

Towards a Psychoneuroimmunendocrine Hypothesis of Breast Cancer

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Abstract. Breast cancer is a neoplastic process thought to arise from the activation of oncogenes in mammary stem cells following chronic exposure to adverse settings (e.g., high estradiol blood concentrations). In spite of the acceptance of this notion, psychological studies support the premise that female personality may influence BC onset, progression and outcome. Medical opinion, however, casts doubts on these assertions. We consider, nonetheless, that controversies arise from the unsupported belief that the workings of the body, including its diseased states, proceed with no consideration for the emotional component. In this review, we first describe and discuss the literature that supports the role of personality on BC onset, progression and outcome in order to propose a physiological mechanism by which personality may influence BC biology. We hope this effort could provide a conceptual framework sufficient enough for the medical establishment to begin considering introducing psychological monitoring among the protocolized prognostic and diagnostic tools aimed at identifying women at risk of developing BC and to have follow up management once diagnosed.

Keywords: Breast cancer, behavioral tendencies, suppression of emotions, stress, health-emotions interaction

INTRODUCTION

Breast cancer (BC) is a highly prevalent malignant neoplastic process in women. It is considered a major public health problem worldwide since, at least for the year 2012, 14.1 million new cases were diagnosed, 32.6 million women lived with it and 8.2 million of them died from medical complications associated to it [1]. Furthermore, BC prevalence is higher in developing countries where the first diag-

nosis occurs at around the age of 50 [2], ten years earlier than in developed countries (although see [3] for recent ciphers in Finland).

BC is an estradiol-sensitive neoplasia. Overexposure to this hormone at sensitive periods along postnatal life increases significantly the risk of developing BC at maturity [4]. Besides estradiol exposure, genetic family history, reproductive history, frequent radiation exposure, obesity, smoking, alcoholism, physical inactivity and low social status all increase the probability of developing BC [5–7]. In addition, there is evidence supporting the fact that certain types of personalities and their related emotional expression predispose women to develop BC and deeply influence the way the disease progresses and

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ends. Conventional medical wisdom, nonetheless, demeans this evidence under the argument that many of the studies on BC psycho-oncology have been conducted in women who have already been diagnosed with BC [8–10]. Nonetheless, other studies have shown that emotional suppression and inadequate stress coping mechanisms compromise the metabolic and immunological status of women, rendering them more susceptible to develop BC [3, 7, 11–14].

Hence, in this review, we seek to invigorate this last notion by providing a reflection on recent literature supporting the role of the woman's personality on the origin, progression and outcome of BC.

PERSONALITY TYPES AND DISEASE: ANCIENT AND MODERN TIMES

Hippocrates probably was the first to infer the existence of connections between personality and the state of health in humankind. Around 2000 years ago, he proposed that each person's temperament was determined by the way the earth elements interacted one another in each subject. From Hippocrates' point of view, the essential trait of each person's temperament was defined by the earth element having the greatest weight in his personality [15, 16; Table 1]. Temperaments were conceived to be associated with specific body fluids released by the heart, liver, brain and spleen. This theory of the four temperaments was updated over time due to advancements in physiology and anatomy. In the 1940's this association of the specific body fluids to the organs of the heart, liver, brain and spleen was changed to organs more related to metabolism such as the pituitary gland, thyroid gland, kidney, gonads, parathyroid gland, or pancreas [17]. If the composite of earth elements and body fluids was balanced and kept in register with each person's temperament, the person would preserve his health. If unbalanced, a disease would emerge affecting the organs responsible of producing the corresponding body fluid. Under these premises, each temperament would make an individual prone to particular sets of seasonal diseases (Table 1). Treatments were devised

considering the opposite qualities of the fluid affected (Table 1).

