Volume 3, Issue 1

Journal of Medical Oncology

Open Access

Cancer Science 2020: Correlation of TNF-α, IFN-γ, IL-6, IL-4 and vitamin D with the ER, PR and HER-2 status of a group of breast cancer patients in Sri Lanka - Isurika Dilshanee Weerasinghe - University of Colombo

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Analysis of gene expression profiles have revealed classical subtypes of breast cancer; presence or absence of hormone receptors, i.e. estrogen (ER+/ER-) or progesterone (PR+/PR-) and excess levels of human epidermal growth factor receptor 2(HER-2+/HER-2-). Understanding the role played by pro-inflammatory cytokines, anti-inflammatory cytokines and vitamin D; a major influencer of immune health, in varying breast cancer subtypes and prognosis of breast cancer is vital to identify novel therapeutics.

Competitive Enzyme Linked Immunosorbant Assay (ELISA) measured the serum 25-hydroxyvitamin D levels while Sandwich ELISAs assayed selected serum cytokine (Interferon gamma [IFN-γ], Tumor Necrosis Factor Alpha [TNF-α], Interleukin 4 [IL-4] and Interleukin 6 [IL-6]) levels of 27 female breast cancer patients. HER-2, PR and ER receptor status were obtained from patients' clinical records. The relationship of serum analytes between the two receptor status of each receptor (negative/positive) were statistically analyzed by SPSS software.

Serum IL-6 and 25-hydroxyvitamin D levels did not differ between the groups with positive and negative receptor status of PR, ER or HER-2. Serum IFN-γ and IL-4 levels were higher in the HER2+ patients compared to the HER2- patients ($p=0.06$). Serum TNF-α level was significantly higher in PR+ patients than in PR- patients ($p<0.05$). TNF-α is known to activate NF-κβ signaling pathway which plays a major role in carcinogenesis; could be a potential reason for the PR upregulation. Few previous studies support this observation where inactivating NF-κβ has been reported to significantly decrease PR-A in human decidua after labor onset and a strong correlation between TNF-α gene expression and PR positivity had also been recorded. In conclusion, TNF-α may have a potential role in upregulating PR expression in breast cancer patients.

Breast cancer ranks as the second most frequent type of cancer globally, and the fifth leading cause of cancer-related deaths overall. In women, breast cancer is considered the most commonly diagnosed cancer in the vast majority of countries around the world, making up approximately one-quarter of all cancers diagnosed. The high incidence of breast cancer can be attributed to a variety of factors, most importantly increasing age and lifestyle. Migration to urban areas is also considered a palpable factor associated with increased incidence due to the lifestyle change this migration gives rise to. This increase in incidence is largely attributed to the adoption of a Westernised lifestyle, whereupon unhealthy dietary habits are adopted and physical activity is decreased. The effect on breast cancer incidence is more evident amongst premenopausal than postmenopausal women. A Western diet is typically low in fresh fruit and vegetable intake and high in animal fats, processed foods, salt and sugars.

Diet is an important pillar of any lifestyle, and can be used as a beneficial factor to help prevent cancer in general, and breast cancer in particular. In addition, it may also reduce the risk of cancer progression and thus improve treatment outcomes and decrease human suffering. We recognise that a reduction in breast cancer risk requires a holistic approach but in order to obtain good-quality scientific evidence, we need to address the various components individually. For this reason, we consider the interaction between numerous foods/nutrients and genotype/gene expression, and their influence or potential influence on breast cancer.

Genetic variants are relevant not only to breast cancer risk, but genotype may influence an individual's nutritional behaviour as well as response to specific nutrients. For example, some genetic variations related to adiposity could affect energy intake by influencing satiety/appetite. In addition, personal preference for specific foods, such as sugar and carbohydrate, is identified as an effect of genetic variation, with sugar consumption being explained by 48% of the genetic variation. Furthermore, in some cases, there are interactions between dietary patterns/nutrients and genotype, and this interaction could impede or accelerate breast cancer risk and/or progression. The genotype (CC vs. CT/TT) of the catalase gene, which helps determine the functioning of the catalase antioxidant enzyme, may also influence the benefit received from consuming adequate quantities of fruit and vegetables. The CC genotype resulted in a 17% reduced risk of breast cancer development.

Breast cancer is a disease that may develop and/or progress due to several possible reasons, including non-modifiable factors such as increasing age and genotype, as well as modifiable factors such as smoking, alcohol consumption and lack of physical activity, poor diet and obesity. Obesity and being over-weight play a critical role in increasing the risk of breast cancer recurrence and arises due to an energy imbalance. In a meta-analysis of 43 studies carried out by Rock et al., the risk of recurrence was markedly higher amongst obese

This work is partly presented at 40th Euro Congress on Cancer Science & Therapy May 25-26, 2020

breast cancer survivors than those who were not obese. A recent study revealed an interaction between diet–gene predisposition and long-term changes in body mass index (BMI) and body weight in two independent prospective cohorts of US men and women. In addition to an energy imbalance, the interaction between several dietary nutrients and gene expression is of interest in the field of tumorigenesis.