



2-Dimethylamino-4,5,6,7-tetrabromo-1H-benzimidazole (DMAT) - A Kinase Inhibitor as Oncology Therapeutic

A potential broad spectrum cancer treatment

Contact

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Inventors

Michael Kalafatis, Ph.D.

Field

Biochemistry and Molecular Biology

Technology

Drug that selectively targets cancer cells independently of the tissue of origin

Key Features

Kills only cancer cells

Key Benefits

- Appears to have low/no toxicity or side effects
- Appears to be applicable to a broad spectrum of cancer types

Stage of Development

Preliminary in vitro and in vivo work (mice) has been accomplished

Status

Seeking partner for licensing and development

Patent Status

US Patents filed

Background

Using a novel therapeutic compound, the inventor has developed extensive preliminary data with cells in culture and with mice xenografts demonstrating that inhibition of a protein that is normally located in the cytoplasm of normal cells, and is translocated into the nucleus of tumor cells may be a general therapeutic treatment for all cancers. The data shows that cell growth can be stopped or controlled by this specific compound that doesn't appear to have any effect on the surrounding normal tissue, since the liver, brain, kidney and muscle tissue of all mice treated with the inhibitor appear to be normal following histological analysis. Therefore, the abnormal cell growth may potentially be eliminated independently of the tissue/organ with minimum or no side-effects.

One molecule can kill cancer cells in vivo and in vitro

Megakaryoblasts are hematopoietic progenitor stem cells that differentiate to the stage of megakaryocytes. MEG-01 cells are malignant megakaryoblasts isolated from a patient with chronic myelogenous leukemia in blast crisis. MEG-01 megakaryoblasts were found to release platelets that are morphologically indistinguishable from normal blood platelets, viable and functional, when treated with apoptosis inducers. These cells are of interest for cancer research because they are cytokine independent, and as a consequence, do not respond to interferon and thrombopoietin treatments. MCF-7 is a breast cancer cell line established from the mammary gland of a 69-years old woman.

The assays:

1) Anchorage independence in "soft agar" assay It has been well established that malignant cells form colonies when grown on soft agar, while normal cells do not grow under similar experimental conditions. Agarose was mixed with growth media specific for MEG-01 cells. Colonies formation was observed and micrograph images were taken. Figure 1A shows MEG-01 cells in the absence of this CK2 Inhibitor, while Figure 1B shows MEG-01 cells grown in the presence of this CK2 Inhibitor.

2) Creation of mice xenografts (using MEG-01, MCF-7, and brain carcinoma cells U-87 cells). Immunodeficient male and female athymic nude nu/nu mice were used. For engraftment, cells in cell culture media were injected. We used: MCF-7 cells. Cells were injected subcutaneously into the lower flanks of mice (left and right). Tumors were visible after 6-7 days from inoculation. Treatment was initiated when tumors were at least 100-200 mm³ volumes. Time 0 is when injections (subcutaneous) were initiated (Fig.2).

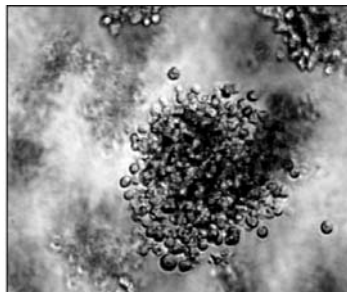


Fig 1A

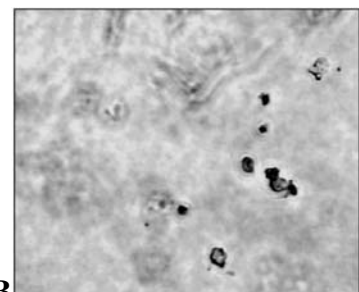


Fig1B

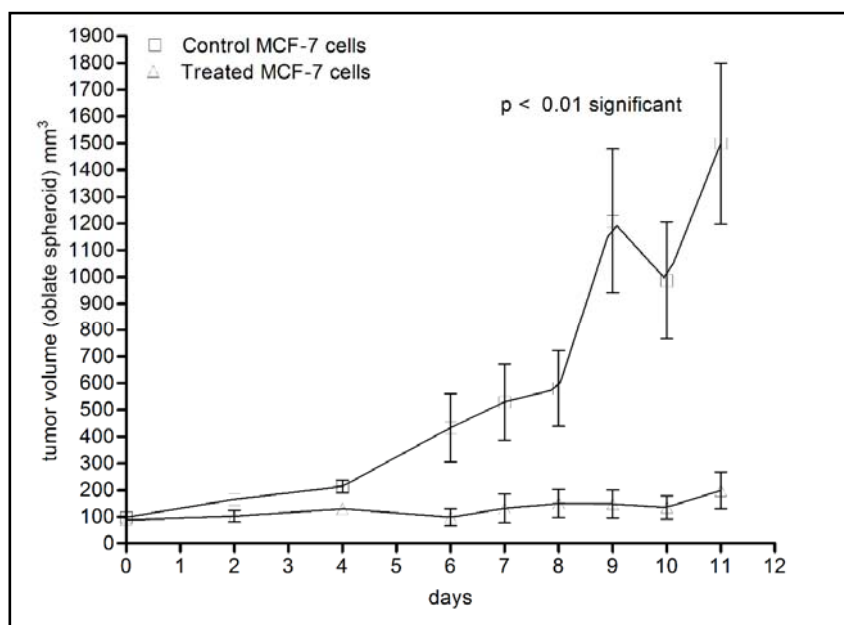


Fig. 2

The inventor's data shows that the area and the number of the colonies formed by untreated MEG-01 cells are extensive (Figure 1A), whereas the CK2 Inhibitor - treated MEG-01 cells do not form colonies (Figure 1B). The data shown in Figure 2 demonstrate no further cancer growth in treated mice. Overall, the data demonstrate that the compound can be used as a therapy to treat tumors *in vivo*. All tumors from treated mice showed high necrotic and apoptotic areas versus untreated (vehicle only) control tumors. All other organs of the treated mice appeared normal, based on hematoxylin-eosin staining. Toxicity experiments have been performed. A mouse was treated with 10 mg (of compound /day/animal) for a period of 2 weeks. Histological analyses of all organs didn't show any difference between a control animal (not injected) and the mouse injected with the compound. In conclusion, this CK2 Inhibitor appears to be of significant importance as a tool in developing a new cancer therapy both because of its potential efficacy and its apparent lack of toxicity.

The National Institutes of Health (NIH) have agreed to test Dr. Kalafatis' drug/molecule in an independent forum to determine if the injections produce similar results on 60 different human cancer cell lines. It is very important to note that the NIH agreed to do this independent analysis (phase I and phase II). Both sets of experiments from the NIH analysis confirmed Dr. Kalafatis' initial findings on a multitude of cancer cells.

Opportunity

CSU is looking for a commercial partner for licensing and development.

Inventor

Michael Kalafatis, Ph.D., is Professor of Chemistry at Cleveland State University. Dr. Kalafatis is an international scholar in blood clotting research, supported by the National Institutes of Health and the American Heart Association.