In an updated version of Hippocrates' temperament theory, researchers presumed that each individual's personality traits remained relatively constant throughout their lifetime. It is precisely this constancy what would provide such traits prognostic value on the individual's present and future state of health or disease [18]. Two basic assumptions constitute the collarbone of this theoretical framework. The first one sustains that persistent, specific personality traits render each individual susceptible to develop a particular set of diseases. The other assumption claims that the conjunction of personality traits provides the context that conditions each person's susceptibility to develop a particular set of illness [18]. Regardless of the approach followed, both assumptions presumed that personality affects not only the individual's quality of life, but the manner in which they experience symptoms, as well as the way in which they cope with the disease [19]. Thus, personality is not merely a factor of disease predisposition, it may also intensify its signs and symptoms once manifested.

PERSONALITY AND BREAST CANCER

It was 1975 when a Londoner research team headed by Steven Greer proposed, for the first time, that people displaying type C personality (Table 2), with a marked tendency towards emotional suppression, were prone to develop BC [20]. Since then, other authors (Table 2) have complemented Greer's proposition by substantiating with empirical evidence that the inability to communicate unpleasant emotions such as anger, anxiety and sadness [21, 22], exerting excessive rationality and sociability, anti-emotional and repressing coping mechanisms and an obsessive need for harmony [23, 24] predispose women to develop BC [25]. As an example, a recent study conducted in Spanish women showed that those that ended up being diagnosed with BC scored high in Rationality/Emotion Defensiveness and the Need for Harmony Tests; significantly lower scores were

Table 1
Hippocrates' Theory of Temperaments

Temperament	Fluid	Main Trait	Organ associated	Element	Season	Quality of the humor
Sanguine	Blood	Joy and optimism	Heart	Air	Spring	Hot and wet
Choleric	Yellow bile	Aggression	Liver	Fire	Summer	Hot and dry
Phlegmatic	Phlegm	Slowness and inactivity	Brain	Water	Winter	Cold and wet
Melancholic	Black bile	Sadness and depression	Spleen	Earth	Fall	Cold and dry

Table 2
Type C personality constructs

Author	Characteristics
Greer y Morris (1975)	Kind of emotional expression (anger, hostility, etc.) Number of stressful live events
Greer, Morris, Pettingale and Watson (1981)	Less expressions of negative emotions Emotional suppression to stressful situations
Temoshok and Heller (1984)	Emotional control Chronically blocked expression of one's needs and feelings Develop feelings of helplessness under extremely stressful situations
Eysenck (1994)	Extremely cooperative Liabilities Conflict avoidant Suppressors emotions, such as anger or anxiety, They are using repression as a coping mechanism Rigid and increased susceptibility to experience hopelessness and depression
Sebastian, Mateos de la Calle and Bueno (1997) and Watson (1981)	Emotional expression deficit Stressful situations that the person has experienced in his life The reactions to abandonment and hopelessness in the face of stressful situations. Some personality characteristics like low neuroticism and anxiety
Bleiker (quoted on López, Esteve-Ramírez and Anarte, 1998) (----)	Emotional suppression Emotional defensiveness Rationality Emotional expression Emotional repression Need for harmony

obtained by healthy women and by those later diagnosed with benign breast pathology [23]. Hence, empirical data supports the theory that some personality traits might be used to predict the chances of developing cancer in women. Evidence also supports the theory that emotional repression (i.e., low anxiety and high defensiveness) and suppression (i.e., deliberate retention of emotional expression) accelerate BC progression, thus shortening the patients' life expectancy [Table 2; 26–29]. On the contrary, when individuals express their emotions freely and openly acknowledge them when confronting traumatic events, their psychological and physical health improves [30–32].

In sum, type C personality in women appears to represent a failed stress coping style that frames a premorbid condition that increases the possibility of developing BC and speeds up its progression towards a negative outcome once seeded [23, 25, 33–36]. Traits of type C personality may also determine the way each patient copes emotionally with the diagnosis and with the way they manage cancer therapy [20, 21]. To reassure these assertions, nonetheless, future studies must improve their design, be prospective and oriented towards finally establishing casual links.

