Nutrigenomic gene expression profile of NCI-60 cancer cell lines

Perfil de expressão de genes nutrigenômicos de linhas celulares de câncer NCI-60

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ABSTRACT
Cancer occurs due to uncontrolled growth and proliferation of abnormal cells, which is a result of molecular alterations in genes associated with a variety of cellular processes. In order to support the development of incipient tumors, cancer cells are expected to require a constant and increasing supply of nutrients. Although it is evident that this increase in nutrients demand would be accompanied by adjustments in expression of genes associated with cellular nutrition, little is known about the regulation of these genes and its implication for cancer development and treatment. In this study a literature based list of 90 genes associated with cellular nutrition was compiled and used to establish nutrigenomic expression signatures across the NCI-60 cancer cell line panel. In order to understand the possible interplay between nutrition genes and cancer genes a literature consolidated gene list of 119 cancer driver genes was used for analysis and comparison. Then, the public available NCI-60 data was used for correlations between nutrigenomic signatures, cancer driver genes and antineoplastic drugs. The results obtained showed several robust correlations between the gene lists and drugs. The expression of GPX2 (Glutathione Peroxidase 2 gene) was strongly correlated with several cancer driver genes and antineoplastic drugs, suggesting that GPX2 may play an important in cancer development and treatment.

Keywords: cancer, nutrition, NCI-60, gene expression, GPX2.
RESUMO
O câncer ocorre devido ao crescimento descontrolado e proliferação de células anormais, que é um resultado de alterações moleculares em genes associados a uma variedade de processos celulares. A fim de apoiar o desenvolvimento de tumores incipientes, espera-se que as células cancerosas necessitem de um fornecimento constante e crescente de nutrientes. Embora seja evidente que esse aumento na demanda de nutrientes seria acompanhado de ajustes na expressão de genes associados à nutrição celular, pouco se sabe sobre a regulação desses genes e suas implicações para o desenvolvimento e o tratamento do câncer. Neste estudo foi compilada uma lista baseada na literatura de 90 genes associados à nutrição celular e utilizada para estabelecer assinaturas de expressões nutrigenômicas em todo o painel da linha celular do câncer NCI-60. A fim de compreender a possível interação entre genes nutricionais e genes cancerígenos, foi utilizada para análise e comparação uma lista de genes 119 genes causadores de câncer, consolidada na literatura. Em seguida, os dados do NCI-60 disponíveis ao público foram utilizados para correlações entre assinaturas nutrigenômicas, genes causadores de câncer e drogas antineoplásicas. Os resultados obtidos mostraram várias correlações robustas entre as listas gênicas e as drogas. A expressão do GPX2 (gene da glutationa peroxidase 2) foi fortemente correlacionada com vários genes que conduzem ao câncer e drogas antineoplásicas, sugerindo que o GPX2 pode desempenhar um papel importante no desenvolvimento e tratamento do câncer.


1 INTRODUCTION
Cancer is a collection of diseases that are caused by abnormal cell growth, resulting from changes in genes which are responsible for controlling a variety of biological processes including cell growth and division. The most altered genes in cancer are considered cancer driver genes and they include proto-oncogenes, tumor suppressor genes and DNA repair genes (NIH, 2015).

The most recent estimated incidence rate performed by Globocan (2018) shows that there have been 18 million new cases of cancer in the world. Given the current scenario, with the help of bioinformatics, it is possible to advance scientific cancer research and, thus, evaluate high-yielding genomic and molecular data using science, statistics, as well as molecular biology for an evaluation of a large-scale set of molecular expression data. In this way, it allows the identification of personalized strategies for
oncologic patients and, in this way, provide better prevention diagnostics as well as antineoplastic directed therapy (CREIGHTON, 2018).

Bioinformatics allows the evaluation of several genes simultaneously and grant the biological analysis of gene expression data through the panel of human tumor cell lines NCI-60, in which it is possible to evaluate several molecular targets in the 60 cell lines. With this, it is possible to select compounds with greater probability of interacting with a specific molecular target (NIH, 2020). Due to the need for cancer cells to need nutrients to sustain their rapid growth, in this study we seek to find nutrigenomic genes that can play an important role in cancer. Given the above, a in silico approach was used to evaluate the expression of genes involved in the processes of nutrigenomics and their correlations with genes related to cancer and, similarly, with antineoplastic drugs.

