

Can Affective Processes Influence Cancer Biology?

Giovanna Zappalà

Shadia Kawa

Paige McDonald

Affective Science Perspectives on Cancer Control
October 12, 2011

Affect & Cancer: Historical Overview

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- 1970ies: Robert Ader, PsychoNeuroImmunology (PNI)

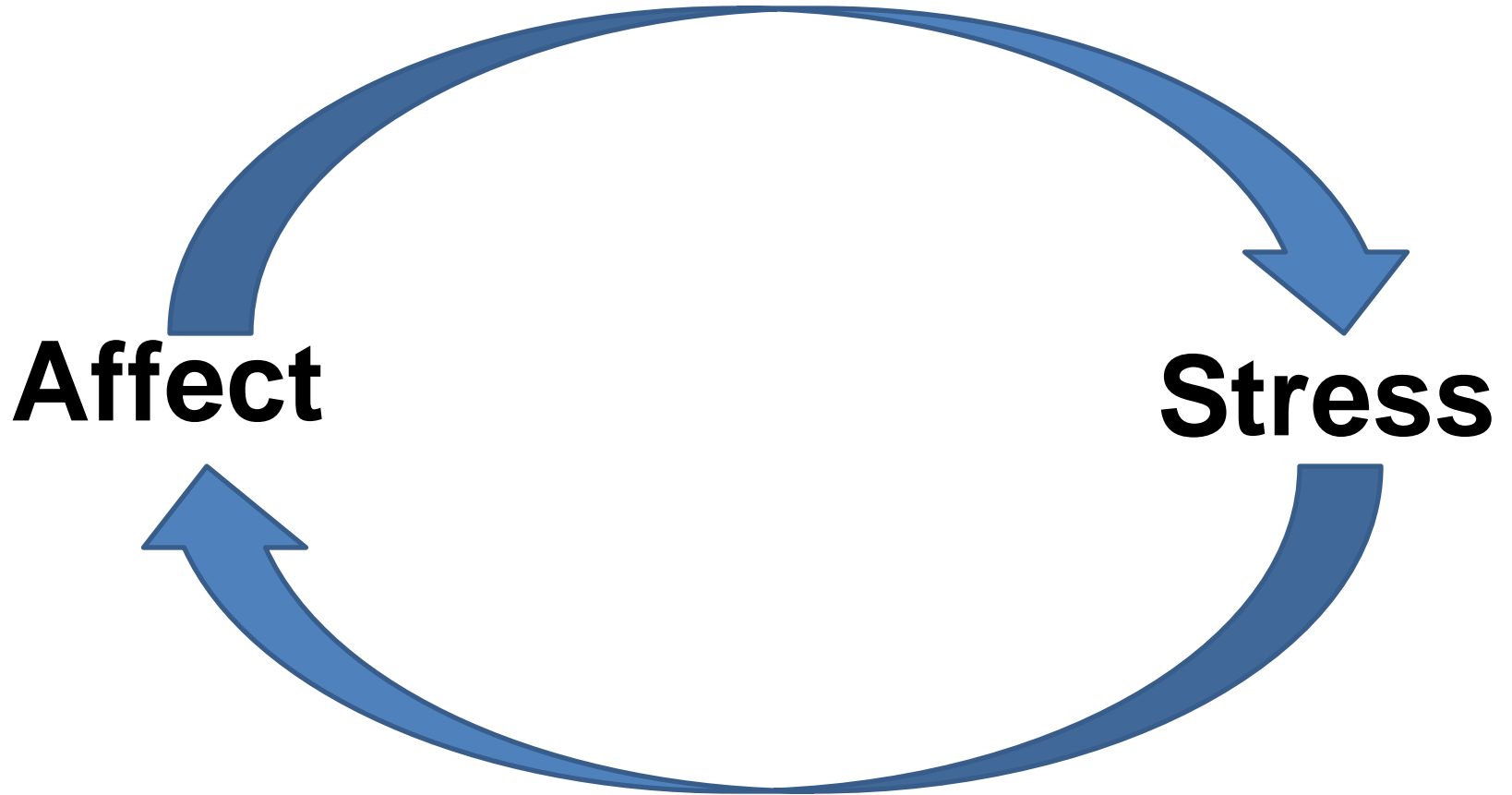
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- ***State of the science: Epidemiological, prospective, psychological intervention, & pharmacological intervention studies suggest a link!***