EMOTIONS AND CANCER

The relationship between emotions and disease is presumed to proceed in a context in which the person develops internal negative responses to external stimuli [37]. This circumstance apparently occurs because emotions are universal and culture-independent expressions. Indeed, emotions influence the way humans experience affection (i.e., cognitive-subjective dimension) and express their behavior (i.e., behavior-expression dimension) while modifying their physiological responses (i.e., physiological-adaptive dimension) [13]. These effects are not equal in all individuals since they vary in accord to their distinct personalities. Hence, for emotional assessments to be comprehensive in relation to disease development, they must evaluate aspects representative of all three dimensions. For instance, they could evaluate the language used by the subject (e.g., expressive and/or evaluative, cognitive-subjective dimension), reflexive physiological responses (somatic and autonomous; physiological-adaptive dimension) and behavioral (behavior-expression dimension) [38]. In this regard, fear-anxiety, anger, sadness-depression and disgust

are basic emotional reactions associated with both an unpleasant affective experience and with an intense physiological response. Of those mentioned above, the first three emotions are by far the ones most researched, probably because they have the greatest impact on the development of pathological processes since they lead to unhealthy behavioral choices [13]. In support of this contention, Lilja et al. [39] reported that patients diagnosed with cancer that express their aggression and depression handle stress in a healthier way and have better prognosis since they are more flexible, creative and skillful [39]. In contrast, patients displaying no signs of depression and aggression have an inability to deal with stress and have poor prognosis [40]. Thus, the suppression of negative emotions foments physical illness and worsens diseased states. In this context, three possible scenarios may explain the links between emotions, health or disease. In the first scenario, intense, recurrent and chronic maladaptive reactions (e.g., anxiety, sadness-depression, and anger) may favor the development and consolidation of noxious habits (e.g., addiction and sedentarism) that, in the long run, become detrimental to the person's health. Second, maladaptive reactions may induce excessive physiological activation that, in the long term, could deteriorate the person's health by promoting chronic stress, immune-depression or chronic inflammation [13, 41]. Lastly, negative emotions could also favor diseased states following an emotional deregulation if cognitive assessments of previous stimuli were inadequate or if voluntary emotional suppression was not engaged in a timely manner [42]. All these scenarios might be applicable to BC susceptible patients. Accordingly, negative emotions might contribute to unfold carcinogenic processes, which in turn could feedback negatively on emotional and behavioral expressiveness. Hence, once again, future studies must evaluate the benefits that psychological intervention might have on the genesis, progression and outcome of neoplastic processes as a whole and in BC in particular [43].

STRESS, EMOTIONAL SUPPRESSION AND CANCER

According to Lazarus and Folkman [44], emotions allow people to perceive themselves stressed after assessing the ongoing circumstances as harmful, threatening or challenging [45]. Consequently, if emotions are unbalanced, the individual's stress

responses will likely exacerbate, thus increasing his chances of becoming ill [46, 47].

The idea that stress and cancer are related is long lasting. Traditionally, two theoretical perspectives have been thoroughly explored in the field. The first one considers that chronic stress primes the body to develop cancer since it decreases immune surveillance [48]. Studies conducted in both experimental animals and humans show that, under healthy conditions, natural killer cells protect against tumors by inhibiting their growth and reducing its metastatic potential [49, 50]. Chronic stress, however, suppresses natural killer and T cell responses [51], mononuclear cell counts [52] and increases serum levels of the pro-inflammatory interleukins IL-6 and IL-8 [53].

The second avenue that has been explored with regard to the relationship between stress and cancer claims things are the other way around. Fair enough, there are reports indicating that around 80% of patients having cancer display high stress levels after diagnosis [54]. A similar trend has been reported for women diagnosed with BC [3]. At this point it is worth recalling that stress perception, regardless of whether it is caused by or results from cancer, depends upon each individual's personality [55].

