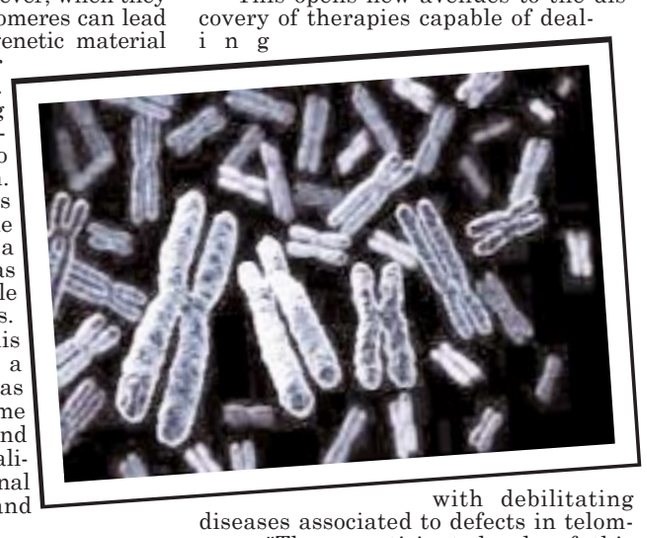
What controls the tips of our chromosomes

IN a new, a research team from Instituto Gulbenkian de Ciencia (IGC; Portugal), led by Jose Escandell and Miguel Godinho Ferreira, discovered a key aspect of the regulation of telomeres – structures that appear at the tips of our chromosomes.

They work as a protective cap that prevents genetic material from unfolding and corroding away. However, when they do not work properly, telomeres can lead to the total erosion of genetic material and can trigger cancer and age-related diseases. There is an increasing number of human syndromes attributed to telomeres malfunction. One such disease was recently identified as the result of a malfunction of a protein complex known as CST, which is responsible for maintaining telomeres.



Deficiencies in this complex give rise to a telomeropathy known as Coats Plus. This syndrome is genetically inherited and characterised by abnormalities of the gastrointestinal system, bones, brain and other parts of the body.

The work of the IGC researchers now unveils the regulation of the "S" component of that CST complex. The researchers discovered that STN1 (the protein that corresponds to the S component) is regulated by a chemical modification that results in the insertion of phosphorus in this protein, and it can be reversed by an enzyme, the phosphatase SSU72. In this way, it allows telomere duplication and telomerase regulation, which is the enzyme that elongates telomeres. The researchers also showed that this process is identical both in yeast and in human cells. This means that the regulation of the 'S' component has been conserved throughout evolution of species, which somehow reveals the importance of this process for the correct functioning of cells.

This opens new avenues to the discovery of therapies capable of dealing with debilitating diseases associated to defects in telomeres. "The unanticipated role of this evolutionary conserved phosphatase is reminiscent of the regulation of the cell cycle by phosphatases that counteract the role of kinases, thus re-establishing the ground state of 'once and only once' cell cycle processes", said investigator Miguel Godinho Ferreira.

"With this work, we now understand better how telomere regulation works, a key process in cancer and ageing", says Jose Escandell, first author of the publication," Ferreira added.

Moderate alcohol consumption associated with high blood pressure: Study

IF you believe that moderate alcohol consumption is harmless, a recent research is here to prick that bubble. The study shows that moderate alcohol consumption-seven to 13 drinks per week-substantially raises one's risk of high blood pressure.

The findings contrast with some previous studies that associated moderate drinking with a lower risk of some forms of heart disease. Most previous studies, however, have not assessed high blood pressure among moderate drinkers. Since hypertension is a leading risk factor for heart attack and stroke, the new study calls into question the notion that moderate alcohol consumption benefits heart health.

Alcohol's impact on blood pressure could stem from a variety of factors, according to researchers. Because alcohol increases appetite and is, itself, very energy-dense, drinking often leads to greater caloric intake overall. Alcohol's activities in the brain and liver could also contribute to spikes in blood pressure.

Data for the research came from the National Health and Nutrition Examination Study (NHANES), a large, decades-long study led by the Centers for Disease Control and Prevention. Specifically, the researchers analyzed data from 17,059 U.S. adults who enrolled in the NHANES study between 1988 and 1994, the NHANES phase with data that is considered most complete and representative of the U.S. population.

