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## **RESEARCH BRIEFS** – continued from page 3

#### **Cancer-fatigue Genes Identified**

Researchers suspect that cancer-related fatigue is associated with proinflammatory cytokines—chemicals kicked into action by injury or infection. Now, three specific cytokine gene variants have been linked to higher levels of fatigue among a group of women treated for early-stage breast cancer. Each of the so-called "high-expression alleles" increased the risk of more severe fatigue by 45 percent. The findings, the authors note, "further implicate inflammatory processes as contributors to cancer-related fatigue and suggest a new strategy for identifying and treating patients at risk for this symptom based on genetic variants in proinflammatory cytokine genes." *Journal of Clinical Oncology* 31 (2013) 1656-1661

## **Yogic Meditation Benefits Dementia Caregivers**

The stress of caring for a loved one with dementia can leave family members vulnerable to depression, inflammation, and impaired immune function. A new study shows that these effects might be offset by daily yogic meditation. In the study, 39 caregivers completed an eight-week program in which they performed either a daily Kirtan Kriya meditation—a 12-minute guided chanting practice—or listened to relaxing music for 12 minutes. Blood samples showed that the yoga meditation reversed the altered expression of a suite of inflammation-related genes, and, the authors say, "might potentially counteract the adverse effects of caregiving on inflammation, responses to vaccination, and resistance to viral infections." *Psychoneuroendocrinology* 38 (2013) 348-355



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## Happiness Influences Gene Expression

Different ways of being happy may have surprisingly different correlates in the body, according to a recent study by researchers at the UCLA Cousins Center for Psychoneuroimmunology. The study, published in August in the *Proceedings of the National Academy* of Sciences, shows that the two types of happiness manifest as different patterns of gene expression in the cells of the immune system.

In the study, led by Steve Cole, Professor of Medicine, Hematology-Oncology, 80 healthy subjects first completed a questionnaire about why they felt satisfied with their lives. Blood samples were then collected from the subjects, to evaluate the expression pattern of genetic markers for molecules that influence the production of diseasefighting antibodies and that promote inflammation—which is linked to an increased risk of cancer, heart disease, and other illness.

Cole and his colleagues found that individuals who reported high levels of hedonic well-being (from experiencing, acquiring, or consuming nice things) showed high levels of proinflammatory markers and lower levels of markers linked to enhanced antibody production; the converse was true in individuals who reported high levels of eudaimonic well-being (working toward a higher life purpose beyond simple self-gratification). "The most surprising finding to me was the extent to which people with high levels of hedonic well-being and those with high levels of eudaimonic well-being showed similar emotional states but different patterns of gene expression," Cole says. "Doing good and feeling good may be



experienced very similarly at the level of conscious emotion but have very different correlates at the level of immune cell gene expression." It is important to note, Cole points out, that this is an early discovery in the field of "social genomics" and it is not yet known if the different types of happiness cause these variations in gene expression, or whether the patterns of gene expression would change if a person changed their path to happiness.

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Cole cautions those who would over-interpret the findings: "I do not think that the connection we document in this study necessarily stems from some process by which the genome 'judges' us by wrecking our health if we are selfish," he says.

Rather, he suspects, it may be that those individuals who place their personal value in goals and interests outside of themselves are less stressed when bad things happen to them "because they feel the things they really care about in life will 'live on without them' in the broader communities. movements, interests and achievements they are invested in." However, "when one's sense of happiness and well-being stems largely from self-satisfaction, then any adversity that affects one personally affects most everything one cares about, which might differentially impact immune cell gene expression."

"If the pattern of results we observed here continues to hold, that would suggest that focusing psychological interventions on helping people connect with purpose and meaning in their lives might ultimately be more successful in warding off stress-related disease than would be interventions focused mainly on helping people simply feel good."

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## Parental Warmth Mitigates Health Impact of Childhood Abuse

A study by researchers at the Cousins Center offers new insight into the lingering health effects of childhood physical and emotional abuse - and how parental affection can mitigate some of the damage.

The study, published this fall in the Proceedings of the National Academy of Sciences, examined the relationship between reported childhood abuse, parental warmth, and health index known as "allostatic load."

Allostatic load, notes Adjunct Assistant Professor Judith E. Carroll, is "a state of chronic dysregulation across multiple systems of the body, thought to occur over time through excessive demands placed on the systems resulting in wear and tear." Higher levels of allostatic load have been associated with a higher risk of health problems like heart attack or stroke.