A PSYCHOPHYSIOLOGICAL MODEL TO EXPLAIN BREAST CANCER DEVELOPMENT AND PROGRESSION

In 2014, Kruk introduced to the specialized literature a multifactorial model to explain women's BC morbi-mortality, based on the interaction of metabolic, genetic and life style factors. Given the information provided along the preceding sections, we set out to enrich this model by incorporating psychological factors known to predispose and/or favor BC onset and progression [56]. We also considered it was important to incorporate the physiological variables that sustain chronic stress [57–60] to Kruk's model. As it now stands, the integrated model is diagrammed in Fig. 1. Briefly, the psychoneuro-immunendocrine model postulated predicts that women with type C personality traits, most importantly emotional suppression, are prone to over-dimensioning environmental challenges, thus leading them to generate allostatic/pantostatic stress loads [29, 59, 61], supported by the chronic activation of hypothalamic-pituitary-adrenal/gonadal axes (HPA/G) [62]. As a result, increased circulating lev-

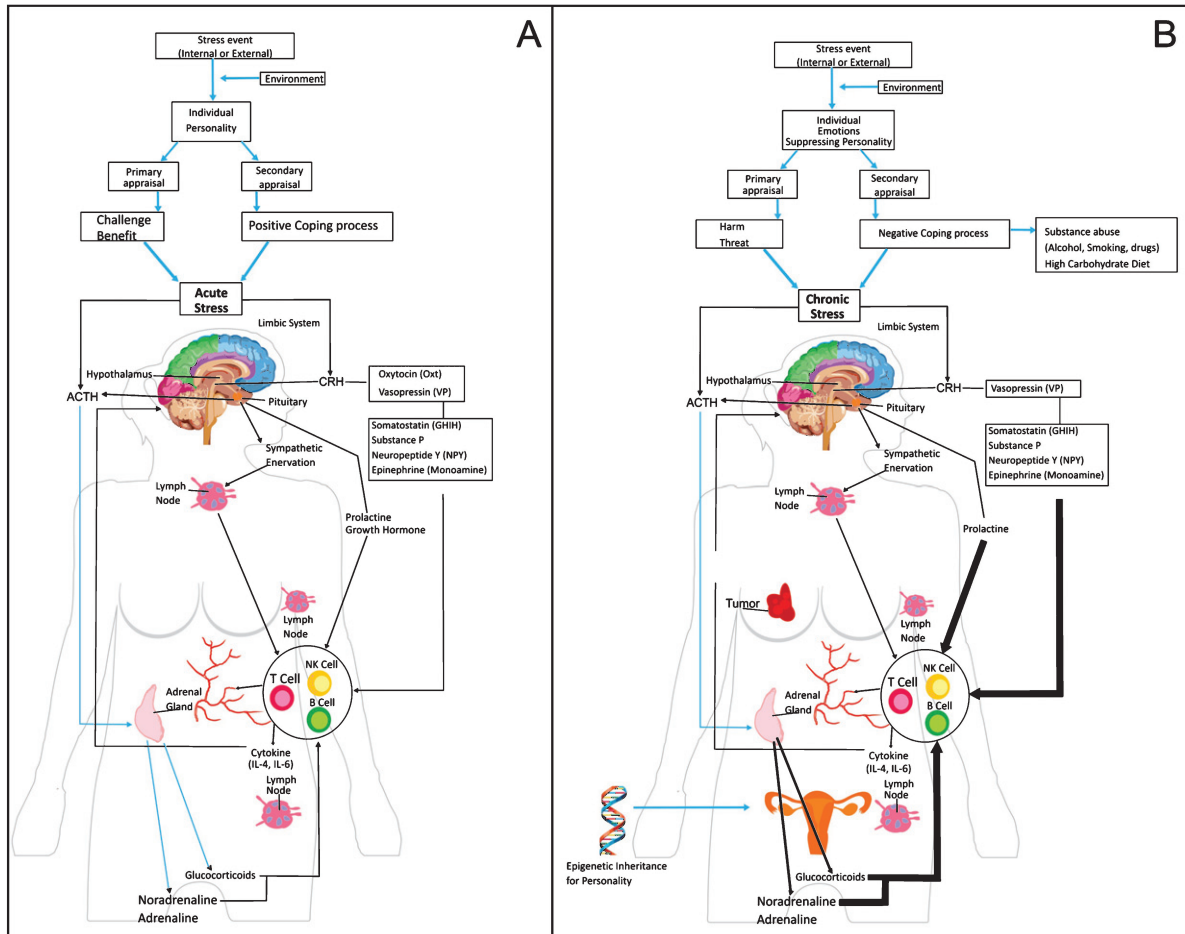


Fig. 1. Psycho-physiological Model for Breast Cancer Development. In this modified version of Kruk's model we suggest that women featuring emotional suppression frequently perceived environmental challenges as excessively stressful. This circumstance puts them on the verge of suffering chronic stress. Panel A diagrams what we think occurs in a woman that does not suppress emotions. In this case, the woman's appraisal of the challenge might be stressful at first. On second thought, she recognizes her ability to contend with it. Under these circumstances, even though her body engages the stress mechanism, it rapidly modulates the physiological chain of events by feeding back the stress response and thus getting her body back into homeostasis. In sharp contrast, women incapable of freeing their emotions (Panel B), after first appraisal of the challenge, consider themselves incapable of confronting it successfully. Then, they turn to use negative coping skills (e.g., drinking alcohol, smoking and/or consuming high-carbohydrate diet) to "deal" with the challenge. This circumstance throws her bodies into an exacerbated chronic stress response in which the modulatory negative feedback is dysfunctional. These events will tend to promote inflammation initially but, in the long run, will suppress NK cell mediated innate and T and B cell mediated adaptive immune responses and, with this, will eventually promote the emergence of BC. The altered endocrine milieu perpetuates this condition. Finally, since gametes may be affected in these altered conditions, the possibility that children will inherit them through epigenetic memory is high.

els of estrogens secreted by the ovaries and by body fat could elevate the risk of developing BC [62]. On the other hand, chronic stress loads could raise prolactin serum concentrations leading to decreased immune surveillance [57–59, 63–66]. Circumstantial evidence of these concepts comes from observations that show that Type C personality is associated with depressed immunity in patients having BC. Also, studies in experimental animal models have revealed that socially inhibited behavior depresses natural

killer lymphocyte function, thus increasing cancer susceptibility in mice [67] and that inflammatory cytokine and glucocorticoid serum levels concentrations correlate positively to tumor growth in rats exposed to carcinogenic agents [68].

Lastly, even though epigenetic inheritance is not a theme that has been touched along the lines of this review, we think it must be also added to Kruk's model since some personality traits might be inherited.

CONCLUSIONS

- Personality traits, as stable characters, may condition the onset, progression and outcome of BC. Breast cancer prevention, diagnosis and prevention programs must evaluate them thoroughly.
- Negative emotions are frequent sources of chronic stress. Breast cancer prevention, diagnosis and prevention programs must monitor them thoroughly.
- It is strongly recommended a re-integration of the psychological component into medical evaluation with the aim of identifying women at risk of developing BC.

COMPETING INTERESTS

All authors declare that there are no conflicts of interest.