Nutrigenomics makes it possible to investigate new interactions of genes associated to nutrition in cancer lines and how these can present metabolic functions in the patterns of gene expression, providing to investigate the activity of several genes in the cellular and molecular mechanisms of cancer and to identify new interventions of regulation of genes that are altered in cancer processes. Thusly, it is possible to designate targeted therapeutic measures and provide a better prognosis, as well as develop new prophylaxis and promote increased survival of cancer patients (FARHUD; YEGANEH, 2010).

Based on the activity of genes in cancer lines, it is possible to determine beneficial responses to treatment by means of drugs that are applied in cancer therapy. This is a research field with an important potential to understand new results of therapeutic efficacy by identifying the genes of the entire genome, as well as by evaluating cellular responses to antineoplastic treatment based on genetic activity (WENG et al., 2013; HUANG; RATAIN, 2009).

Antineoplastic drugs associated with genetic evaluation are fundamental to direct the treatment. Hence, this allows applying new pharmacological approaches with a personalized and targeted therapeutic intervention according to the genes that are altered in cancer patients (CRISCI et al., 2019).
From this perspective, new research on therapeutic approaches and treatments directed to assist oncologic therapy is essential. In this sense, the various genes that are related to the study of nutrition are prominent for identifying new therapeutic targets by way of the analysis of genes that are commonly altered in cancer lines. Therefore, nutrigenomics provides new conducts to oncology regarding the evaluation of nutrition genes in the molecular pathways of cancer, enabling the identification of positive prevention responses, as well as treatment by way of the interaction with cancer drivers and drugs. Then, with bioinformatics, it is possible to identify the gene interaction and how the correlation of both allows the development of new strategies for effective responses.

2 MATERIALS AND METHODS

By means of a in silico approach, a gene expression correlation was performed on 60 cell lines of 9 different types of cancer on the NCI-60 panel, a database of cancer cell lines that assesses genomic and pharmacological data provided by the United States National Cancer Institute (REINHOLD et al., 2012).

In this study, after an extensive literature review, genes associated with nutrigenomics and driver cancer were identified upon articles available on the PubMed platform. Subsequently, these genes were compiled into two lists: one for cancer driver genes and another for nutrigenomics; and with the aid of the GeneCards database, information was collected for each identified gene. Through the CellMiner platform: a database with important molecular profile data resources on the NCI-60 and other types of cancer cells; the genes selected for this study were correlated with each other by the of mathematical analysis and R programming language to identify new patterns of correlation of gene expression and, upon CellMiner, these data were made available by way of a correlation of 60 cell lines.

Besides, a mathematical correlation was performed with nutrigenomics genes and antineoplastic drugs available on the CellMiner platform to identify of genomic and pharmacological activity in cancer lines and distinguish new molecular data sets for possible targeted therapeutic approaches.
3 RESULTS AND DISCUSSION

The mathematical analysis of gene expression between different genes lists resulted in 11080 correlations. As shown in Figure 1, 4245 correlations were obtained for cancer driver and nutrigenomics gene lists; 4558 correlations were obtained between cancer driver genes with themselves; and 2277 correlations were obtained between nutrigenomics genes with themselves.

Figure 1: Results of the interaction of genes associated with nutrigenomics and referring to cancer. The 119 cancer driver genes were correlated with the 90 nutrigenomics genes through a database in R programming language for cell lines available in NCI-60, obtaining the respective results:

<table>
<thead>
<tr>
<th>GENES</th>
<th>CANCER DRIVER</th>
<th>NUTRIGENOMICS &amp; CANCER DRIVER</th>
<th>NUTRIGENOMICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>CANCER DRIVER</td>
<td>4.558</td>
<td>4.245</td>
<td>2.277</td>
</tr>
</tbody>
</table>

Source: Author's own elaboration (2023)

It is possible to verify that the alterations in the metabolism of cancer cells are associated with activities between the genes and their co-expressions. Therefore, classifying the genes that are deregulated is essential to investigate the analysis of the expression of different genes in cancer processes, because, co-expression can occur with common factors and functions. Thus, the analysis of gene correlations, it becomes possible to evaluate potential therapeutic targets and identify new strategies in the area of oncology (REZNIK; SANDER, 2015). That said, in Table 1, the main genes that showed promising results in this in silico analysis will be demonstrated.
Table 1: Genes associated with cancer and referring to nutrigenomics with their respective locations in cytogenetic bands.