The researchers assessed allostatic load in 756 adult subjects-all participants in the Coronary Artery Risk Development in Young Adults (CARDIA) study-by measuring 18 different biological markers such as blood pressure, heart rate, stress hormones, cholesterol, waist circumference, inflammation, and blood sugar regulation.

The study revealed that individuals who recalled childhood emotional and physical abuse and who also experienced limited parental love and affection had the highest allostatic load score. In contrast, subjects who experienced emotional and physical abuse during childhood but received love and affection from a parental figure had lower scores. In them, parental warmth acted as "a buffer," Carroll says. "Our findings highlight the extent to which these early social relationships are associated with biological risk across nearly all of the body's major regulatory systems," says the paper's senior author Teresa Seeman, Professor of Medicine and Epidemiology at UCLA-

Because the study is cross-sectional—that is, it looks at a population at one point in time, rather than over a period of



time (as is the case in a so-called longitudinal study)-it does not prove that abuse plus a lack of affection causes allostatic load, Carroll cautions. "To move this area of research forward, our next step should be to show that giving love and affection to a child who has been abused can provide some protection from the development of a higher biological risk profile," she says. "There is currently preliminary evidence suggesting that early interventions with families and their caregivers can improve developmental and mental health outcomes. Future work should now also focus on whether these types of interventions improve biological risk for adult disease."

## **Untreated Depression Influences Shingles Risk**

A person's mental well-being can also influence their physical health—including their risk of contracting the infectious disease shingles, a painful, blistering skin rash affecting older adults that is caused by the varicella-zoster virus, the same virus that leads to chickenpox in children.

According to a study by Cousins Center researchers, untreated depression in older adults significantly decreases the effectiveness of the shingles vaccine. The study, which appeared in the journal Clinical Infectious *Diseases*, is among the first to examine the association between depression and infectious disease risk or disease-relevant immunologic endpoints, such as vaccine responses.

Michael Irwin, Cousins Professor of Psychiatry at the Semel Institute for

Neuroscience and Human Behavior at UCLA and Director of the Cousins Center. and his colleagues measured immune responses to the shingles vaccination in 40 patients aged 60 or older who had suffered from a major depressive disorder. Irwin and colleagues found that depressed patients who were not being treated with antidepressants were less able to respond to the shingles vaccine than a group of control (not depressed) patients and patients with depression who were taking antidepressants; the protective effect of the antidepressants in this latter group of patients was noted even when the drugs were not actually effectively managing the emotional disorder.

The study suggests, Irwin says, that among depressed elderly individuals,

## **RESEARCH BRIEFS**

Brain Region Linked to Sickness-induced Social Withdrawal When they are sick, organisms display "sickness behavior" – a coordinated set of responses including fatigue, reduced appetite, and social withdrawal that are thought to encourage recovery. A recent brain study provides new evidence that this desire to withdraw has a more important function: preventing the spread of infection by reducing social contact. In the study, volunteers were given an injection of endotoxin, which experimentally induces inflammation, or a placebo. They then viewed a number of different images, including "non-social, non-threatening" images (like household objects) and "socially threatening" images (faces showing fear). Brain imaging showed that inflammation increases the activation of the amygdala, a brain region linked to social avoidance and phobias, specifically in response to the socially threatening images; this activity was also associated with heightened feelings of social disconnection. NeuroImage 59 (2012) 3222-3226

## **Yoga Aids Cancer-related Fatigue**

Debilitating fatigue is a common side effect of cancer treatment that can linger for years even after treatment ends. Yoga may be the answer, a study by Cousins Center researchers suggests. The study involved 31 breast cancer survivors randomly assigned to either health education classes (control) or an Iyengar-based yoga program that focused on passive inversions (upside-down positions supported by props, for example) designed to allow even highly fatigued individuals to complete the postures. Compared to controls, women in the yoga group reported significant reductions in fatigue after the 12-week program, as well as increased vigor and decreased depression and stress. The benefits persisted through a three-month follow-up period. Cancer 118 (August 1, 2012) 3766-3775

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"treatment with an antidepressant medication such as a selective serotonin uptake inhibitor"-such as Prozac and Celexa-"might increase the protective effects of zoster vaccine," although further research is needed to understand why depressed patients have a reduced immune response in the first place. In addition, Irwin notes, "efforts are needed to identify and diagnose depressed elderly patients who might benefit from either a more potent vaccine or a multi-dose vaccination schedule."

A similar immune phenomenon may be present with other infectious diseases, such as influenza, suggesting that untreated depression could be used to identify a subgroup of elderly individuals who are likely to respond poorly to other vaccines.

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