

THE NEW THERAPEUTIC PROTOCOLS: FROM THE HISTOLOGICAL MODEL TO THE MUTATIONAL MODEL. THE ROLE OF ZINC IN CANCER PATIENTS SUFFERING FROM DIABETIC DISEASE OR HYPERGLYCAEMIA.

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Abstract: The study of the genetic mutations of tumors is changing the therapeutic approach, as the focus is shifting from the study of the tissue modifications of the tumor to the study of the modifications and proliferation of the neoplastic cells, thus moving to a different advanced and strategic phase, which directs us towards precision and personalized medicine. A parameter to be taken into consideration in these studies is diabetic disease or hyperglycemia, since according to various scientific researches, it is considered a personal risk factor, not so much in the formation phase of the neoplastic disease, but in the therapeutic response phase.

Hyperglycemia, accompanied by insulin resistance, and consequent hyperinsulinemia, pushes towards rapid cell proliferation, while the high amount of sugars and lipids in the blood act as metabolic fuel for the spread of the tumor. The high insulin-glucose ratio in diabetics causes some cells to lose control of the regulatory genes of the DNA, starting a transformation mechanism as occurs, in particular, in tumors of the gastrointestinal tract. All this is due to a high proliferation, migration and infiltration of tumor cells that make the disease particularly aggressive.

Furthermore, recent studies have shown that hyperglycemia is the cause not only of a delayed and reduced immune response but also of an increase in co-morbidity as well as mortality, due to possible organ-specific complications, thus predicting in which patients it could arise a rapid and aggressive evolution of the disease with an individual-specificity and organ-specificity.

When a person's immune defenses do not respond to a certain disease, it is because the body is unable to produce or activate specific lymphocytes and antibodies against that disease. This may be the cause of lack of therapeutic response or recurrence of the disease. These therapeutic programs, which involve the transition from the histological model to the genetic mutation (mutational) model, must take into account the zinc deficiency in cancer patients which can become a personal risk factor, especially if linked to diabetic disease or hyperglycemia. A fundamental role in planning the treatment of a tumor is played by genomic tests which are carried out directly on the modified neoplastic tissue, in addition to genetic tests and the dosage of toxic substances (heavy metals, dioxins, furans, PCBs, etc.) analyzed "primarily" in the tumor and subsequently in the various biological matrices (modified tissues, blood, urine, hair, nails, breast milk, saliva, skin appendages, etc.). In addition to these tests, just mentioned, the search for trace elements useful for normal cellular metabolism is also fundamental, but also and above all for the control mechanisms of genetic modifications. Unfortunately, little attention is paid to the importance of having a healthy, complete and balanced diet for the prevention of neoplastic and chronic-degenerative diseases. In this context, Nutrigenomics plays a fundamental role, which studies how some nutrients can induce a change by acting on genetic expressions and consequently on the individual phenotype.

These nutrients are: Copper, Zinc, Selenium, Magnesium, Cobalt, Iron and Manganese, essential for improving cellular functionality and for modulating the therapeutic response. In addition, in oncological diabetic patients, another parameter to be taken into consideration is hyperglycemia, which is considered a personal risk factor not so much in the formation phase of the neoplastic disease, but mainly in the therapeutic response phase. Zinc, in particular, improves the immune system as it is present in the enzyme molecules essential for the functioning of lymphocyte cells and the structure of antibodies. It also

participates, through the Zinc Finger Proteins, in the DNA repair process and therefore in the recovery of the immune system. It performs an action that supports the cognitive function of the organism. It also appears in recent literature that in cases in which there have been no or reduced therapeutic responses in diabetic cancer patients, these have been related to the lack of activation of certain genes related to the immune defences, which are not activated. Their non-activation could be referred to low concentrations (or values) especially of Zinc, but also of Copper, Selenium, Cobalt, Manganese and Iron.

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