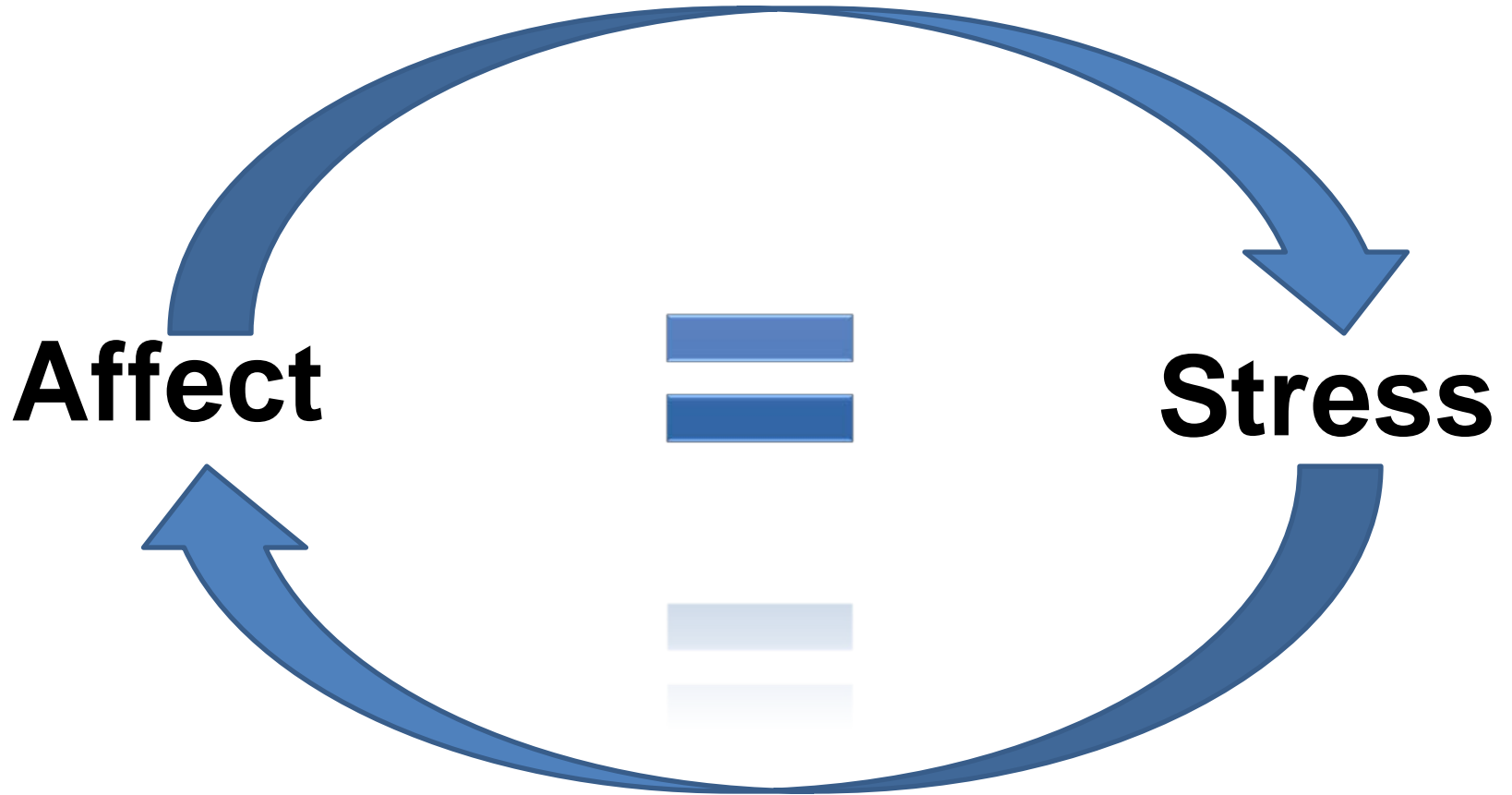
Stress & Affect



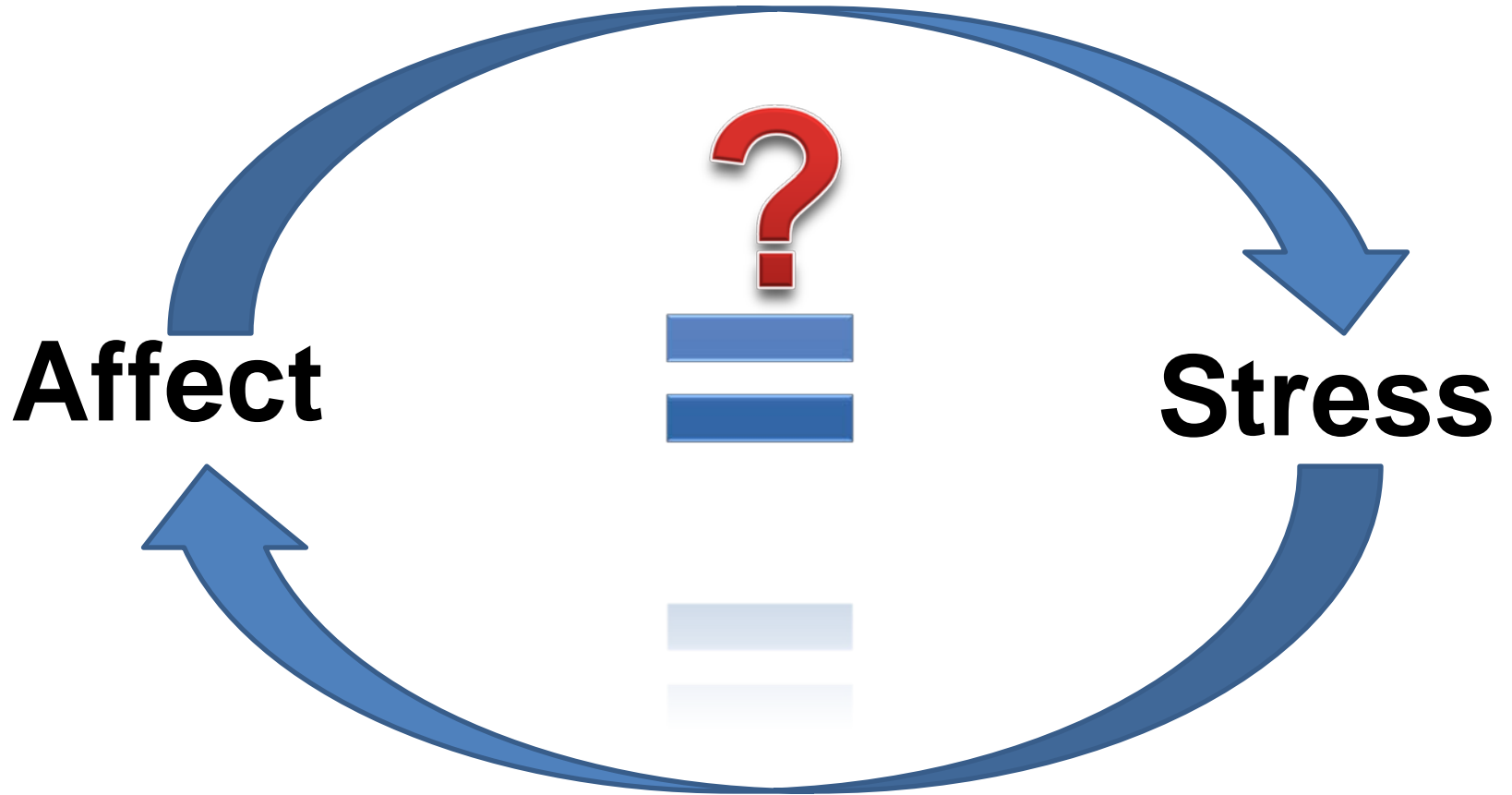
Stress & Affect



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Stress

Hans Selye:

Stressor = “a change in an organism’s internal or external environment which is perceived by the organism as threatening”.

Stress = perceived threat associated with “an alteration in the body’s hormonal and neuronal secretions caused by the central nervous system in response to a perceived threat”.

Distress – “negative stress” v/s **Eustress** – “positive stress”

Selye, H (1955), Stress and disease. Science, 122: 625-631.