<table>
<thead>
<tr>
<th>GENE</th>
<th>CYTOGENETIC BAND</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutrigenomics</td>
<td>GPX2</td>
</tr>
<tr>
<td>Cancer driver</td>
<td>HNF4A</td>
</tr>
<tr>
<td>Cancer driver</td>
<td>GCNT3</td>
</tr>
<tr>
<td>Cancer driver</td>
<td>TYMS</td>
</tr>
<tr>
<td>Cancer driver</td>
<td>OGG1</td>
</tr>
<tr>
<td>Nutrigenomics</td>
<td>LIPC</td>
</tr>
<tr>
<td>Nutrigenomics</td>
<td>APOA2</td>
</tr>
</tbody>
</table>

Gene interaction indicates that genes share a functional relationship in cells and which can present positive interactions, being this a determining factor to evaluate co-expression and activity in a cancer cell. When genes are altered, it becomes possible to evaluate how they can affect molecular processes and contribute to the pathogenesis of cancer. Otherwise, the genes also present negative correlations that may occur due to the altered activity in the cancer lines, indicating that one gene is being expressed, while another is being repressed. Likewise, this negative activity may besides be evident when genes present altered phenotypes in cellular processes (BOUCHER; JENNA, 2013).

Because of this, Table 2 will show the analyses selected for this study with the respective correlation results between nutrigenomics genes and cancer drivers.

Table 2: Values of correlation between nutrigenomics genes and cancer genes.

<table>
<thead>
<tr>
<th>CORRELATION</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutrigenomics &amp; Cancer</td>
<td>GPX2 &amp; HNF4A</td>
</tr>
<tr>
<td>Nutrigenomics &amp; Cancer</td>
<td>GPX2 &amp; GCNT3</td>
</tr>
<tr>
<td>Cancer &amp; Cancer</td>
<td>GCNT3 &amp; HNF4A</td>
</tr>
<tr>
<td>Nutrigenomics &amp; Cancer</td>
<td>GPX2 &amp; TYMS</td>
</tr>
<tr>
<td>Nutrigenomics &amp; Cancer</td>
<td>OGG1 &amp; APOA2</td>
</tr>
<tr>
<td>Nutrigenomics &amp; Cancer</td>
<td>OGG1 &amp; LIPC</td>
</tr>
</tbody>
</table>

Among the analyses obtained, a strong correlation of the nutrigenomics gene GPX2 (Glutathione Peroxidase 2) with the genes associated with cancer HNF4A (Nuclear...
Factor 4α of hepatocytes) and GCNT3 (Glucosaminyl n-acetyl transferase 3) was found. These cancer driver genes also showed positive correlations with each other. This high correlation is evidenced because both genes have activities in liver cells and colon (GUPTA, et al., 2020; LIU et al., 2017; LENNICKE et al., 2018; WALESKY; APTE, 2015). As shown in Figure 2, the genes have a positive functional relationship with cancer cell lineages, and also a negative correlation.

Figure 2: The Network of interaction between the GPX2 nutrigenomics gene and cancer-associated genes using String. The blue lines indicate positive interactions and the negative red line.

The GPX2 presents a function in the antioxidant protection of biological systems, acting in the reduction of the high levels of reactive oxygen species (ROS). Through this antioxidant defense, it prevents the formation of EROs and free radicals (IGHODARO; AKINLOYE, 2018). Furthermore, the GPX2 gene is a selenoprotein, so it uses the mineral selenium as a cofactor to exercise its activity, which also plays a role in cancer prevention and demonstrates important antioxidant activities protecting cells from oxidative damage, in addition to contributing to the reduction of high levels of ROS. Therefore, the appropriate levels of selenium can contribute and act as an adjunct to cancer treatment (TAN et al., 2019; LENNICKE et al., 2018).

In carcinogenic processes, GPX2 deregulation can contribute to oxidative stress. Therefore, the positive regulation of this gene in the cancer lines is fundamental for a
better prognosis and, thus, to maintain the regulated activity of this gene in the antioxidant defense (WANG et al., 2019).

Oxidative stress occurs due to the imbalance between oxidants (reactive oxygen species) and antioxidants. When ROS prevails, they are associated with oxidative cell stress and oxidative damage (IGHODARO; AKINLOYE, 2018).

In conditions of metabolic stress, pro-oxidants outnumber antioxidants, thus, high levels of ROS can increase cell proliferation and induce DNA damage, thus contributing to cancer progression. Therefore, antioxidant mechanisms must overcome the activities of pro-oxidants, fighting ROS to prevent the growth of the tumor cell, as well as preventing a normal cell from proliferating in an uncontrolled way (REUTER et al., 2010).