Participants reported their drinking behavior on several questionnaires administered by mail and in person. Their blood pressure was recorded by trained personnel during visits in participants' homes and at a mobile examination center.

The researchers split participants into three groups: those who never drank alcohol, those who had seven to 13 drinks per week (moderate drinkers) and those who had 14 or more drinks per week (heavy drinkers). They assessed hypertension according to the 2017 ACC/AHA high blood pressure guideline, which defined Stage 1 hypertension as having systolic blood pressure between 130-139 or diastolic pressure between 80-89, and Stage 2 hypertension as having systolic pressure above 140 or diastolic pressure above 90. Compared with those who never drank, moderate drinkers were 53 percent more likely to have stage 1 hypertension and twice as likely to have stage 2 hypertension. The pattern among heavy drinkers was even more pronounced; relative to those who never drank, heavy drinkers were 69 percent more likely to have stage 1 hypertension and 2.4 times as likely to have stage 2 hypertension. Overall, the average blood pressure was about 109/67 mm Hg among never-drinkers, 128/79 mm Hg among moderate drinkers and 153/82 mm Hg among heavy drinkers.

Findings of the study were discussed in a meeting held at American College of Cardiology 68th Annual Scientific Session. In their analysis, researchers adjusted for age, sex, race, income and cardiovascular risk to separate the effects from alcohol consumption from other factors with known links to hypertension. "This study is not only large but diverse in terms of race and gender," Aladin said. "The results are very informative for future research and practice.

If you are drinking a moderate or large amount of alcohol, ask your provider to check your blood pressure at each visit and help you cut down your drinking and eventually quit," said Amer Aladin, study's lead author.

Menstrual cycle affects cocaine addiction risk

MENSTRUAL cycle may influence cocaine craving risk in women, a recent study suggests. According to the findings, menstrual cycle may influence addiction risk in women. In female rats, craving for cocaine during abstinence from the drug was stronger during estrus--the phase in which ovulation occurs--than non-estrus, and female rats were more prone to relapse of cocaine use than male rats. "Sex differences are extremely important in addiction. This new study suggests that the period around ovulation is the most vulnerable period for promoting addiction. This knowledge has implications for both prevention and treatment," said John Krystal, lead author of the study.

"To the degree that results from animal models generalize to humans, our findings implicate the phase of the menstrual cycle as a risk factor for relapse in women and, therefore, should be taken into consideration in the development of relapse prevention treatments," said senior author Satoshi Ikemoto.

To assess the influence of the menstrual cycle on addiction, a group of researchers used a model of cocaine use in rats that mimics the intermittent binge-like pattern of human cocaine use.

They compared this model with the standard rat model of cocaine use that provides continuous access to the drug. Although both access models led to progressively increased cocaine seeking during abstinence, referred to as incubation of cocaine craving, cocaine seeking was higher after intermittent access.

Regardless of the type of access provided to the rats, cocaine seeking was higher in female rats than male rats. "In female rats, the magnitude of cocaine craving was critically dependent on the phase of the estrous cycle, demonstrating a novel role of ovarian hormones in incubation of cocaine craving," said Ikemoto.

Previous studies in humans suggest that women relapse faster after quitting cocaine and have stronger craving than men. The new findings reveal that the estrous cycle may contribute to these differences between women and men and highlight a potential target to help prevent relapse in women.

A nap a day keeps high blood pressure away: Study

NAPPING may do more than just rebooting our energy level and improve our mood. It can also keep high blood pressure at bay, a recent study suggests.

"Midday sleep appears to lower blood pressure levels at the same magnitude as other lifestyle changes. For example, salt and alcohol reduction can bring blood pressure levels down by 3 to 5 mm Hg," said co-author Manolis Kallistratos. Overall, taking a nap during the day was associated with an average 5 mm Hg drop in blood pressure, which researchers said is on par with what would be expected from other known blood pressure-lowering interventions. In addition, for every 60 minutes of midday sleep, 24-hour average systolic blood pressure decreased by 3 mm Hg.

"These findings are important because a drop in blood pressure as small as 2 mm Hg can reduce the risk of cardiovascular events such as heart attack by up to 10 per cent. Based on our findings, if someone has the luxury to take a nap during the day, it may also have benefits for high blood pressure. Napping can be easily adopted and typically doesn't cost anything," Kallistratos said.

