The team at MCIP, Inc. applies Quantum Computational Biology (QCB) and Metalloendocrinology modeling to the following Chargaff maxim to identify near certain causes of chronic diseases.

"Science is wonderfully equipped to answer the question 'How?' but it gets terribly confused when you ask the question '**Why**'?" Erwin Chargaff - Member of Watson and Crick Team (1895-2002)

To identify factors that cause aggressive skin cancers, reference to DDX3 and MITF in the following article, based on our mission to pursue the <u>WHY</u> causal path factors, the results for discussion with qualified computational biology professionals were.

Modeling of DDX3 identified the following as likely epigenetic factors:

- It is a member of a trefoil DDX1 3 with selenium zinc as the base elements with phenylalanine – tyrosine – tryptophan as the amino acids. These findings identify it as a selenoprotein.
- An alternative designation of this selenium binding protein 1 3 (SBP1 – 3)

MITF is Microphthalmia-associated transcription factor.

With many studies correlating TXNIP (Thioredoxin Interacting Protein) with MITF, QCB tools were applied to thioredoxin activies with the following being verifiable results.

Thioredoxin, thioredoxin-interacting protein (TXNIP) and thioredoxin reductase comprise a modulated pair of enzymes (signaling molecules) that are byproducts of iron - sulfur based pancreatic polypeptide (PP).

For discussion with qualified computational biologists, subsequent modeling identified DNAJB2 and DNAJB3 as the DNA binding

molecules that, if mutated and unable to be subjected to autophagy, are near certain causal factors for aggressive skin cancers.

https://medicalxpress.com/news/2019-07-protein-linked-aggressive-skin-cancer.html

JULY 1, 2019 Protein linked to aggressive skin cancer

by Lund University

Almost 300,000 people worldwide develop malignant melanoma each year. The disease is the most serious form of skin cancer and the number of cases reported annually is increasing, making skin cancer one of Sweden's most common forms of cancer. A research team at Lund University in Sweden has studied a protein that regulates a gene linked to metastasis of malignant melanoma.

Over the past 10 years, new treatment alternatives to strengthen the immune system or attack specific cancer cells have been developed for patients with metastatic skin cancer. The introduction of these treatments is due to an increased understanding of how melanoma develops. However, there is still a lack of knowledge about how the tumor cells spread to other parts of the body.

"We have discovered that a specific protein, called DDX3X, regulates the gene that is central to the development of the pigment cells in the skin. The gene is called MITF. Previously, other researchers have found that MITF is a melanoma-specific oncogene, i.e. a gene that can trigger the development of tumors. The general function of DDX3X was known, but the link to the MITF gene was not understood. We understand more about it now," say Cristian Bellodi, who led the study with Göran Jönsson.

The Lund researchers have now seen that the DDX3X protein does not affect whether or not you develop malignant melanoma, but that it plays a considerable role in the aggressiveness of the tumor. The patient's level of DDX3X can therefore serve as a biomarker for predicting how intractable the disease will be.

"The activity of the MITF gene determines the melanoma cells' specific characteristics, which are then linked to the disease prognosis. The lower the level of DDX3X protein the patient has in the tumor cell, the more aggressive the disease and the worse the prognosis will be," says Göran Jönsson, professor of Molecular Oncology at Lund University.

Both researchers consider that more knowledge is needed about how the MITF gene is regulated in order to understand the mechanisms behind how tumor cells move around in the body, with an aim for the future to prevent the spread of the cancer and improve treatment for melanoma patients.