

Chapter 19

Breast Cancer With Relevance for Heavy Metals, Mycotoxines, and Pesticides

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ABSTRACT

Certain environmental contaminants such as heavy metals, pesticides, and mycotoxins are presumed to play a crucial role in the etiology of breast cancer, which is the most common tumor in women worldwide. In fact, the exposure to heavy metals poses risk in causing human cancers. Several investigations indicated strong contribution of heavy metals especially copper, arsenic, zinc, cadmium, lead, and aluminum in breast cancer. Furthermore, it has been reported that the excessive use of pesticides in agriculture in order to improve the productivity contaminates food materials and can be responsible to induce breast cancer in women. It is also noted that some fungi produce several type of mycotoxins such as zearalenone, aflatoxin, and ochratoxin that are dangerous for human health and can especially cause breast cancer. Thus, the objective of this chapter is to discuss the experimental data regarding the involvement of heavy metals, pesticides, and mycotoxins as well as the recent insights on the molecular mechanisms involved in the progress of breast cancer.

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INTRODUCTION

Breast cancer is the most frequently diagnosed cancer among woman worldwide in terms of incidence and mortality, accounting for about 2.4 million new cases and 523,000 estimated mortalities recorded global in 2015, which corresponds to about 29% of the total incident cancer cases and 14% of all cancer deaths (Fitzmaurice et al., 2017) representing therefore a real public health problem. In Morocco, the occurrence of breast cancer, particularly in young women ranges from 8 to 25.4%, which represent the highest rates published so far (Slaoui et al., 2016). Till now, breast cancer remains highly frequent especially for women under the age of 35 in which it is aggressive (Axelrod et al., 2008). In fact, there are four stages of breast cancer: cancer in the earliest stage is appointed stage 0 (carcinoma *in situ*) and varies from stage I through IV. Stage IV is the most aggressive stage of the disease. A higher stage involves a more advanced metastatic cancer.

Depending on the expression of estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (Her2), mammary carcinomas can be classified into five molecular subtypes: Luminal A, Luminal B, HER2, Basal-like (or triple-negative) and normal-like (Tao et al., 2015). The last one was unnecessary because it is artifactual and corresponds to tumors contaminated by healthy breast tissue (Tao et al., 2015). The luminal A and luminal B subtypes account for about 65% of all breast cancers. These two subtypes are characterized by the expression of estrogen receptors (ER) and progesterone receptors (PR) (Dunnwald et al., 2007). However, there are many differences between these subtypes; mammal carcinomas of the Luminal A molecular subtype tend to express a greater amount of hormonal receptors, particularly progesterone receptors (PR) compared to luminal B (Tao et al., 2015). Due to the expression and activity of receptors hormonal mammal carcinomas luminal A and luminal B are systematically treated with endocrine treatments, including selective estrogen receptor (ER) modulators such as tamoxifen, selective negative ER regulators such as fulvestrant and inhibitors of aromatase such as letrozole which block the systemic production of the native ligand; β -estradiol (Manning, Buck, & Cook, 2016). In contrast, luminal B tumors are generally poorly studied, although they are often more proliferative, clinically more aggressive and have a lower prognosis than luminal A tumors (Tao et al., 2015). Her2 and basal-like subtypes were found to be the most aggressive breast tumors. Her2 oncogene is correlated to epidermal growth factor receptor family, overexpressed in about 20% of the breast tumors and associated with poorer short-term prognosis compared to PR and ER positive breast cancer (Tao et al., 2015). Basal-like subtypes do not express ER, PR, or Her2 and called triple negative breast cancer (Dent et al., 2007). Approximately 15% of the breast cancers fall basal-like breast cancers category and the incidence of this type is generally higher in younger women, African-American women and in patients with mutated BRCA1 (Dent et al., 2007). The precise causes of cancer are still unknown; however, several factors have been linked to its occurrence. The etiological factors such as genetics, family history, age and hormonal changes are associated to a high risk of breast cancer. Moreover, breast cancer might also be induced by external or environmental factors, like smoke, unhealthy diet, exposure to environmental contaminants, etc. There is growing evidence that exposure to environmental pollutants, including heavy metals, pesticides, persistent organic pollutants and mycotoxins is associated with increased incidence of breast cancer. The present chapter is dedicated to emphasizing the involvement of heavy metals, pesticides and mycotoxins on the incidence and progress of breast cancer.

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