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REFERENCES

- [1] Cancer Statistics Worldwide. International Agency for Research on Cancer. <http://globocan.iarc.fr/> (accessed 8.02.14)
- [2] Chávarri-Guerra Y, Villareal-Garza C, Liedke PER, et al. Breast cancer in Mexico: A growing challenge to health and the health system. *Lancet Oncol.* 2012;13:e335-345.
- [3] Eskelinen M, Korhonen R, Selander T, Ollonen P. Emotional Personality/Proximity versus emotional authenticity in patients-physician communication in healthy study participants, and in patients with benign breast disease, and breast cancer: A prospective case-control study in Finland. *Anticancer Research.* 2015;35:1627-34.
- [4] Russo J, Russo I. Development of the human breast. *Maturitas.* 2004;49:2-15. doi:10.1016/j.maturitas.2004.04.011
- [5] Danaei G, Vander S, Lopez AD, Murray CJ, Ezzati M. Causes of cancer in the world: Comparative risk assessment of nine behavioural and environmental risk factors. *Lancet.* 2005;366(9499):1784-1793. doi: 10.1016/S0140-6736(05)67725-2.
- [6] Peled R, Carmil D, Siboni-Samocho O, Shoham-Vardi I. Breast cancer, psychological distress and life events among young women. *BMC Cancer.* 2008;8:245. doi:10.1186/1471-2407-8-245
- [7] Khazae-Pool M, Montazeri A, Majlessi F, Foroushani AR, Nedjat S, Shojaeizadeh D. Breast cancer-preventive behaviors: Exploring Liranian women's experiences. *BMC Women's Health.* 2014;14:41.
- [8] Carvalho A, Mesquita E, De Almeida I, De Figueiredo Z. Aspectos culturales en el proceso de padecer cáncer de mama. *Avances En Enfermería.* 2005;XXIII(2):28-35. julio-diciembre.
- [9] Ornelas-Mejorada RE, Tufiño MA, Sánchez-Sosa JJ. Ansiedad y depresión en mujeres con cáncer de mama en radioterapia: Prevalencia y factores asociados. *Actas de Investigación Psicológica.* 2011;1(3):401-14.
- [10] Llantá MC, Massip C, Martínez Y. La significación de la esperanza en el paciente oncológico. *Rev Electrónica Medicina, Salud y Sociedad.* 2012;2(3):155-75.
- [11] Bowman G. Emotions and illness. *Journal of Advanced Nursing.* 2000;34(2):256-63.
- [12] Rojas-May G. Estrategias de intervención psicológica en pacientes con cáncer de mama. *Rev Med Clin Condes.* 2006;17(4):194-7.
- [13] Piqueras JA, Ramos V, Martínez AE, Oblitas LA. Emociones negativas y su impacto en la salud mental y física. *Suma Psicológica.* 2009;16(2):85-112.
- [14] Cruzado JA. Tratamiento psicológico en pacientes con cáncer Síntesis, España, 2010.
- [15] Allport GW. *La personalidad*, Herder, Barcelona, 1986.
- [16] Alby JC. La concepción antropológica de la medicina hipocrática. *Enfoques.* 2004;XVI(1):5-29.
- [17] Adler A. *Understanding human nature*, Greenberg, New York, 1946.
- [18] Sanderman R, Ranchor A. The predictor status of personality variables: Etiological significance and their role in the course of disease. *European Journal of Personality.* 1997;11:359-382.
- [19] Saita E, Acquati C, Kayser K. Coping with early stage breast cancer: Examining the influence of personality traits and interpersonal closeness. *Frontiers in Psychology.* 2015;6. Doi: 10.3389/fpsyg.2015.00088
- [20] Vinaccia S, Arango C, Cano E, Tobón S, Moreno E, López AE. Evaluación del Patrón de Conducta Tipo C y su relación con la cognición hacia la enfermedad en pacientes colostomizados con diagnóstico de cáncer colorrectal. *Univ Psychol Bogotá.* 2006;5(3):575-83.
- [21] Torres AM. Relación entre el patrón de conducta tipo C y el cáncer de mama. *Univ Psychol Bogotá.* 2006;5(3):563-73.
- [22] Cerezo MV, Ortiz-Tallo M, Cardenal V. Expresión de emociones y bienestar en un grupo de mujeres con cáncer de mama: Una intervención psicológica. *Revista Latinoamericana de Psicología.* 2009;41(1):131-40.
- [23] Sebastián J, León M, Hospital A. Variables psicosociales y cáncer de mama: Un estudio cuasiprospectivo de la personalidad tipo C. *Revista Latinoamericana de Psicología.* 2009;41(3):461-479.
- [24] Eskelinen M, Ollonen P. Assessment of "Cancer-prone Personality" characteristics in healthy study subjects and in patients with breast disease and breast cancer using the commitment questionnaire: A prospective case-

