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Novel anticancer compound that targets metabolic plasticity

F-MN-D1 compound targets metabolic plasticity common to many solid tumors through inhibition of glycolysis and oxidative phosphorylation facilitating tumor growth reduction.

Technology No. 2019-124

IP Status: Pending US Patent; **Application #:** 17/076,527

Applications

- Cancer therapeutic
- Basic cancer research
- Metabolism research

Key Benefits & Differentiators

- **Potent anti-cancer potential:** F-MN-D1 inhibition of glycolysis and oxidative phosphorylation facilitates tumor growth reduction.
- **Reduced toxicity:** F-MN-D1 inhibits glycolysis and oxidative phosphorylation via a reversible mechanism leading to improved systemic tolerance and a broad therapeutic window.

Metabolic plasticity: an enticing but tricky anti-cancer target

Cancer cells are resilient because they rewire their metabolism to promote cell proliferation, survival, tumour growth and long-term maintenance. Solid tumors exhibit metabolic plasticity that allows them to produce energy from either glycolysis or oxidative phosphorylation, or both. This necessitates that effective therapies must target and inhibit both pathways. There is abundant interest in developing small molecules that selectively target these two aberrant metabolic pathways. The search for dual-activity molecules has been impaired by the toxicity of many agents targeting mitochondrial function resulting in a therapeutic window that is too restrictive. To overcome these challenges, researchers at the University of Minnesota designed

a molecule, F-MD-1 and its derivatives, that exhibits potency in inhibiting glycolysis and mitochondrial function with a large therapeutic window.

Hitting two targets with one (molecular) stone

F-MD-1 works through inhibition of monocarboxylate transporters (MCT1/4) and the mitochondrial pyruvate carriers (MPC1/2) involved in glycolysis and oxidative phosphorylation. This dual inhibition mechanism is necessary for the elimination of cancer as opposed to only tumor reduction. The chemical structure includes a lipophilic cyanocinnamate template designed to create a potent, but reversible, inhibition mechanism. This reversibility makes the molecule generally well tolerated when administered systemically, a drastic improvement on the current toxic compounds that target mitochondrial function. Using various cancer cell lines, F-MD-1 effectively inhibits mitochondrial function and ATP production as well as the glycolytic capacity of cells. The compound also exhibits improved kinetics and stability compared to its predecessors. These properties lend F-MN-D1 to development as a new anticancer agent that targets tumor metabolic plasticity that is common in many solid tumors.

Phase of Development

In vitro data showing F-MN-D1 inhibits glycolysis and oxidative phosphorylation in aggressive triple negative breast cancer cells (MDA-MB-231) and colorectal cancer cells (WiDr).

Researchers

Venkatram Mereddy, PhD
Professor, Dept. of Pharmacy Practice and Pharmaceutical Sciences
External Link (www.pharmacy.umn.edu)

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