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From the Histological Model to the Mutational Model: The Study of Heavy Metals and Other Substances in New Antineoplastic Therapies

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From the Histological Model to the Mutational Model: The Study of Heavy Metals and Other Substances in New Antineoplastic Therapies

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Abstract- The study of genetic mutations in tumours changes the therapeutic approach; in fact, we move into a different advanced and strategic phase by entering personalized precision medicine and shifting the focus from the tissue study of the tumour to the modification and proliferation of neoplastic cells. The therapeutic programs, especially in oncology, are changing. We are in a phase of transition from the histological model to the model of genetic mutation (mutation). When a person's immune defences do not respond to a disease it is because the body cannot produce or activate specific lymphocytes and antibodies against that disease. This causes of a lack of therapeutic response or recurrence of the disease. A fundamental role is played by genomic tests, which are carried out directly on the neoplastic tissue and other modifies tissues, and the dosage of toxic substances (heavy metals, dioxins, furans, PCBs, etc.) analysed 'primarily' in the tumour and subsequently in the various biological matrices (tissues, modified, blood, urine, hair, nails, breast milk, saliva, etc.) as well as genetic tests. A significant role is a search for toxic substances and therapeutic integration of trace elements beneficial for cellular metabolism, especially for defence mechanisms, absent or deficient in these patients, such as Copper, Selenium, Zinc, Cobalt, Iron, and Manganese to improve or modify a lack of therapeutic response. Another parameter to consider is hyperglycaemia in diabetic subjects, which according to various scientific research, is considered a personal risk factor not so much in the formation phase of the neoplastic disease, but in the healing response phase.

Keywords: tumour disease, therapeutic response, complications, genomic modification, genomic and genetic tests, trace elements, immune response, nutritional supplementation, heavy metals, dioxins, hyperglycaemia, and hyperinsulinemia.

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Introduction

Environmental pollution is today one of the major global problems with significant repercussions on human health. Despite this, little has been done to highlight the possible correlations between the different forms of pollution and the many related diseases, especially neoplastic ones. Unfortunately, little attention is paid to the importance of having a healthy, complete, and balanced diet to prevent neoplastic and chronic-degenerative diseases and to support the various therapeutic approaches. In this context, Nutrigenomics plays a fundamental role, which studies how nutrients can induce a modification or suppress genetic expressions, consequently acting on the individual phenotype. Nutrition (www.cestraecologia.it), with the possible introduction of toxic substances and a few substances useful for our body's defence mechanisms, such as vitamin D and vitamin C as well as Zinc and Copper, etc., as well as the environment in which we live, both due to soil, water and atmospheric pollution and the presence of electromagnetic fields and industrial sites (Sima Study; Rapporti ISTISAN 10/22, Ambiente salute, www.iss.it), can affect our DNA. Among the toxic substances with which we come into contact, both for environmental pollution and food, we have taken into consideration some dioxins because they are linked to immune defence deficits since they cause a reduced production of B and T lymphocytes as well as the PAHs which especially damage the lungs and nervous system.

We must start from the assumption that the genome is not a rigid structure, but interacts dynamically and evolutionarily with the environment, so that pollution, global warming, and climate change will bring about phenotypic changes as an expression of the new genetic, with loss of biodiversity, but also of fertility. The many energy sources, now used for decades, further contribute to polluting our environment by acting accordingly on the genetic structure. A world that evolves with little respect for the environment will always make recent changes to our DNA which unfortunately can hardly be co-managed or controlled by the many increasingly current therapeutic approaches, denying us the right to health if there is no due respect for the