Affective processes in the context of cancer

Environmental & psycho-social factors with an affective dimension

Stress...

Chida et al (2008), *Do stress-related psychosocial factors contribute to cancer incidence and survival? Nature Clinical Practice Oncology*, 5(8):466-475.

Adverse life events (bereavement, divorce, loss of loved one...)

Duijts SFA, et al (2003), *The association between stressful life events and breast cancer risk: A meta-analysis. International Journal of Cancer*, 107(6):1023-1029.

Lillberg K et al (2003), *Stressful life events and risk of breast cancer in 10,808 women: a cohort study. American Journal of Epidemiology*, 157:415-423.

Social support/social isolation

Pinquart M & Duberstein PR (2010), *Associations of social networks with cancer mortality: a meta-analysis. Critical Reviews in Oncology/Hematology*, 75(2;403-415.):122-137.

Nausheen B, et al (2009), *Social support and cancer progression: a systematic review. Journal of Psychosomatic Research*, 67

Depression, Anxiety

Pinquart M & Duberstein PR (2010), *Depression and cancer mortality: a meta-analysis. Psychological Medicine*, 40:1797-1810.

Giese-Davis J et al (2011), *Decrease in depression symptoms is associated with longer survival in patients with metastatic breast cancer: A secondary analysis. Journal of Clinical Oncology*, 4(1):413-420.

Emotional distress, poor QOL

Hamer M, Chida Y, Molloy GJ (2009), *Psychological distress and cancer mortality. Journal of Psychosomatic Research*, 66:255-258.

Psychological interventions

Creswell JD, Lam S, Stanton AL, Taylor SE, Bower JE, Sherman DK (2007), *Does Self-Affirmation, Cognitive Processing, or Discovery of Meaning explain cancer-related health benefits of expressive writing? Personality and Social Psychology Bulletin*, 33(2):238-250.

Antoni MH, Lechner S, Diaz A, Vargas S, Holley H, Phillips K, McGregor B, Carver CS, Blomberg B (2009), **Cognitive behavioral stress management effects on psychosocial and physiological adaptation in women undergoing treatment for breast cancer**, *Brain, Behavior and Immunity*, Vol. 23, pp. 580-591

In animals:

Psychological stress paradigms

Kawa S, et al (forthcoming), *The effects of psychological stress on cancer progression: a systematic review and meta-analysis of animal models.*

Affective processes in the context of cancer

Environmental & psycho-social factors with an affective dimension

Emotion regulation, Coping, & Personality

Type C personality/coping style & emotional suppression

Temoshok L (1987) *Personality, coping style, emotion and cancer: towards an integrative model. Cancer Surveys*, 6(3):545-567.

Hopelessness/pessimism

Schulz et al (1996) *Pessimism, age, and cancer mortality. Psychol. Aging*, 11, 304–309.

Active coping/avoidance

Butow et al (2000), *Epidemiological evidence for a relationship between life events, coping style, and personality factors in the development of breast cancer. J. Psychosom. Res.*, 49, 169–181.

Denial/minimization

Butow et al (1999); Butow et al (2000)

Fighting spirit

Greer et al (1979); Greer et al (1990); Pettingale (1984); Pettingale et al (1985)

Dispositional optimism

Allison PJ et al (2003), *Dispositional optimism predicts survival status 1 year after diagnosis in head and neck cancer patients. Journal of Clinical Oncology*, 21:543-548.

No relationship between personality & cancer?

Bleiker EMA et al (2008), *Personality factors and breast cancer risk: a 13-year follow-up. JNCI*, 100:213-218.

Nakaya et al (2010) *Personality traits and cancer risk and survival based on Finnish and Swedish registry data. American Journal of Epidemiology*, 172(4):377-385.

Post-traumatic growth; benefit-finding – adaptive?

Bussell VA, Naus MJ (2011) *A longitudinal investigation of coping and posttraumatic growth in breast cancer survivors. Journal of Psychosocial Oncology*, 28:61-78.

Sumalla EC, Ochoa C, Blanco I (2009), *Posttraumatic growth in cancer: Reality or illusion? Clinical Psychology Review*, 29:24-33

Emotional wellbeing

Coyne JC, Pajak TF, Harris J, Konski A, Movsas B, Ang K, Bruner DW (2007), *Emotional well-being does not predict survival in head and neck cancer patients: A radiation therapy oncology group study. Cancer*, 110(11):2568-2575

In animals:

