

Novel Therapy for Melanoma

Each year melanoma affects over 76,000 people and causes about 10,000 deaths in the US alone. According to estimates of the National Cancer Institute, there are currently over 900,000 people living with melanoma in the US and the American Cancer Society estimates that melanoma affected over 87,000 people in 2017. If detected and treated at an early stage, melanoma cases are mostly curable. When treated before metastasis the 5-year survival rate is 98%, but in cases that remain untreated until metastasis, the 5-year survival rate is only 10-15%. Although there are multiple approved therapies for melanoma, the disease known to acquire resistance to most of them. A number of currently used melanoma treatments also result in toxicity for healthy cells. Moreover, the overall survival period of patients suffering from late stage metastatic melanoma is only about 3 years. Hence, there is a need for developing effective combination therapies that result in higher survival rates and/or offer longer periods of progression free survival (PFS). The invention described here offers an innovative approach for treating melanoma and potentially other cancers by targeted inhibition of cellular proteins. This strategy implements a combination of a pharmaceutically acceptable carrier and a therapeutically active compound that specifically interacts with particular cellular proteins. Such targeted therapies are of interest to medical professionals as the treatments tend to demonstrate better efficacy against malignant cells and lower probability of serious adverse events.

Technology

NSU's Dr. Minond discovered a novel therapeutic method in collaboration with researchers at two other institutions. The invention proposes a combination of a pharmaceutically acceptable carrier and a therapeutically active agent to treat metastatic melanoma. This intervention has the potential to be an efficient and specific treatment of metastatic melanoma that has a mutation in BRAF and/or NRAS genetic pathways. The compounds to be used in the treatment will be antagonists of at least one of lamin A/C, ATP-dependent RNA helicase DDX1, heterogeneous nuclear ribonucleoproteins H1/H2 (hnRNP H2), and heterogeneous nuclear ribonucleoproteins A2/B1 (hnRNP A2/B1). Their mechanisms of action involve either substantially decreasing or blocking an activity or a specific function of these cellular proteins, which will then inhibit the proliferation of primary and metastatic melanoma cells. The invention utilizes anti-melanoma therapeutic agents that induce basal autophagy and perturb mitochondrial potential, resulting in death of melanoma cells with mutations in BRAF and NRAS genes. To enhance therapeutic efficacy, a pharmaceutically acceptable carrier for delivering the active ingredient is proposed. The technology presented here describes a novel approach for using lamin A/C, DDX1, hnRNP H2 and hnRNP A2/B1 as drug targets for an anti-melanoma therapy. An innovative screening method utilized to evaluate and select these therapeutic agents indicated that the compounds inhibited two different types of cancer cells (A549 and M14) but did not have significant deleterious effect on healthy cells (CHO-K1).

Application

- This technology has the potential to be an efficient therapy for the treatment of metastatic melanoma that has a mutation in BRAF and/or NRAS genetic pathways
- It may be used for treating cancers other than melanoma, malignant tumors and alternate conditions of unregulated cellular growth
- This method of melanoma treatment can be used by itself or in combination with another therapy

Advantages/Benefits

- Melanoma often develops resistance to monotherapies. A combination therapy such as the technology described here can be a more effective method as cancer cells are less likely to develop resistance
- Toxicity towards normal/healthy cells is a major drawback of existing melanoma therapies. The molecules selected by the researchers for melanoma treatment did not exhibit significant toxicity against healthy cells
- An efficient treatment for melanoma offers significant economic potential as the global melanoma treatment market is estimated to reach \$12.4 billion by 2025

Status of Development

Two compounds have been tested on cancer cell lines. The agents demonstrated anticancer properties while not having significant toxicity in normal cells.

The anti-cancer potency exhibited by the two compounds was comparable to that of a leading FDA-approved metastatic melanoma drug, vemurafenib (Zelboraf®).

Patent Status

PCT application published on 21st June 2018.

Information on Inventors



- Dr. Dmitry Minond is Affiliate Associate Professor at Rumbaugh-Goodwin Institute for Cancer Research and Dr. Kiran C. Patel College of Allopathic Medicine at Nova Southeastern University. Dr. Minond's research interests include protein chemistry, oncology, drug discovery, high throughput screening (HTS) and enzymology.
- Dr. Gregg Fields is Professor and Chair of the Department in the Department of Chemistry and Biochemistry at Florida Atlantic University.
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