

A Novel Class of Anti-MIF Compounds as Therapeutic Agents Against Cancer and Other Diseases (05037 / 08065 / 10066)

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Technology description



A class of extremely potent inhibitors of Macrophage Migration Inhibitory factor (MIF)-dependent disease processes and represents novel anti-cancer and anti-inflammatory therapeutics.

Technology

U of L researchers have identified a class of novel, small molecule antagonists of Macrophage Migration Inhibitory Factor (MIF)-dependent pathological functions. This new class of MIF inhibitors targets a novel amino acid in the base of the hydrophobic pocket of MIF's catalytic active site. The new target appears to inhibit MIF activity as well as, if not better than, current candidate compounds that target the side of the catalytic pocket. The new MIF inhibitors are suicide substrate/inhibitors that covalently attach to MIF and are therefore potentially irreversible. The new class of inhibitors is active against the enzymatic activity of MIF at 20X less the concentration than the best described competitor MIF inhibitor.

This was achieved by conducting a virtual screen of several small compound libraries against the catalytic active site of MIF. A subset of candidate inhibitors were identified and screened. One candidate, 4-iodo-6-phenylpyrimidine, has proven to be a remarkably potent and potentially irreversible inhibitor of both MIF-mediated catalytic and biologic functions. Several analogs or derivatives of 4-iodo-6-phenylpyrimidine that stably interact with MIF and inhibit MIF activity have also been identified. These MIF antagonists represent a new generation of less toxic and more potent anti-cancer and anti-inflammatory disease therapeutics than those currently in use.

Markets Addressed

Several aggressive cancers possess very low oxygen tensions and hypoxia is known to induce MIF expression. MIF expression is increased in pre-cancerous, cancerous and metastatic tumors. MIF levels have been found over-expressed in a large variety of human neoplasias, including breast, prostate,

colon, brain, skin and lung-derived tumors. Furthermore, MIF may be important in the progression of inflammatory disorders. The newly identified MIF inhibitors can be used as therapeutic agents for cancers and inflammatory disorders involving elevated plasma levels of MIF with 10X more potency than the previously tested anti-MIF compounds. The new class of MIF inhibitors for treatment of autoimmune disorders can be used in the later stages of the disease and need not be administered in the early stages of disease onset to achieve the desired therapeutic effect.

Publications: Winner et al, Cancer Research, 2008, vol. 68(18): 7253-7257

Application area

Fields of Use Available: All commercial fields

Advantages

This Technology is available for licensing, further development, or industrial partnering

Institution

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