Environmental enrichment

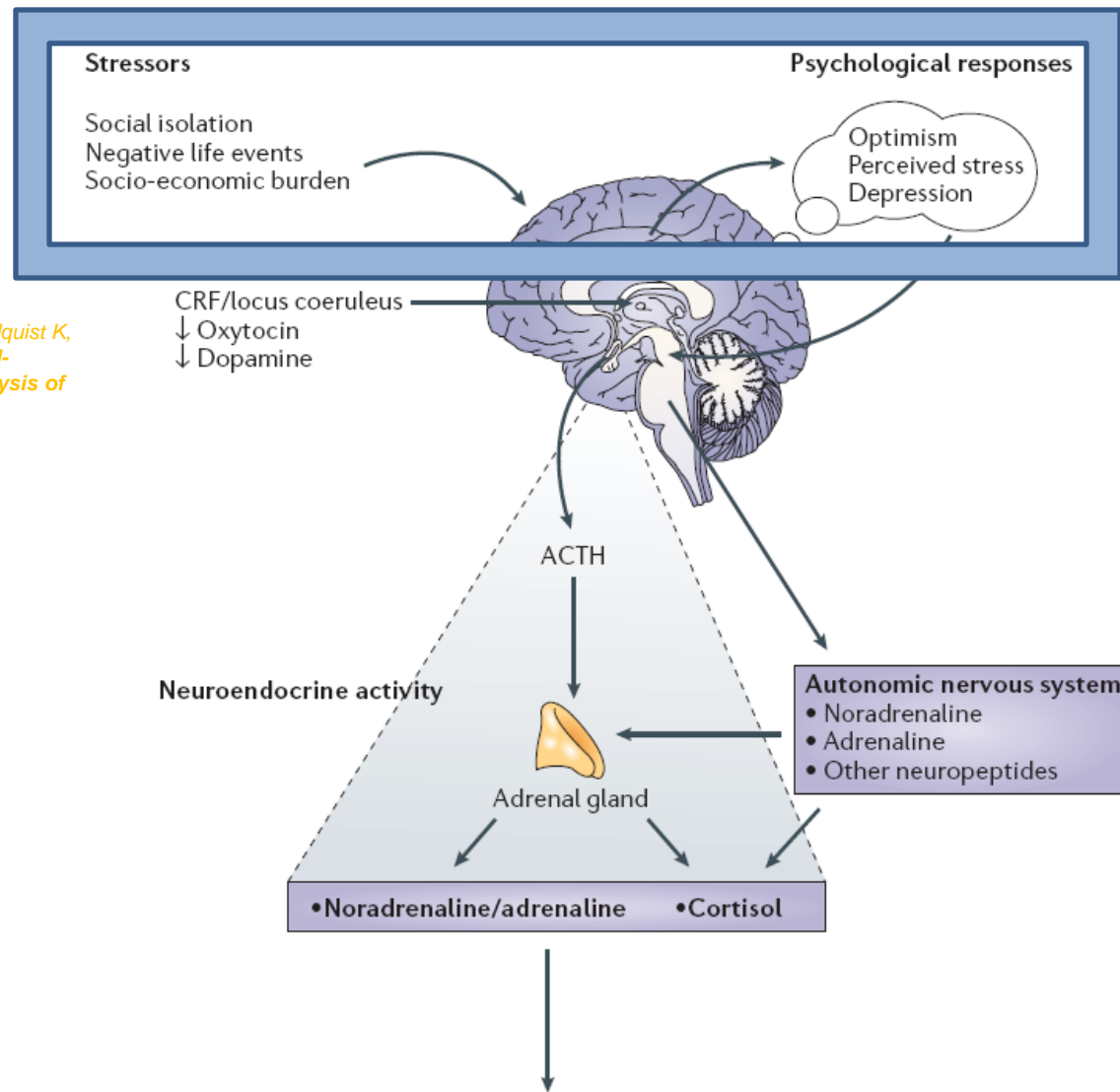
Cao L et al (2010), *Environmental and genetic activation of a brain-adipocyte BDNF/Leptin axis causes cancer remission and inhibition. Cell*, 142(1):

At the interface of affect and cancer: From affect & brain to neuroendocrine system

Affect

Core limbic structures-
Amygdala
Periaqueductal Gray (PAG)
Hypothalamic activations (Hy)

*Kober H, Barrett LF, Joseph J, Bliss-Moreau E, Lindquist K, Wager T (2008), **Functional grouping and cortical-subcortical interactions in emotion: A meta-analysis of neuroimaging studies.** Neuroimage, 42:998-1031*



Does Stress influence Cancer?



Inconsistent or weak associations have been identified regarding **cancer incidence**

The association between stressful life events and breast cancer risk: A meta-analysis

Dujts SFA et al. (2003) *Int J Cancer* 107: 1023-1029

Do stress-related psychosocial factors contribute to cancer incidence and survival?

Chida Y et al. (2008) *Nature Clinical Practice Oncology* 56 (8): 466-475

Does Stress influence Cancer?



Epidemiological and clinical studies document **significant evidence for cancer progression**

Social network, social support, and survival after breast cancer diagnosis

Kroenke CH et al. (2006) *JCO* 24 (7): 1105-1111

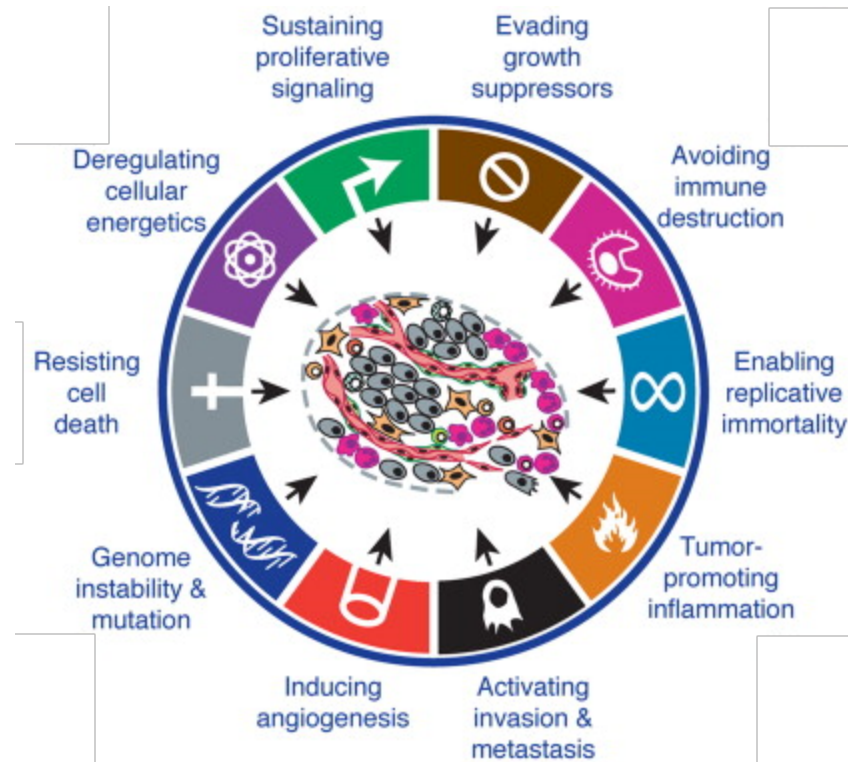
Psychological distress and cancer mortality