Concerning HNF4A, when this gene is repressed, it can promote carcinogenesis. In this way, its inhibition can increase the risk of cancer progression, and its re-expression results in a decrease in cancer growth (TANIGUCHI et al., 2018; WALESKY; APTE, 2015). GCNT3 is also seen in cancer when the activity is unregulated. For this reason, the positive regulation of this gene allows a better prognosis of cancer (AGUIRRE-PORTOLÉS; FERNÁDEZ E MOLINA, 2017).

Taking into account the aforementioned correlations, when GPX2 is highly expressed it can potentiate the negative effect of HNF4A and GCNT3, which can be harmful to cancer patients. However, when GPX2 demonstrates its regulated activity, demonstrates important functions in the antioxidant defense system, acting against oxidative damage and reducing the deleterious effects of high levels of ROS. In addition, it can favor the positive regulation of genes that are altered in cancerous processes.

This being said, this mechanism may be promising to identify possible therapeutic targets, as well as being used as a target for drugs, making it possible to target the treatment of liver and colon cancer by regulating the activity of genes that are commonly altered in cancer. Therefore, the correlation analysis between different genes is essential to develop new clinical interventions. Due to this, the gene regulation may benefit patients from whom the cancer cells present alterations in the expression of the above-mentioned genes.
In another way, genes can also have negative interactions. In this analysis, GPX2 demonstrated a negative correlation with TYMS (Thymidylate synthase), which may be associated with the risk of cancer development when it presents its dysregulated function and shows polymorphisms (FENG et al., 2018). Thus, this may be due to the activity of distinct genes in opposite directions in cancer lines, while one gene is driving gene transcription, another is highly expressed or muted, indicating its unregulated activities in the molecular mechanisms of cancer.

Besides, among other genes that showed negative correlations, the cancer-associated gene OGG1 (8-Oxoguanine DNA Glycosylase) stands out, which showed interactions with the LIPC (liver lipase C) and APOA2 (Apolipoprotein 2) genes (Figure 3).

Figure 3: Network of negative interaction between the cancer gene OGG1 and the nutrigenomic genes LIPC and APOA2 using String.

OGG1 has a repair function by base excision, which corrects DNA damage caused by oxidation, deamination, and alkylation (KROKAN; BJORAS, 2013). However, when this mechanism is impaired, polymorphisms of this gene can lead to the accumulation of DNA damage and the development of several types of cancers, such as breast, lung, pancreas, and colorectal cancer (LAI et al., 2016; ALI et al., 2015; YAN et al., 2014; XU; YU; ZHANG, 2013). OGG1 repairs 8-oxoguanine, an oxidative lesion formed by reactive oxygen species, which can oxidize lipid macromolecules (NAKABEPPU, 2014). This
gene repairs 8-OH-Gua in genomic DNA, cutting it into 8-hydroxy-2′-deoxyguanosine (8-OHdG) (OCK et al., 2012).

Otherwise, the APOA2 and LIPC genes have functions in the activities of lipid metabolism. APOA2 is the second most common protein in high-density lipoproteins (HDL). Its levels can impair the reverse cholesterol transport and the antioxidant function of HDL (ZAKI; AMR; ABDEL-HAMID, 2015). Besides, inadequate levels of Apolipoproteins can contribute to oxidative stress, since the excess of circulating lipids induces the formation of ROS, in which they affect cellular structures, including lipids and DNA (LAY et al., 2014).

The LIPC gene, synthesized mainly by hepatocytes, catalyzes the hydrolysis of triglycerides and phospholipids in various lipoproteins (KOBAYASHI et al., 2015). The LIPC variants were related to the lipid profile and oxidative stress, and demonstrated an association with increased levels of 8-OHdG, resulting from lipid levels and adiposity, showing a relationship with oxidative stress levels (TENG et al., 2019). 8-OHdG is related to the oxidation of nucleic acids, so its increased levels may be associated with cancer (GUO et al., 2017; GUO et al., 2016).

In view of this, the analysis of the mapping of genes related to lipid metabolism and the regulation of the activity of the LIPC and APOA2 genes are essential to assess the activity of lipid levels in the body and its correlation with cancer. Therefore, maintaining the levels of oxidative stress reduced in cancer patients, as well as the reduction of 8-OHdG levels, is essential for the regulation of gene expression in cancer lines.

