

HUMAN TRISOMY 21 FIBROBLASTS RESCUE METHOTREXATE TOXIC EFFECT AFTER TREATMENT WITH 5-METHYL-TETRAHYDROFOLATE AND 5-FORMYL-TETRAHYDROFOLATE

Vitale L. (1), Serpieri V. (2), Lauriola M. (1), Piovesan A. (1), Antonaros F. (1), Cicchini E. (1), Locatelli C. (3), Cocchi G. (3,4), Strippoli P. (1), Caracausi M. (1)

(1) *Unit of Histology, Embryology and Applied Biology, Department of Experimental, Diagnostic and Specialty Medicine (DIMES), University of Bologna, Bologna (Italy)*

(2) *Unit of Genetics and Applied Biology, Department of Molecular Medicine, University of Pavia, Pavia (Italy)*

(3) *Neonatology Unit, St. Orsola-Malpighi Polyclinic, Bologna (Italy)*

(4) *Department of Medical and Surgical Sciences (DIMEC), University of Bologna, Bologna (Italy)*

Trisomy 21 causes Down syndrome (DS), the most common human genetic disorder and the leading genetic cause of intellectual disability. The alteration of one-carbon metabolism was described as the possible metabolic cause of the intellectual disability development in subjects with DS. One of the biochemical pathways involved in the one-carbon group transfer is the folate cycle. The cytotoxic drug methotrexate (MTX) is a folic acid (FA) analogue which inhibits the activity of dihydrofolate reductase enzyme involved in the one-carbon metabolic cycle. Trisomy 21 cells are more sensitive to the MTX effect than euploid cells, and in 1986 Jérôme Lejeune and Coll. demonstrated that MTX was twice as toxic in trisomy 21 lymphocytes than in control cells. In the present work, the rescue effect on MTX toxicity mediated by FA and some of its derivatives, tetrahydrofolate (THF), 5-formyl-THF, and 5-methyl-THF, in both normal and trisomy 21 skin fibroblast cells, was evaluated. A statistically significant rescue effect was obtained by 5-formyl-THF, 5-methyl-THF, and their combination, administered together with MTX. In conclusion, trisomy 21 fibroblast cell lines showed a good response to the rescue effects of 5-formyl-THF and 5-methyl-THF on the MTX toxicity almost as normal cell lines.

XIX Congresso Nazionale
AIBG

Milano | 4 - 5 Ottobre 2019