Hamer M et al.(2009) *J Psychosomatic Res* 66: 255-258

How does Stress influence Cancer

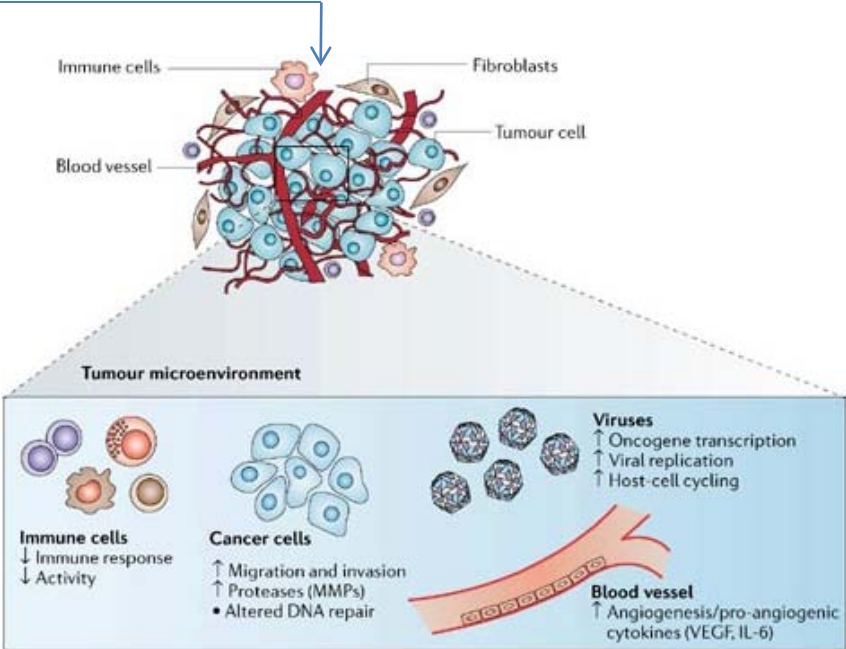
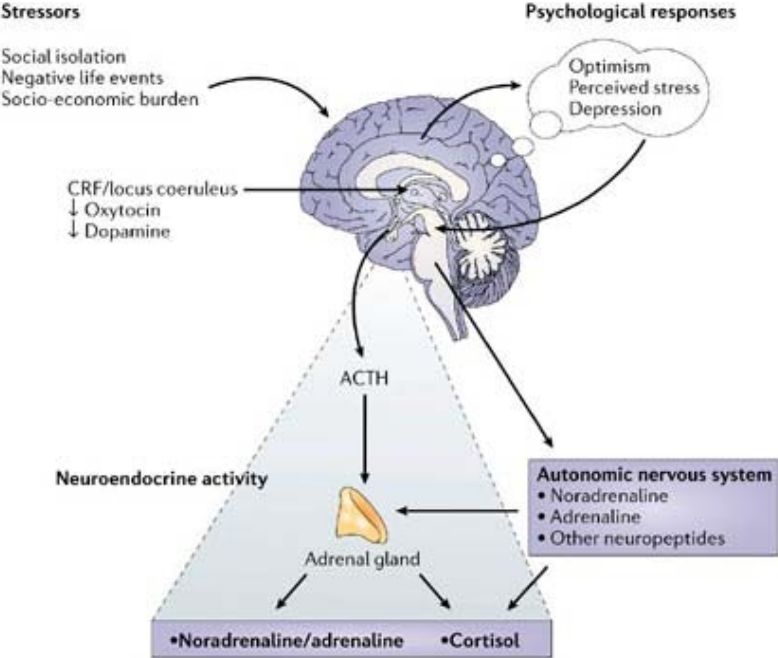


The Hallmarks of Cancer

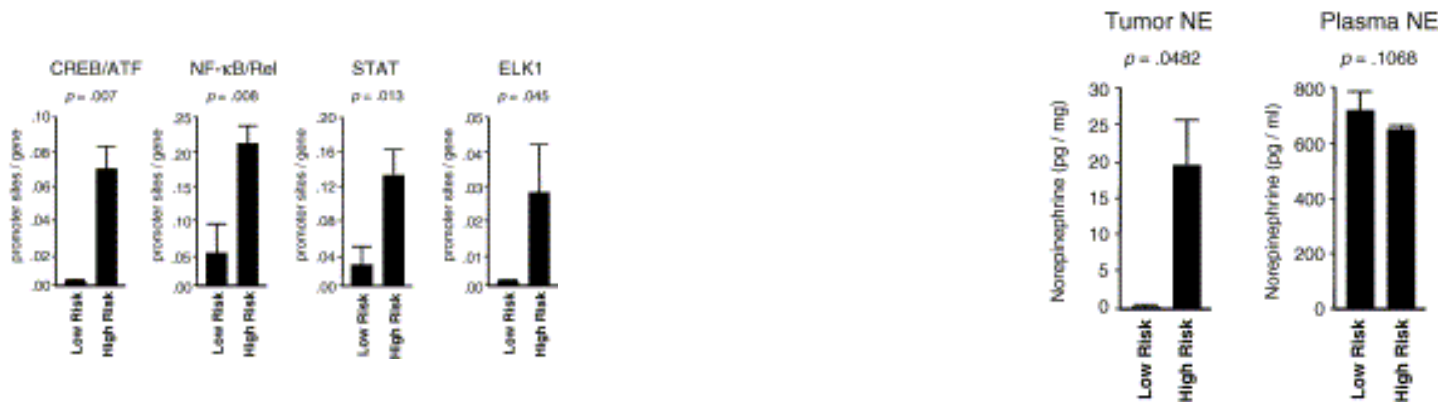
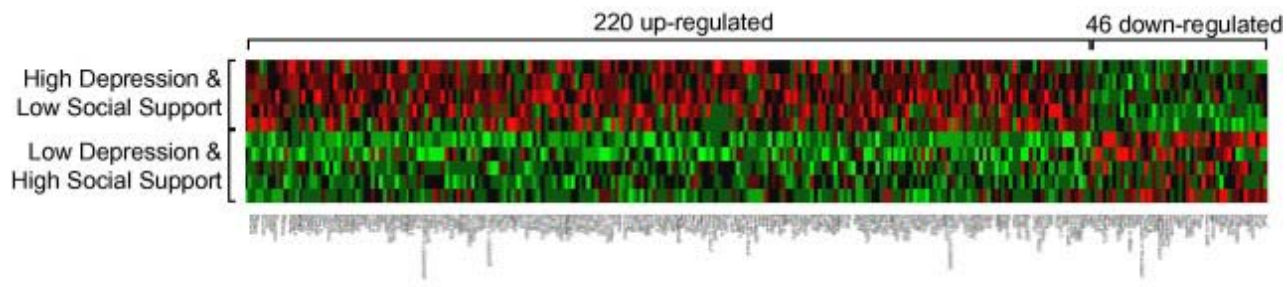