- control study in Finland. *Anticancer Research*. 2011;31:4013-4018.
- [25] Sebastián J, Mateos de la Calle N, Bueno MJ. Expresión emocional y personalidad tipo C: Diferencias entre mujeres con patología mamaria maligna, benigna y normales. *Revista de Psicología de la Salud*. 1997;9(1):93-126.
- [26] Weinberger DA. The construct validity of the repressive coping style. In: Singer JL, editor. *Repression and dissociation: Implications for personality theory, psychopathology, and health*. Chicago: University of Chicago Press, 1990, pp. 337-86.
- [27] Giese-Davis J, Koopman C, Butler LD, et al. Change in emotion-regulation strategy for women with metastatic breast cancer following supportive-expressive group therapy. *J Consult Clin Psychol*. 2002;7:916-25.
- [28] Córdova ML, Giese-Davis J, Golant M, et al. Mood disturbance in community cancer support groups. The role of emotional suppression and fighting spirit. *J Psychosom Res*. 2003;55:461-467.
- [29] Giese-Davis J, Wilhelm FH, Conrad A, et al. Depression and stress reactivity in metastatic breast cancer. *Psychosom Med*. 2006;68:675-83.
- [30] Pennebaker JW. The effects of traumatic disclosure on physical and mental health: The values of writing and talking about upsetting events. *Int J Emerg Ment Health*. 1999;1:9-18.
- [31] Iwamitsu Y, Shimoda K, Abe H, Tani T, Okawa M, Buck R. The relation between negative emotional suppression and emotional distress in breast cancer diagnosis and treatment. *Health Commun*. 2005a;18:201-15.
- [32] Iwamitsu Y, Shimoda K, Abe H, Tani T, Okawa M, Buck R. Anxiety, emotional suppression, and psychological distress before and after breast cancer diagnosis. *Psychosomatics*. 2005b;46:19-24.
- [33] Iwamitsu Y, Shimoda K, Abe H, Tani T, Kodama M, Okawa M. Differences in emotional distress between breast tumor patients with emotional inhibition and those with emotional expression. *Psychiatry and Clinical Neurosciences*. 2003;57:289-94.
- [34] Nieto-Munuera J, Abad M, Esteban M, Tejerina M. *Psicología para Ciencias de la salud*, Mc Graw Hill, España, 2004.
- [35] Bleiker E, van der Ploeg H, Hendriks J, Adér H. Personality factors and breast cancer development: A prospective longitudinal study. *Journal of the National Cancer Institute*. 1996;88(20):1478-82.
- [36] Llantá MC, Grau J, Massip C. La psicología de la salud y la lucha contra el cáncer. En Hernández E, Grau J. (Comps.). *Psicología de la Salud: Fundamentos y aplicaciones*. Centro Universitario de Ciencias de la Salud: Guadalajara, 2005.
- [37] Frazetto G. *Cómo sentimos* Anagrama, Barcelona, 2014.
- [38] Lang P. Emotion and motivation: Toward consensus definitions and a common research purpose. *Emotion Review*. 2010;2(3):229-33.
- [39] Lilja A, Smith G, Malmström P, Salford LG. Attitude towards aggression and creative functioning in patient with breast cancer. *Perceptual and Motor Skills*. 1998;87:291-303.
- [40] Lilja A, Smith G, Malmström P, Salford LG, Idvall I, Horstman V. Psychological profile in patients with stages I and II breast cancer: Associations of psychological profile with tumor biological prognosticators. *Psychological Reports*. 2003;92:1187-98.
