Skysong Innovations
Advancing the Arizona State University Knowledge Enterprise

1475 N. Scottsdale Road, Suite 200
Scottsdale, AZ 85287-3538
Phone: 480 884 1996 Fax: 480 884 1984

Case ID:M18-031LC
Published: 1/4/2019

Inventors

Shengxi Chen

Contact

Jovan Heusser
jovan.heusser@skysonginnovations.com

Diazeniumdiolate Derivative Anti-Cancer Agents

Nitric oxide (NO), a signaling molecule, is involved in many physiological and pathological processes and as such plays an important role in tumor biology. It is involved in vascular permeability and angiogenesis as well as controlling the growth, migration and invasion of cancer cells. Thus, interfering with NO signaling could be a promising strategy in developing novel cancer treatments.

O2 -arylated diazeniumdiolates are NO donors that allow spontaneous NO generation after catalysis. These compounds have been shown to have cytotoxic activities to many cancer types including leukemia, prostate cancer, multiple myeloma, hepatoma and lung cancers.

Prof. Shengxi Chen, at the Biodesign Institute of Arizona State University, has designed and synthesized derivatives of diazeniumdiolate compounds which have antiproliferative effects on cancer cells, especially for Leukemia cancer. When tested in vitro in various cancer cell lines, these compounds showed comparable cytotoxic activity to the parent compound which was highly inhibitory to cellular proliferation. The mechanism of action is through arylation of GSH, activation of caspases -3, -8 and -9, induction of protein kinases p38, JNK and (MAPK) ERK and other cellular nucleophiles. This MOA essentially increases generation of intracellular nitric oxide, affecting various pathways leading to cell death.

These compounds show great potential using a promising pathway and target to treat many different cancers, including some cancers that are known to be multidrug resistant.

Potential Applications

- Cancer therapeutics
- Leukemia, prostate cancer, multiple myeloma, hepatoma, lung cancer, breast cancer, pancreatic cancer, bile duct carcinoma, neuroblastoma, colon cancer, gastric cancer, liver cancer, lung cancer, kidney cancer, esophageal cancer, stomach cancer, cervical cancer or lymphoma tumors
- Therapeutics for conditions where an increase in intracellular nitric oxide is

beneficial

Benefits and Advantages

- Increased delivery efficiency of nitric oxide
- Some compounds had higher selectivity than the parent compound
- Comparable cytotoxic activity to parent compound
- Each compound can release up to four nitric oxide molecules

For more information about the inventor(s) and their research, please see Dr. Chen's departmental webpage