Adapted from Hanahan D and Weinberg RA (2011) *Cell* 144: 646-674

Neuroendocrine Influences on the Tumor Microenvironment

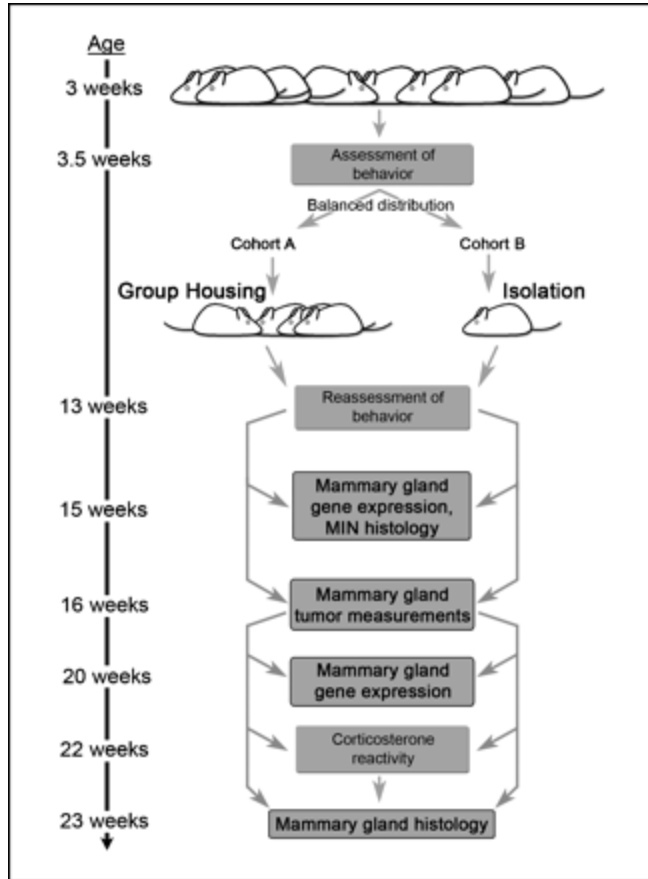


Behavioral Factors and Gene Expression Regulation



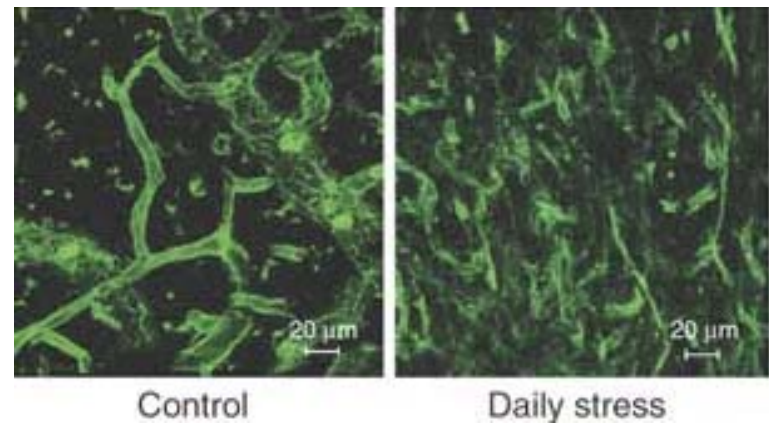
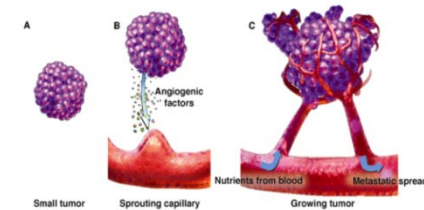
Lutgendorf SK et al. (2009) *BBI* 23: 176-183

Social Isolation Alters Mammary Gland Gene Expression and Increases Tumor Growth



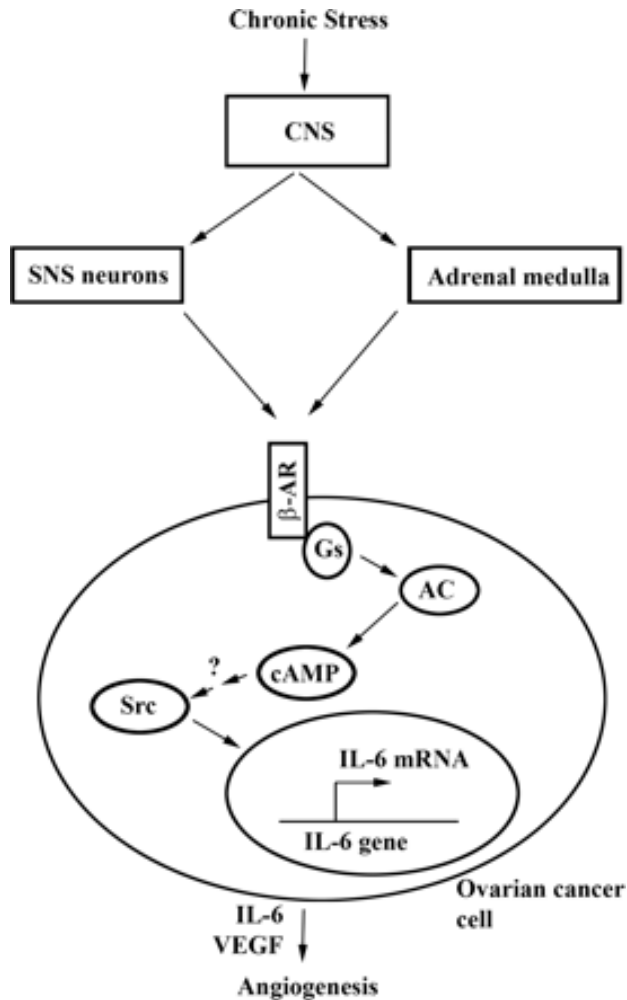
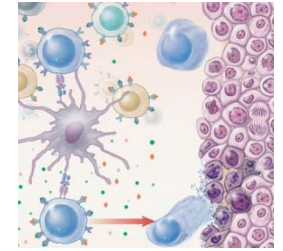
Alteration in Lipid Synthesis and Glycolytic Pathway Gene Expression