- [41] Martin P. *The Healing Mind*, Thomas Dunne Books, New York, 1998.
- [42] Cano-Vindel A. Bases teóricas y apoyo empírico de la intervención psicológica sobre los desórdenes emocionales en atención primaria. *Una Actualización Ansiedad y Estrés*. 2011;17(2-3):157-84.
- [43] Cano A. Control emocional, estilo represivo de afrontamiento y cáncer ansiedad y cáncer. *Psicooncología*. 2005;21:71-80.
- [44] Rodríguez-Marín J, Neipp M. *Manual de Psicología social de la salud*. Síntesis España. 2008.
- [45] Lazarus R. *Estrés y emoción*, Desclée de Brouwer, España, 2000.
- [46] Barroilhet S, Forjaz MJ, Garrido E. Conceptos, teorías y factores psicosociales en la adaptación al cáncer. *Actas Esp Psiquiatr*. 2005;33(6):390-7.
- [47] Rodríguez J. *Psicología Social de la Salud*. España: Síntesis, 1995.
- [48] Kruk J. Lifestyle components and primary breast cancer prevention. *Asian Pac J Cancer Prev*. 2014;15(24):10543-55.
- [49] Vissoci EM, Odebrecht S, Kaminami H. Stress, depression, the immune system, and cancer. *Lancet Oncol*. 2004;5:617-25.
- [50] Sabbioni ME, Siegrist HP, Bacchi M, et al. Association between immunity and prognostic factors in early stage breast cancer patients before adjuvant treatment. *Breast Cancer Res Treat*. 2000;59:279-87.
- [51] Andersen BL, Farrar WB, Golden-Kreutz D, et al. Stress and immune responses after surgical treatment for regional breast cancer. *J Natl Cancer Inst*. 1998;90(1):30-6.
- [52] Zelig U, Barlev E, Bar O, et al. Early detection of breast cancer using total biochemical analysis of peripheral blood components: A preliminary study. *BMC Cancer*. 2015;15:480. Doi: 10.1186/s12885-015-1414-7
- [53] Yokoe T, Iino Y, Morishita Y. Trends of IL-6 and IL-8 levels in patients with recurrent breast cancer: Preliminary report. *Breast Cancer*. 2000;7(3):187-90.
- [54] Parikh D, De Ieso P, Garvey G, et al. Post-traumatic stress disorder and post-traumatic growth in breast cancer patients—a systematic review. *Asian Pac J Cancer Prev*. 2015;16(2):641-46.
- [55] Florez-Alarcón L, Mercedes M, Moreno B. *Psicología de la salud*. Temas actuales de investigación en Latinoamérica. Bogotá: ALAPSA. 2005;59-76.
- [56] Sirera R, Sánchez P, Camps C. Inmunología, estrés, depresión y cáncer. *Psicooncología*. 2006;3(1):35-48.
- [57] Chambers DA, Schauenstein K. Mindful immunology: Neuroimmunomodulation. *Immunology Today*. 2000;21(4):168-70.
- [58] Heinze G. Mente-Cerebro: Sus señales y su repercusión en el sistema inmunológico. *Salud Mental*. 2001;24(1):3-9.
- [59] Gómez B, Escobar A. La psiconeuroinmunología: Bases de la relación entre los sistemas nervioso, endocrino e inmune. *Rev Fac Med UNAM*. 2002;45(1):22-6.
- [60] Glaser R, Kiecolt-Glaser J. Stress-induced immune dysfunction: Implications for health. *Nature*. 2005;5:243-51.
- [61] McEwen B. *The end of stress as we know it*. Washington: Joseph Henry Press, 2002.
- [62] Nava-Castro K, Palacios-Arreola M, Ostoa-Salama P, et al. The immunoendocrine network in breast cancer. *Advances in Neuroimmune Biology*. 2014;5:105-131.
- [63] Kenne E, Martensson LB, Holmberg SB, Andersson BA, Odén A, Bergh I. Mindfulness based stress reduction study design of a longitudinal randomized con-