Findings of the study were discussed in a recent meeting held at the American College of Cardiology 68th Annual Scientific Session.

This is the first study to prospectively assess midday sleep's effect on blood pressure levels among people whose blood pressure is reasonably controlled, according to the researchers. The same research team previously found midday naps to be associated with reduced blood pressure levels and fewer anti-hypertensive medications being prescribed among people with very high blood pressure readings.

"The higher the blood pressure levels, the more pronounced any effort to lower it will appear. By including people with relatively well-controlled blood pressure, we can feel more confident that any significant differences in blood pressure readings are likely due to napping," Kallistratos said. In their analyses, researchers adjusted for factors known to influence blood pressure levels, including age, gender, lifestyle and medications. There were no differences in terms of the number of anti-hypertensive medications taken between the two groups, and pulse wave velocity tests and echo-cardiograms were also similar.

Overall, average 24-hour systolic blood pressure was 5.3 mm Hg lower among those who napped compared with those who didn't (127.6 mm Hg vs 132.9 mm Hg). When looking at both blood pressure numbers, people who slept during the day had more favourable readings (128.7/76.2 vs 134.5/79.5 mm Hg).

There also appeared to be a direct linear relationship between time asleep and blood pressure; as reported, for each hour of napping, the average 24-hour systolic blood pressure lowered by 3 mm Hg.

"We obviously don't want to encourage people to sleep for hours on end during the day, but on the other hand, they shouldn't feel guilty if they can take a short nap, given the potential health benefits," Kallistratos said. "Even though both groups were receiving the same number of medications and blood pressure was well controlled, there was still a significant decrease in blood pressure among those who slept during midday."

Researchers said the findings are further bolstered because patients had similar dipping blood pressure rates at night (natural drops during night-time sleep), meaning that any reductions in ambulatory blood pressure were separate from this phenomenon and give greater confidence that reductions in ambulatory blood pressure could be due to daytime napping.

Older biologic age associated with increased breast cancer risk: Study

ACCORDING to a new study, biologic age, a DNA-based estimate of a person's age, is linked with the development of breast cancer..

The results of the study were published in the Journal of the National Cancer Institute. Biologic age was determined by measuring DNA methylation, a chemical modification to DNA that is a part of the normal aging process. The study showed for every five years a woman's biologic age was older than her chronologic or actual age, known as age acceleration and she had a 15 per cent increase in her chance of developing breast cancer.

Scientists from the National Institute of Environmental Health Sciences (NIEHS), part of National Institute of Health, speculated that biologic age may be tied to environmental exposures. If so, it may be a useful indicator of disease risk. They used three different measures, called epigenetic clocks, to estimate biologic age. These clocks measure methylation found at specific locations in DNA. Researchers used these clocks to estimate biologic age, which can then be compared to chronologic age.

The researchers used DNA from blood samples provided by women enrolled in the NIEHS-led Sister Study, a group of more than 50,000 women in the U.S. and Puerto Rico. The study was specifically designed to identify environmental and genetic risk factors for breast cancer. The research team measured methylation in a subset of 2,764 women, all of whom were cancer-free at the time of blood collection.

"We found that if your biologic age is older than your chronologic age, your breast cancer risk is increased. The converse was also true. If your biologic age is younger than your chronologic age, you may have decreased risk of developing breast cancer. However, we don't yet know how exposures and lifestyle factors may affect biologic age or whether this process can be reversed," said corresponding author Jack Taylor. Lead author Jacob Kresovich had read studies that used epigenetic clocks to predict age-related mortality. Since age is the leading risk factor for breast cancer, he hypothesized that age acceleration may be associated with higher breast cancer risk.

"If you look at a group of people who are all the same age, some may be perfectly healthy while others are not. That variability in health may be better captured by biologic age than chronologic age," Kresovich said. Kresovich suggested that using DNA methylation to measure biologic age may help scientists better understand who is at risk for developing cancer and other age-related diseases.

Breast cancer study confirms importance of multigenerational family data to assess risk

IN the largest study of its kind, a team of researchers evaluated four commonly used breast cancer prediction models and found that family-history-based models perform better than non-family-history based models, even for women at average or below-average risk of breast cancer.