environment, we live in. In this article, our main objective is to analyse the presence in cancer patients, not only of nutritional deficiencies, but also of food toxicity that causes the accumulation of toxic substances that act by modifying, reducing, or blocking the immune response. For this reason, we must start from the analysis of the genetic mutations of tumours, changing the therapeutic approach; in fact, we move from the histological study of the tumour to a different advanced and strategic phase, entering a personalized precision medicine, shifting the focus to genetic modifications and neoplastic cell proliferation. The therapeutic programs, especially in oncology, are changing, as we are in a phase of transition from the histological model to the model of genetic mutation, called mutational model. To this new diagnostic model, according to our studies, it is essential to add the in-depth analysis of certain substances, such as heavy metals, dioxins, PCBs, etc., in the tumour and in the biological matrices and which can reduce or modify the therapeutic response. When a person's immune defences do not respond to a specific disease, it is because the body cannot produce or activate specific lymphocytes and antibodies against that disease. This causes the lack of therapeutic response or recurrence of the disease. A fundamental role is played by genomic tests, which are carried out directly on the neoplastic tissue, and modified tissues, but also the dosage of toxic substances (heavy metals, dioxins, furans, PCBs, etc.) analysed "firstly" in the tumour and subsequently in the various biological matrices (tumoral tissues, blood, urine, hair, nails, mother's milk, saliva, etc... skin appendages), as well as specific genetic tests. A key role is also the therapeutic integration in case of the absence of trace elements useful for cellular metabolism, especially for the defence mechanisms, such as Zinc, Copper, Selenium, Magnesium, Cobalt, Iron and Manganese and essential vitamins to improve or modify lack of therapeutic response.

The lack of trace elements could be seen as a possible "predisposition" to lack of response to immunological therapies and, therefore, to a greater risk of aggravation of the disease due to lack of therapeutic response. It is reported in the literature that the lack of Selenium, Zinc, Copper, Magnesium, Manganese, Iron, and Cobalt can be correlated to states of immunodeficiency.

In fact, in several studies, it appears that an absent or reduced therapeutic response of the cancer patient has been related to the lack of activation of specific genes associated with the immune defences, which are not activated. Their non-activation could be referred as low concentrations (or values), especially of Copper and Zinc, but also of Selenium, Cobalt, Manganese, and Iron. For example, Zinc participates, through the Zinc Finger Protein, in the DNA repair processes, and therefore, in the recovery of the immune defences.

Even the altered dosage of these trace elements in different organs and systems finds some correspondences in the possible organ-specific complications, giving us the possibility of predicting in which patients a rapid and aggressive evolution of the disease could arise with an individual-specificity and organ-specificity, but also in which patients a severe or pauci-symptomatic form.

It is important to clarify that the dosage of heavy metals in the tumour and in the various biological matrices does not and cannot be a methodology for preventing neoplastic disease, but a helpful method for improving the therapeutic response of the several therapeutic approaches.

Another parameter to consider is hyperglycaemia in diabetic subjects which, according to various scientific research, is considered a personal risk factor not so much in the formation phase of the neoplastic disease, but in the healing response phase. Recent studies have shown that hyperglycaemia is the cause not only of a delayed and reduced immune response but also of an increase in co-morbidity and mortality. (Updates of the FNOMCeO).

Hyperglycaemia, accompanied by insulin resistance, and consequent hyperinsulinemia, push towards rapid cell proliferation, while the high number of sugars and lipids in the blood act as metabolic fuel for the spread of the tumour. The high insulin-glucose ratio in people with diabetes causes the loss of control of the DNA regulatory genes in some cells, starting a transformation mechanism, as occurs in cancers of the gastrointestinal tract. This brings to a high proliferation, migration, and infiltration of tumour cells that make the disease particularly aggressive.

Following our mutational therapeutic approach, it should be emphasized that even the deficiencies of some substances in diabetic subjects can compromise the extent of the response and modify it. This is the case of Zinc deficiency which could damage the immune response due to reduced production of Zinc Finger Protein.

According to our conclusions, therefore, in the diabetic oncological patient treated with immunotherapy, the therapeutic program must be adjusted with the dosage, both in the tumour and in the various biological matrices, of Zinc and with careful control of the glucose/insulin ratio to avoid a reduced or no response therapeutic.

Once again, environmental pollution has proven to be a severe danger to human health, since many neoplastic diseases have shown a greater incidence, diffusion, aggressiveness, and mortality in the most polluted areas.

This research, still in an early stage, requires considerable resources and more patients, and is meant

to be a further invitation to start a multi-center clinical-scientific program for a broader study of heavy metals, dioxins, PAHs, polychlorinated biphenyls in cancer patients, being treated with immunotherapy, but also for many patients who do not respond to the several standard therapeutic programs. In fact, this program allows to study in these patients, in addition to the genetic mutations, also the presence or deficiency of some substances. Then we pass from the histological model to the model of genetic mutation (mutation) both in the cancer and in the biological matrices, and we can positively affect the therapeutic approach even in cancer patients who do not respond to immunotherapy or who have had a recurrence of the disease after immunotherapy, so as to implement precision and personalized therapeutic programs.

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