4 DRUGS AND NUTRIGENOMICS

The genes associated with nutrigenomics have been correlated with the drugs available in CellMiner. As shown in figure 4, the interaction between genes and drugs allows to observe new mathematical models and, thus, to evaluate possible therapeutic approaches in the field of cancer therapy. Although there are no studies that associate the genes of nutrition with antineoplastic drugs, with the help of bioinformatics, this is a field
of nutrition that makes it possible to verify new correlations with drugs and evaluate new responses to treatment based on nutritional genomics.

Figure 4: Result of the correlation between nutrigenomics genes and drugs. The genes associated with nutrigenomics were correlated by a mathematical computational analysis with the drugs available in the CellMiner platform, being obtained 34,592 correlations between genes and drugs.

![Diagram showing the correlation between genes nutrigenomics and drugs with 34,592 correlations]

Source: Author's own elaboration (2023)

The study of genetic mapping in response to drugs contributes significantly to assess the applicability of drugs aimed at treating cancers based on genetic activity. This evaluation allows to direct the neoplastic drug treatment using genomic approaches (JOHNSON, 2013)

The studies of nutrigenomics, together with pharmacogenomics, provide the investigation of new therapeutic targets that can be used to direct cancer treatment and, wherefore, obtain satisfactory clinical results. In this study, we verified the association of genes to which nutrition demonstrated important correlations, positive and negative, with antineoplastic drugs proven by the FDA, as well as others that are in the clinical trial. In this sense, Table 3 will show the results selected for this study between the correlations of genes of nutrigenomics and drugs.
Table 3: Values of drug x genes of the nutrigenomics.

<table>
<thead>
<tr>
<th>GENE</th>
<th>DROGA</th>
<th>R</th>
<th>MECANISMO DE AÇÃO</th>
<th>STATUS DA FDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLP1R</td>
<td>Nelarabine</td>
<td>0,58</td>
<td>Ds</td>
<td>FDA Approved</td>
</tr>
<tr>
<td>GPX2</td>
<td>Barasertib</td>
<td>0,48</td>
<td>AURKB</td>
<td>Clinical trial</td>
</tr>
<tr>
<td>G6PD</td>
<td>Anthrapyrazole derivative</td>
<td>0,46</td>
<td>T2</td>
<td>Clinical trial</td>
</tr>
<tr>
<td>FTO</td>
<td>Barasertib</td>
<td>-0,44</td>
<td>AURKB</td>
<td>Clinical trial</td>
</tr>
<tr>
<td>G6PD</td>
<td>Parthenolide</td>
<td>-0,48</td>
<td>APO</td>
<td>FDA Approved</td>
</tr>
<tr>
<td>LEP</td>
<td>Tanespimycin</td>
<td>-0,51</td>
<td>HSP90</td>
<td>Clinical trial</td>
</tr>
<tr>
<td>LEP</td>
<td>Alvespimycin</td>
<td>-0,53</td>
<td>HSP90</td>
<td>Clinical trial</td>
</tr>
</tbody>
</table>

Mechanism of action: Ds: DNA synthesis inhibitor; AURKB: aurora kinase B inhibitor; T2: topoisomerase II inhibitor; APO: Apoptosis inducer. HSP90: heat shock protein 90, enzymatic inhibition with effect on protein synthesis; (Source: CellMiner).

Among the interactions of nutrigenomics genes with drugs, it was possible to identify a correlation of the GLP1R gene (peptide receptor 1 similar to glucagon) with a drug Nelarabine. This gene stimulates glucose-induced insulin secretion. Studies show that GLP1R expression in endometrial cancer lines may be related to a better prognosis in patients with this cancer (KANDA et al., 2018). Nelarabine is an anticancer drug, normally used to treat acute T-cell lymphoblastic leukemia and lymphoma. This drug is metabolized in cells by the cytotoxic metabolite ara-G triphosphate (ara-GTP), which competes with deoxyadenosine triphosphate for incorporation into DNA, resulting in inhibition of DNA synthesis (SANFORD; LYSENG-WILLIAMSON, 2008). Given the example of this positive correlation, GLP1R with this drug may be used as a treatment target in endometrial cancer. Furthermore, with the use of bioinformatics, it is possible to investigate whether the drug Nelarabine can be beneficial in other cancer lines.