The findings are published online in The Lancet Oncology. The study saw women between the ages of 20 to 70 being selected for the study who had no previous history of bilateral prophylactic mastectomy or ovarian cancer, and whose family history of breast cancer was available. The researchers calculated 10-year risk scores for the final cohort of 15,732 women, comparing four breast cancer risk models which all vary in how they use information regarding multi-generational and genetic information as well as non-genetic information: the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm model (BOADICEA), BRCAPRO, the Breast Cancer Risk Assessment Tool (BCRAT), and the International Breast Cancer Intervention Study model (IBIS).

A second analysis was conducted to compare the performance of the models after 10 years based on the mutation status of the BRCA1 or BRCA2 genes. The results showed that the BOADICIA and IBIS models which have multigenerational family history data were more accurate in predicting breast cancer risk than the other models. This held true even for women without a family history of breast and without BRCA1 and BRCA2 mutations. The other two models BRCAPRO and BCRAT models did not perform as well overall and in women under 50 years of age.

The BCRAT model was well-calibrated in women over 50 years who were not known to carry deleterious mutations in the BRCA1 and BRCA2 genes. Of the 15,732 eligible women, 4 percent were diagnosed with breast cancer during the median follow-up of 11-plus years.

Speaking about it, Dr Terry, author of the study said: "Our study, which was enriched based on family history, was large enough to evaluate model performance across the full spectrum of absolute risk, including women with the highest risk of cancer in whom accurate prediction is especially important," adding, "Independent validation is particularly important to understand the utility of these models across different settings."

Co-author of the study Dr Robert MacInnis added, "Mathematical models can help estimate a woman's future risk of breast cancer. There are several available, but it is uncertain which models are the most appropriate ones to use. These findings might help provide better guidance to women with their decision-making on breast cancer screening strategies."

Integrated therapy treating obesity and depression is effective: Study

AN Integrated therapy directed towards curing obesity and depression together, has proven to be affective, a recent study suggests.

According to the study, an intervention combining behavioural weight loss treatment and problem-solving therapy with as-needed antidepressant medication for participants with co-occurring obesity and depression improved weight loss and depressive symptoms more effectively, when compared with routine physician care. Obesity and depression commonly occur together. Approximately 43 per cent of adults with depression are obese, and adults with obesity are at increased risk of experiencing depression.

The study suggests that to treat both conditions, patients must visit multiple practitioners including dietitians, wellness coaches and mental health counsellors or psychiatrists. The burden associated with visiting multiple health care providers consistently over the long periods of time required to treat obesity and depression can be significant and lead to dropping out of therapy altogether.

Additionally, these health services may not be available due to a lack of trained providers or reimbursement, and the cost of seeing numerous specialists can be prohibitive.

"We have shown that delivering obesity and depression therapy in one integrated program using dually trained health coaches who work within a care team that includes a primary care physician and a psychiatrist, is effective at reducing weight and improving depressive symptoms," said Dr. Jun Ma, principal investigator on the study.

As part of the study, 204 participants were randomly assigned to receive the integrated collaborative care program and were seen by a health coach for one year.

In the first six months, they participated attended nine individual counselling sessions and watched 11 videos on healthy lifestyles. In the following six months, participants had monthly telephone calls with their health coach. Two hundred and five participants randomly assigned to the usual care control group did not receive any additional intervention.

Participants in the integrated care program experienced more weight loss and decline in the severity of depressive symptoms over one year compared with control participants receiving usual care. On average, patients in the integrated program experienced a decline in body mass index from 36.7 to 35.9 while participants in the usual care group had no change in BMI. Participants receiving integrated therapy reported a decline in depression severity scores based on responses to a questionnaire from 1.5 to 1.1, compared with a change from 1.5 to 1.4 among those in the control group.

"While the demonstrated improvements in obesity and depression among participants receiving the integrated therapy were modest, the study represents a step forward because it points to an effective, practical way to integrate fragmented obesity and depression care into one combined therapy, with good potential for implementation in primary care settings, in part because the integrated mental health treatment in primary care settings is now also reimbursable by Medicare.

For patients, this approach is an attractive alternative to seeing multiple practitioners each charging for their services as is done traditionally," Ma said.