–106*

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