

Novel Therapeutic Analogues of Metformin for the Treatment of Cancers

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BACKGROUND

Breast cancer is the most common type of cancer that occurs in women in the US and ranks as the second leading cause of cancer death after lung cancer. Of the 230,480 invasive breast cancer cases diagnosed in the US in 2011, approximately 15-20% were "triple negative breast cancer" (TNBC), a subtype of breast cancer that lacks clinical expression of estrogen receptor-alpha (ER α), progesterone receptor, and HER-2 receptors. TNBC tends to occur often in younger and African American women, and it is associated with high proliferative rates, and poor survival. Despite initial responsiveness to some types of chemotherapy, TNBC often recurs early with distant metastases. Treatment of TNBC has also been hindered by its insensitivity to widely-used targeted therapies including trastuzumab, lapatinib, tamoxifen, and aromatase inhibitors. Due to the aggressive nature of TNBC, it accounts for nearly half of all breast cancer deaths. Therefore, there is an urgent need to develop new and more effective therapies for this deadly subtype of breast cancer. The use of novel metformin analogues detailed below may present a promising new treatment for TNBC.

INNOVATION

Dr. Richard Pietras, Director of the Stiles Program in Integrative Oncology in the UCLA Jonsson Comprehensive Cancer Center, and Dr. Michael Jung from the Departments of Chemistry & Biochemistry at UCLA have recently synthesized novel analogues of metformin, the most commonly prescribed drug to treat type 2 diabetes. These metformin analogues have anticancer activity in breast cancer cell lines, particularly those derived from TNBC. Further, the analogues also exhibit significant antitumor activity in melanoma, lung, and pancreatic cancers. As there are currently no drugs specifically approved for the treatment of TNBC, these metformin analogues may provide a unique breakthrough in treatment of this malignancy.

APPLICATIONS

- ▶ This invention provides the basis for development of novel metformin compounds for treating TNBC and other forms of breast cancer. Other solid tumors, such as melanoma, non-small cell lung cancer and pancreatic cancer may also benefit from metformin analogue treatment. As TNBC, few effective targeted therapies are currently available for lung and pancreatic cancers in the clinic.
- ▶ The metformin-based compounds may also be used to treat noncancerous diseases that have dysregulated signaling pathways, such as lymphangiomyomatosis (LAM) or angiomyolipomas.
- ▶ There is also a potential for use of these compounds in cancer prevention among individuals at high risk for cancer including those with a significant history of diabetes, obesity, metabolic syndrome, tobacco smoking or evidence of premalignant lung or other tissue lesions.

ADVANTAGES

- ▶ Non-invasive, oral route of administration.
- ▶ Several metformin analogues do not exhibit significant toxicity toward normal nonmalignant human cells.

STATE OF DEVELOPMENT

- ▶ Novel analogues of metformin induce cell death in vitro in cell lines derived from TNBC, ER α -positive breast cancers, as well as melanoma, lung and pancreatic cancers.
- ▶ *In vivo* analysis of the anticancer properties of novel metformin analogues is currently underway.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	9,862,693	01/09/2018	2012-733

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OTHER INFORMATION

KEYWORDS

Therapeutics, cell lines, research tools, drug development, drug synthesis

CATEGORIZED AS

- ▶ **Medical**
 - ▶ Disease: Cancer
 - ▶ Disease: Metabolic/Endocrinology
 - ▶ Disease: Women's Health
 - ▶ New Chemical Entities, Drug Leads
 - ▶ Research Tools
 - ▶ Therapeutics
- ▶ **Research Tools**
 - ▶ Cell Lines

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