- trolled complementary intervention in women with breast cancer. *BMC Complementary and Alternative Medicine*. 2013;13:248. Doi: 10.1186/1472-6882-13-248
- [64] Lin Y, Wang C, Zhong, et al. Striking life events associated with primary breast cancer susceptibility in women: A meta-analysis study. *Journal of Experimental Clinical Cancer Research*. 2013;32:53.
- [65] Kim SW, Kim SY, Kim JM, et al. Relationship between a hopeful attitude and cellular immunity in patients with breast cancer. *General Hospital Psychiatry*. 2011;33:371-6.
- [66] Navas C, Villegas H, Hurtado R, Zapata D. La conexión mente-cuerpo-espíritu y su efecto en la promoción de la salud en pacientes oncológicos. *Revista Venezolana de Oncología*. 2006;18(1):28-37.
- [67] Petitto JM, Lysle DT, Garipey JL, Clubb PH, Cairns RB, Lewis MH. Genetic differences in social behavior: Relation to natural killer cell function and susceptibility to tumor development. *Neuropsychopharmacology*. 1993;8(1):35-43.
- [68] Pyter LM, Prendergast BJ. Individual differences in pre-carcinogen cytokine and corticosterone concentrations and depressive-like behavior predict tumor onset in rats exposed to a carcinogen. *Psychoneuroendocrinology*. 2013;38(6):800-7.