In relation to G6PD (Glucose-6-phosphate dehydrogenase), this gene is essential for the synthesis of nucleic acids from the pentose phosphate pathway, which produces NADPH and is fundamental for maintaining redox balance, reducing free radical levels and Oxigen-reactive species. However, when this gene has dysregulated functions, it can contribute to the pathogenesis of cancer (CHEN et al., 2017). Wherefore, adequate levels of this gene are essential for regulating ROS levels to decrease oxidative stress in cancer.
cells. This gene demonstrated positive interactions with the drug Anthrapyrazole derivative (r = 0.46), a topoisomerase II inhibitor, in which it repairs the damage that requires double-stranded break repair pathways and other pathways for removing protein-DNA (NITISS, 2009). On the other hand, G6PD demonstrated negative interaction with the drug Parthenolide, which is responsible for the induction of apoptosis in cancer cells. This drug can lead to alterations in the redox balance, leading to increased production of reactive oxygen species in cancer cells (SUN et al., 2010).

Regarding GPX2, this gene demonstrated a positive association with the drug Barasertib (r = 0.48). Thusly, possibly this drug may potentiate the beneficial effect of GPX2, in which it may lead to the regulation of cancer driver genes that are altered in cancer lines. Barasertib is a prodrug that, by way of phosphatase, undergoes a cleavage in which it releases barasertib-hQPA, which acts as a selective inhibitor of Aurora B kinase. The inhibition of aurora B kinase induces the arrest of the cell cycle and triggers death cells in different types of cancers (DENNIS et al., 2012).

Among other negative interactions of genes with antineoplastic drugs, it was possible to identify genes that are commonly identified in obesity. As an example, the drug Barasertib showed a negative correlation with FTO (Alpha-Ketoglutarate Dependent Dioxygenase), a gene commonly associated with obesity (FONSECA et al., 2020; YANG et al., 2017). Studies demonstrate that polymorphisms in the FTO are related to several types of cancers (DENG et al., 2018; HUANG et al., 2017). As such, the application of Barasertib in the treatment of cancer in patients with an allele in the FTO gene is not entirely favorable, due to the possibility that such a gene may inhibit the efficacy of the drug.

Additionally, among other negative correlations of drugs and genes associated with obesity, it was possible to observe the LEP gene (Leptin). Studies demonstrate that polymorphisms in this gene may be related to carcinogeneses, such as hepatocellular carcinoma, breast and colon cancer (TANG et al., 2019; YANG et al., 2014; SLATTERY et al., 2008).

Elevated levels of leptin, produced mainly by adipose tissue, act as a pro-inflammatory adipokine, where high concentrations may be associated with the
promotion of carcinogenesis. In addition to being a factor in poor prognosis in patients with obesity, cancer cells receive growth-promoting stimuli in an environment where leptin negatively influences through factors such as inflammation, oxidative stress, inhibition of apoptosis, and cell proliferation (RAY; CLEARY, 2018). For this reason, it shows the negative correlation that LEP has demonstrated with the drugs Tanespimycin and Alvespimycin, indicating negative characteristics in the molecular mechanisms of cancer processes. Therefore, the use of these drugs for oncologic treatment in patients with nutritional status classified as obesity may not be efficient, due to over-expression of LEP inhibit the efficacy of these drugs.

Given this, the correlation of genes associated with nutrition with drugs makes it possible to characterize new methods of therapeutic approaches that can benefit patients who present the deregulation of gene expression in cancer processes. Thus, it becomes possible to direct the treatment with the appropriate drug according to the genetic activity of each oncologic patient.

5 FINAL CONSIDERATIONS

The analysis of the genetic interaction of genes of nutrigenomics and driver cancer, as well as the association with the drugs, enabled a better understanding of the pathogenesis of cancer. To obtain the results of correlations between different genes, the use of bioinformatics is essential for the manipulation of biological data. Hence, through the CellMiner platform, it was possible to integrate the set of molecular data to detect new research approaches in the cell lines of the NCI-60. Wherefore, adequate levels of this gene are essential for regulating ROS levels to decrease oxidative stress in cancer cells, the identification of the interaction between different genes in the molecular pathways of cancer made it possible to verify the correlation and functional activity in cancerous processes.

Given the aspects evaluated, the aforementioned research shows that the analysis of this interaction is prominent to identify new therapeutic targets through the regulation of gene expression between cancer driver and nutrigenomic genes. Furthermore, understanding the correlation of genes with drugs allows the applicability of targeted
therapy based on the patient's genetic activity. For this reason, a better understanding of the interactions between different genes, as well as the correlation with drugs, is a promising area for the field of oncology.

As a result, the in silico analyzes carried out in this study must be validated upon new approaches, by way of experimental research, to ascertain whether the considerations mentioned in this mathematical model work correspond to cancer cells in vivo.

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