### Summer 2022 Can Sleep Protect Against Cancer-Related Aging?

There is mounting evidence that poorer concentration and memory, decreased mobility and strength, and increased pain and fatigue, commonly occur at an earlier age or at a higher frequency in cancer patients, suggesting that cancer may accelerate the aging process. A growing body of evidence also now indicates that cancer therapies might have the same effect.

In a recent article in the journal Nature Reviews, Cousins Center researcher Judith Carroll and her colleagues discuss the possible biological mechanisms through which cytotoxic cancer therapies like chemotherapy and radiotherapy might make cancer patients age faster. Even as they target cancerous cells, the researchers say, these therapies can cause damage to DNA and other key cellular components in healthy cells,

causing aging at the cellular level and ultimately accelerated cognitive and physical aging.

"Cancer treatments are necessary and life extending and lifesaving. However, these lifesaving treatments are also thought to cause harm and contribute to secondary complications and symptoms," says Carroll, Associate Professor of Psychiatry and Biobehavioral Science and holder of the George F. Solomon Professorship in Psychobiology. "By studying these late effects of the treatments, we can begin to remediate or reduce the burden of long-term complications and improve the health of survivors."

In the review article, Carroll and her colleagues note that modifiable biobehavioral factors such as poor sleep, stress, a lack of physical

activity, obesity, and tobacco and alcohol use might worsen the accelerated aging seen in cancer patients. "We don't have a complete picture of what behavioral factors might be the most important, and not everyone experiences the same effects. but I suspect sleep is a critical player," Carroll says. In addition to reducing feelings of irritability and anxiety and improving mood and energy levels, sleep is important for healing the body and removing waste products. "We all know the adage of when you are sick with a cold virus you need to get extra rest to recover. We hypothesize that similar processes are at work while undergoing treatments for cancer," she says. "Making sure the patient is sleeping well may have lasting benefits and help reduce the effects of cancer treatments on biological aging."



# Preventing Depression in Older Adults with Insomnia

An estimated 1 in 10 individuals aged sixty or older are likely to suffer an episode of major depression each year, increasing their risk of cognitive decline, disability, and illness, and potentially death through disease or suicide (suicide rates are indeed highest among older men). Few of these individuals, however, receive adequate treatment-if they are even diagnosedand only 30 percent of those treated will have a remission of their depression. Prevention of depression is urgently needed to address this public health crisis.

One way to prevent depression is to selectively target a factor that puts persons at higher risk of developing depression. Insomnia is one such factor. Insomnia occurs in nearly half of older adults, and has been shown to contribute to a two-fold greater risk of depression. No prior study has evaluated whether selectively treating insomnia might prevent depression, even though there are a number of treatments that effectively treat insomnia. Cognitive behavioral therapy for insomnia (CBT-I) is the gold standard for treatment of insomnia; this treatment helps people change their thoughts and behaviors that precipitate and perpetuate insomnia. Another treatment, sleep education therapy (SET), can also improve sleep but these benefits often do not last. In a recent study, Cousin Center Director Michael



Irwin and colleagues assessed the efficacy of CBT-I as compared to this active control, SET, to prevent depression in older adults with insomnia.

The study, published in the journal JAMA Psychiatry, enrolled 291 older individuals from the UCLA area with insomnia disorder, none of whom had experienced a major depression episode or serious health event in the year prior to joining the trial. The participants were randomly divided into two treatment groups: One group (156 people) participated in weekly 120-minute CBT-I treatment sessions for two months, while the other (131 individuals) completed the active

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control treatment, SET, for the same period of time.

SET targets day-to-day behavioral and environmental factors, such as sleep hygiene and stress and its impact on sleep, that contribute to poor sleep. CBT-I consists of five elements: cognitive behavioral therapy, stimulus control, sleep restriction, sleep hygiene, and relaxation.

Individuals in both groups were followed for up to 36 months after the end of their treatment protocols.

#### Summer 2022

Preventing Depression in Older Adults with Insomnia -- continued from page 1

Those in the CBT-I group, as compared to SET, were two times less likely to develop depression during the threeyear follow-up period. In addition, those who had received CBT-I and sustained remission of insomnia were nearly seven times less likely to have depression, as compared to those who received SET and did not have an insomnia remission: this finding indicates that sustained treatment of insomnia was critical in preventing depression. In short, treatment of insomnia prevented the occurrence of depression in older adults who had insomnia, but were not depressed.

As expected, CBT-I was also more effective in the treatment of insomnia than SET. Nearly twice as many persons who received CBT-I had a remission of their insomnia as compared to those receiving SET. Further, remission of insomnia over the 36 months was more likely to occur in those who received CBT-I as compared to SET.

The editors of JAMA Psychiatry applauded this study as being "a completely new and innovative way of increasing the effect of preventive interventions on the disease burden of depression." In addition, because treatment focused on insomnia without using the word "depression," the stigma associated with depression treatment was avoided, meaning that older adults would be more likely to be interested in receiving this treatment to prevent depression and benefits would more broadly impact the community.

Irwin forecasts that "screening for insomnia in older adults and wide delivery of CBT-I-based treatment for insomnia could substantially advance public health efforts to treat insomnia and prevent depression in this vulnerable older adult population."