Chronic Stress promotes Tumor Growth and **Angiogenesis** in Ovarian Carcinoma



Thaker PH et al. (2006) *Nat Med* 12 (8): 939-944

Inflammatory Cytokines



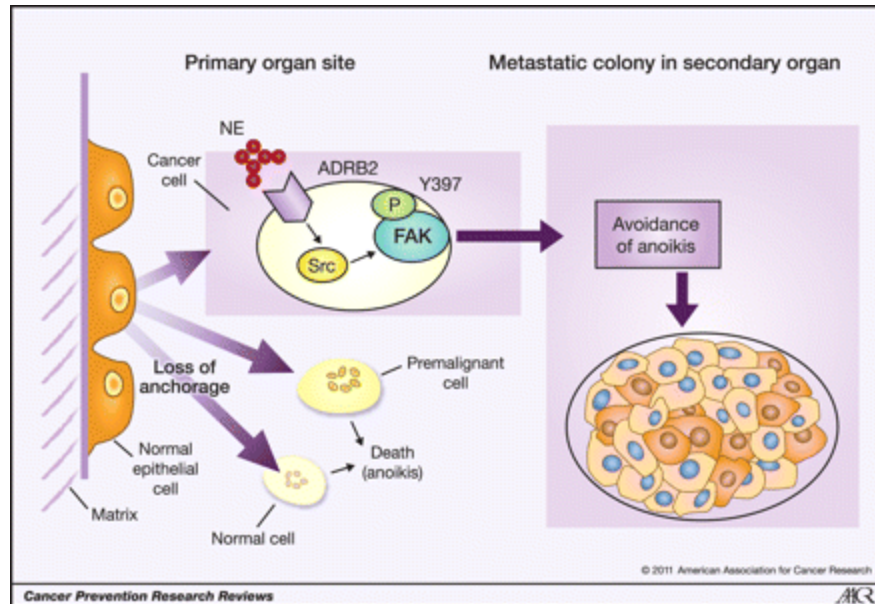
- Stress Hormones regulate **IL-6** expression by human ovarian carcinoma cells via a Src-dependent mechanism
- Stress increases **IL-8** expression associated with ovarian cancer growth and metastasis

Invasion and Migration



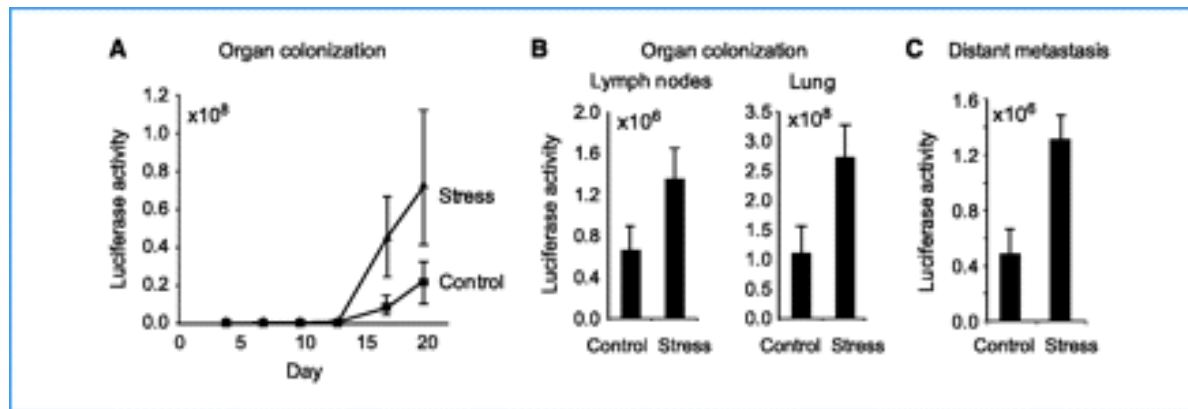
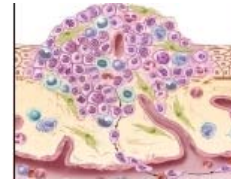
- Stress hormones increase cancer cells production of MMP-2 and MMP-9 through β -adrenergic signaling
- Negative affect and stress associated with higher MMP9 expression from TAMs in ovarian carcinoma

NE and E Protect Human Ovarian Cancer Cells from Anoikis through Adrenergic Pathway



Sood AK and Lutgendorf SK (2011) Cancer Prev Res 4 (4): 481-485

SNS as a novel regulator of Breast Cancer Metastasis

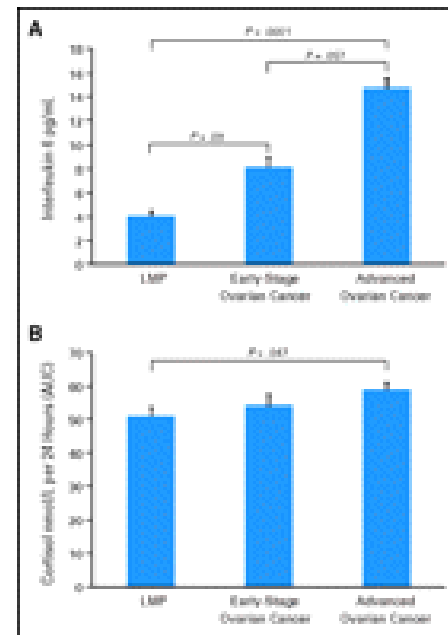


Sloan EK et al. (2010) *Cancer Res* 70 (18): 7042-7052

Can Cancer affect Emotion?



- Peripheral Tumors induce Depressive-like Behaviors and Cytokine production and alter HPA axis Regulation
- In Ovarian Cancer Patients IL-6 and Cortisol are related to Depressive Symptoms



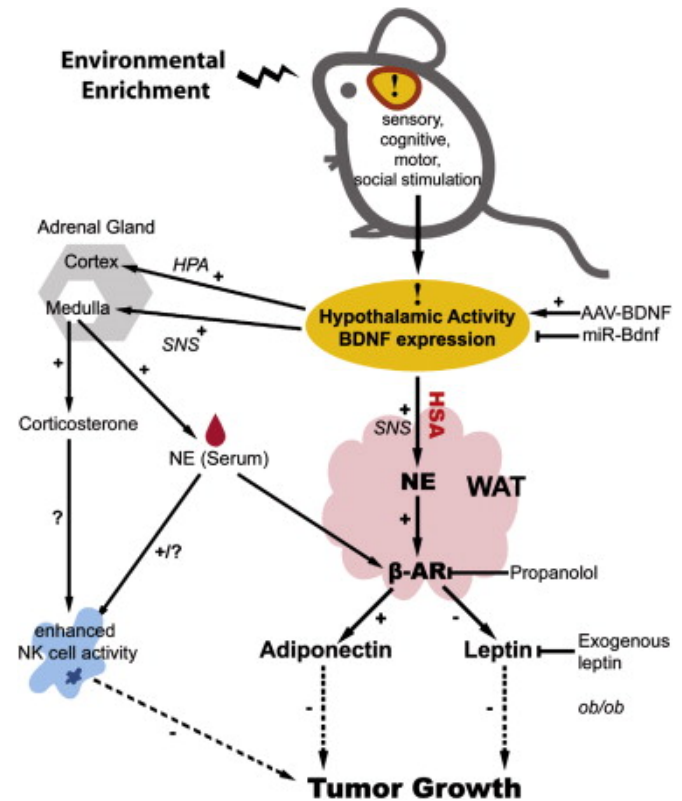
Lutgendorf SK et al. (2008) *JCO* 26 (29): 4820-4827

