The role of tyrosine kinase receptors in the diagnosis and therapy of brain tumors

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Scientific report II (1st of january-31st of december 2012)

General Objectives

1. The evaluation of the cytotoxic effect of Helianthinei on brain tumors

2. The elaboration of „in vitro" experimental models for screening, using combined treatments of tyrosine kinase inhibitors, on which „in vivo" combined treatments can be developed.

3. To continue the collection and processing of biological materials from patients in accordance with medical ethics for the maintenance of the Brain Tumor bank started in 2006.

The objectives of the execution phase:

a. The acquisition of equipement and reactives/consumables

b. The continuation of the experimental phase

c. The processing and preliminary presentation of the results

d. The analysis and interpretation of the existing data

e. The preliminary synthesis of the theoretical conclusions in the studied field

Introduction

The current study aims to discover and improve methods of diagnosis and therapy able of improving the prognosis of patients diagnosed with brain tumors. Signaling pathways of

growth factors are frequently deregulated in brain tumors and may contribute to uncontrolled growth of tumor cells through autocrine and paracrine mechanisms. Excessive stimulation of growth factor receptors may also lead to excessive activity of the Ras signaling pathway, which is frequently aberrant in brain tumors. Inhibition of the tyrosine kinases receptor using antireceptor monoclonal antibodies and antisense oligonucleotides are techniques currently under investigation as methods of regulating aberrant signaling pathways of growth factors in brain tumors. In recent years, we are witnessing a revolutionary development of targeted therapeutic agents and angiogenic growth factors and their signaling pathways. Another recent direction in the therapy of brain tumours is the target of cancer stem cells. Several tyrosine kinase receptor inhibitors including imatinib mesylate (Gleevec), gefitinib (Iressa) and erlotinib (Tarceva) have entered clinical trials for patients with high-grade gliomas. Farnesyl transferase inhibitors such as tipifarnib (Zarnestra) which affect the processing of proRas and inhibit Ras signaling have also entered into clinical trials for patients with malignant gliomas. We need further development and evaluation of targeted therapies in clinical trials of these new agents to improve survival and quality of life for patients with brain tumors. Because brain tumors are heterogeneous in terms of genotype and phenotype, the constitution of a brain tumor bank which includes a larger variety of cases is justified.

Results

In this first stage of the project the following were achieved:

1. Equipment and consumables necessary to the objectives were purchased
2. The collection of tumor samples from patients with brain tumors operated at The Neurosurgery Department of the Emergency Hospital "Bagdasar-Arseni", was continued in order to extend the bank of brain tumors
3. Four brain tumor cell lines have been established
4. Heliantine bound to ferite nanoparticles was obtained
5. The effect of ferrite nanoparticles was assessed on the tumor cell lines

6. The cytotoxic effect of Heliantine was evaluated, administered through ferrite nanoparticles, to the tumor cell lines.

7. The function of growth factor receptors (IGF-1R, PDGFR, VEGFR and EGFR) in cell lines was inhibited, then the effect of inactivating the receptors was analyzed.

Books

1. METHYLATION – FROM DNA, RNA AND HISTONES TO DISEASES AND TREATMENT. Edited by Anica Dricu**.** ISBN 978-953-51-0881-8. Editura InTech. 2012

2. Book chapter: "DNA Methylation, Stem Cells and Cancer**"** Anica Dricu, Stefana Oana Purcaru, Alice Sandra Buteica, Daniela, Elise Tache, Oana Daianu, Bogdan Stoleru, Amelia Mihaela Dobrescu, Tiberiu Daianu and Ligia Gabriela Tataranu. METHYLATION – FROM DNA, RNA AND HISTONES TO DISEASES AND TREATMENT. Edited**.** ISBN 978-953-51-0881-8 **,** pg 153, 2012

Articles.

1. Tropomyosin-receptor-kinases Signaling in The Nervous System. Bogdan Stoleru, Alisa Madalina Popescu, Daniela Elise Tache, Oana Maria Neamtu, Ghazaleh Emami, Ligia Gabriela Tataranu, Alis Buteica, Anica Dricu, Stefana Oana Purcaru. Submitted to Medica, 2012.
2. Angiogenesis and Vascular Endothelial Growth Factor in malignant gliomas. Alisa Madalina Popescu, Oana Stefana Popescu, Bogdan Stoleru, Ligia Tataranu, Daniela Elise Tache, Monica Dosa, Anica Dricu. Submitted to Current Health Sciences Journal**,** 2012.

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