## The Immulogical Impact of Isolation

The "shelter in place" policies enacted in the early days of the COVID-19 pandemic were vital for slowing the spread of infection. But a new study from the Cousins Center finds a surprising irony: They may have left us less able to fight off the virus when we were exposed.

Steve Cole, a Professor of Psychiatry and Biobehavioral Sciences and Medicine at UCLA, and his colleagues simulated shelter-in-place protocols by moving 21 adult male rhesus macaques from communal living in large outdoor colonies to individual indoor shelters. After just 48 hours alone, the animals' circulating immune cells declined by 30 to 50 percent. The animals also showed a striking decrease in the activity of a suite of antiviral genes called the Type 1 interferon system, as well as an increase in "classical monocytes" that play a key role in inflammation. "Reduced antiviral activity and increased inflammation are basically a recipe for severe COVID," says Cole. The effects abated within four weeks after the macaques were

returned to their regular communal housing colony.

Later, the researchers returned the animals to individual housing, but this time with a companion—a previously unknown juvenile macaque. This simple act of taking care of a young partner blocked the decline in antiviral responses and increased inflammation.

According to Cole, the findings, published in the *Proceedings of the National Academy of Sciences*, make sense from a resource-conservation standpoint: When we are not around other individuals who could pass on new viruses, our bodies reduce production of the cellular and molecular defenses that respond to such threats.

"When we are not 'close' to others of our own species, the risk of viral infection declines, but there's another angle we need to take into account, which is what the immune system does with the 'resources' that are being recovered," Cole says. When we feel threatened or uncertain—which is how our brain's interprets social isolation our immune system pivots away from the antiviral immune responses that are needed in times of close social interaction, and instead ramps up inflammatory immune responses that aid wound healing.

"That made sense in our hunter-gatherer history when the things that threaten us and experiences of isolation would routinely increase the risk of physical injury," Cole explains. "In the modern world, that equation no longer holds, but our nervous and immune system is still programmed to execute that shift. Unfortunately, this chronic inflammation serves as a kind of molecular fertilizer for the development of chronic diseases such as cancer, heart disease, and neurodegenerative diseases. That makes it more important than ever that we maintain a good sense of social support and community to help counteract the effects of modern life on immune system resource-shifting."

# Reducing Depressive Symptoms in Breast Cancer Survivors



Younger women-those 50 years of age and under—have higher levels of depression and other symptoms after breast cancer diagnosis and treatment than their older counterparts, in addition to a greater risk of poor outcomes, including cancer recurrence. "It is much more disruptive and stressful to have to deal with a cancer diagnosis when you are building a family, a career, and navigating these other developmental challenges," explains Cousins Center researcher Julienne Bower, whose research is focused on mind-body interactions among individuals facing chronic stressors, including cancer diagnoses.

As part of her continuing effort to understand and improve the quality of life in these women, Bower, a Professor of Psychology and Psychiatry and Biobehavioral Sciences at UCLA, and her colleagues recently conducted the multi-site Pathways to Wellness study, an evaluation of the effectiveness of two group-based behavioral interventions, survivorship education (SE) and mindful awareness practices (MAPs), in younger breast cancer survivors with elevated depressive symptoms. The survivorship education program focused on topics relevant for younger breast cancer survivors, including medical management and quality of care after treatment; relationships and work-life balance; body image, sexuality and fertility; and energy balance, nutrition, and physical activity. The MAPs intervention was based on a program developed at the UCLA Mindful Awareness Research Center (MARC), a part of the Cousins Center, that teaches individuals to understand basic principles of mindfulness, develop a personal meditation practice, and to apply the principles in their daily life In previous work, Bower and colleagues found that the MAPs intervention was effective in reducing stress, depression, and inflammation, and enhancing positive affect and feelings of meaning and peace in life among younger breast cancer survivors.

In the new study, reported in the Journal of Clinical Oncology, 247

Summer 2022

younger female breast cancer survivors participated in either a 6-week inperson survivorship education class or a MAPs program, or were assigned to a wait-list control group. Compared to the control group, both the SE and MAPs participants showed reductions in symptoms of depression. However, the women in the MAPs group also showed improvements in fatigue, insomnia, and vasomotor symptoms, i.e., hot flashes and night sweats. In addition, the MAPs program had beneficial effects on cancer-related stress, positive affect and meaning/ peace in life, and inflammatory activity relative to controls.

With the benefits of MAPs now becoming clear, Bower and colleagues next plan to test versions of the program that can be delivered remotely, which will significantly expand the reach of the intervention. These will be evaluated through a large nationwide network of cancer centers and community clinics. "There is tremendous value to the women being there in-person, but the pandemic has made us all a lot more comfortable with having interactions on line, and this will give us a much larger and more diverse patient population," Bower says. She and her team plan to test a Zoom-based version of the MAPs intervention, and are also working with a technology company to develop a digital, self-directed version of program for use on smart phones and computers. "We are very excited about providing the tools of the MAPs program to women across the country who are dealing with cancer diagnosis and treatment at a relatively young age. Our goal is to promote a long and healthy survivorship for younger women and really for all cancer survivors."