Potential Therapeutic Strategies

Beta adrenergic receptors blockade

Dopamine antagonists

Hypothalamic BDNF stimulation

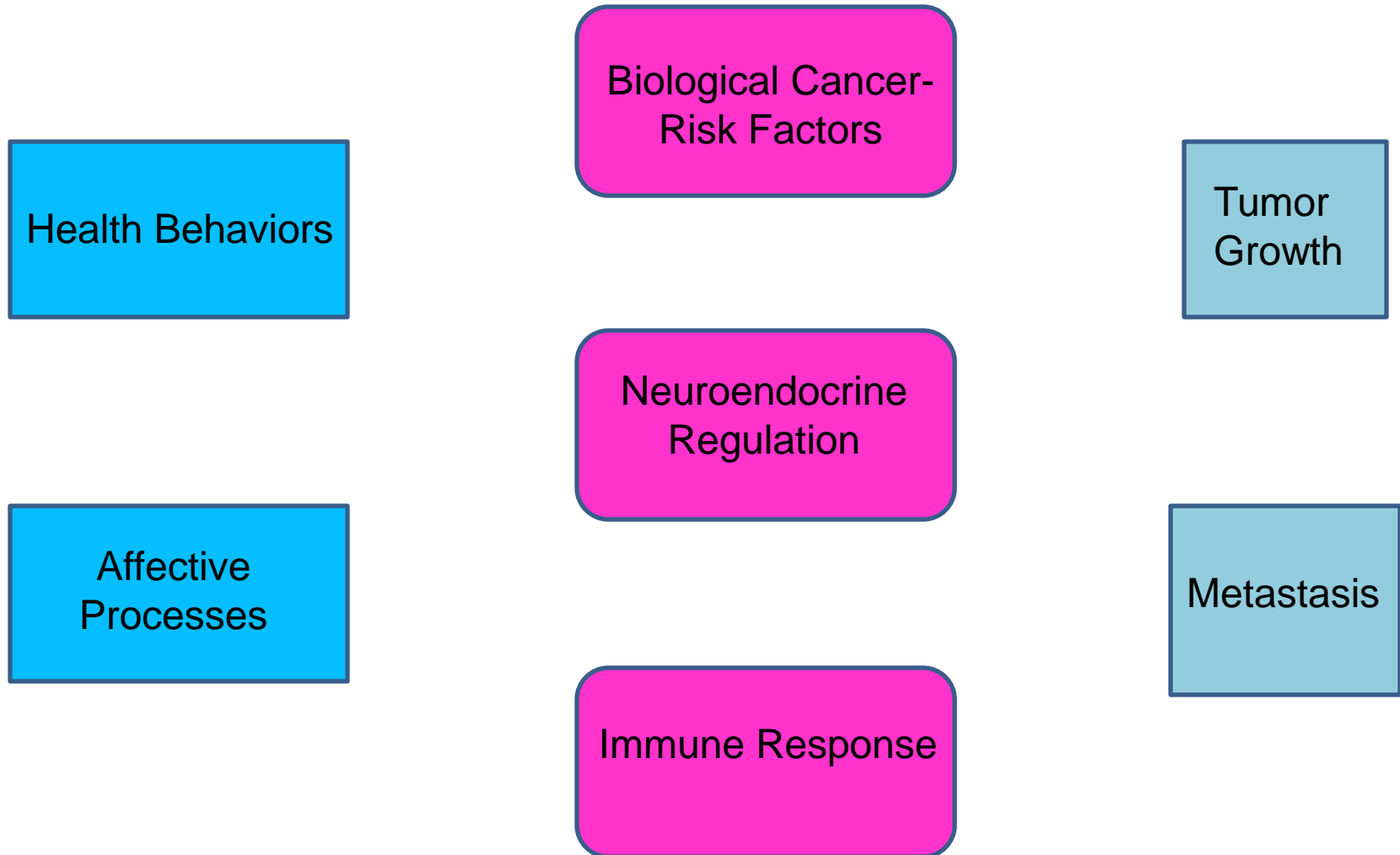


Associations between **Positive Affect** and Health outcomes

Mediating processes:

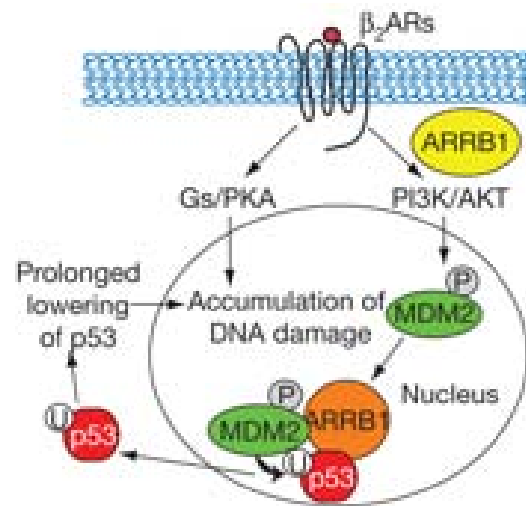
- **Genetic substrate**
- **Lifestyle Factors**
- **Neuroendocrine, autonomic, immune and inflammatory pathways**
- **Psychosocial factors**

Opportunities and Challenges



DNA damage

Stress Response Pathways Regulate DNA Damage through β_2 -adrenoreceptors and β -arrestin-1



Hara MR et al. (2011) *Nature* 477: 349-353

