Hawai'i Journal Watch

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Highlights of recent research from the University of Hawai'i and the Hawai'i State Department of Health

'Longevity Gene' Linked with Lower Cardiovascular Disease Mortality in Japanese Men

Japanese men at risk for cardiovascular disease (CVD) who have certain versions of gene called PIK3R1 may have a lower mortality risk over a 30-year period. Researchers including Timothy Donlon, PhD, of the John A. Burns School of Medicine (JABSOM), investigated whether certain PI3K alleles were associated with life span in individuals with and without type 2 diabetes, cancer, and CVD (including hypertension, coronary heart disease, and stroke). The researchers used data on 3568 Japanese men from the Kuakini Honolulu Heart Program/Kuakini Honolulu-Asia Aging Study cohort. At the study's start, the men's ages ranged from 71 to 93, and during the 29-year follow-up period, 3533 of the participants died. Overall, men with CVD had higher mortality than men without CVD. However, the men with CVD who also had a longevity-associated version of PIK3R1 had survival curves similar to men without CVD. Men without CVD showed no association between the longevity-associated genotype and life span, nor was there an association between the gene and life span for men with diabetes or cancer. More research is needed to determine the mechanisms of the association, and the implications for the heritability of healthy aging.

- Donlon TA, Chen R, Masaki KH, et al. Association of growth hormone receptor gene variant with longevity in men is due to amelioration of increased mortality risk from hypertension. *Aging*. 2021;13:10.18632/aging.203133. doi:10.18632/aging.203133

Antibiotic Hybrids Show Promise in Combating Antibiotic Resistance

Macrocycles are 12- or more membered cyclic molecules that can be synthesized or isolated from natural sources. Recent research suggests that one promising approach to the growing problem of antibiotic resistance is to combine macrocycles with antibiotics into metabolically stable hybrid molecules. In a review article, researchers including Dianqing Sun, PhD, of the Daniel K. Inouye College of Pharmacy, investigated clinical trials of new macrocycle-antibiotic hybrids. Results showed that 2 such compounds are hybrids of vancomycin: TD-1792 has shown activity against MRSA, and TD-1607 has demonstrated a bactericidal effect against Gram-positive organisms. Two other compounds are hybrids of rifamycins. TNP-2092, which is a rifamycin nucleus hybridized with a quinazolinone, shows activity against several types of *Staphylococci* and *Streptococci* bacteria. TNP-2198, a conjugate of rifamycin and another antibiotic called metronidazole, may be effective against bacteria that cause certain vaginal infections. Finally, DSTA3647S, a hybrid of rifamycin and an artificially engineered antibody, may be effective against *Staphylococci* infections. More studies are needed to determine whether these macrocycle-antibiotic hybrid clinical candidates will be developed as new and potential treatment options in the clinic.

- Surur AS, Sun D. Macrocycle-antibiotic hybrids: A path to clinical candidates. *Front Chem*. 2021;9:659845. doi:10.3389/fchem.2021.659845

Metabolic Syndrome in Native Hawaiians

The prevalence of metabolic syndrome in a population can be difficult to determine because there are varying criteria for diagnosing the condition. The criteria include having high cholesterol, high blood pressure, diabetes or raised glucose levels, and a large waistline. But, for example, the World Health Organization uses a blood pressure of 140/90 mmHg or greater, while the International Diabetes Federation guidelines use a blood pressure of 130/85 mmHg or greater. Researchers including Chloe Asato, a recent bachelor's degree graduate from the Office of Public Health Studies and a current student at JABSOM, examined data from the Native Hawaiian/Multiethnic Health Research project on 1452 Filipino, Native Hawaiian, Japanese, and white residents of Kohala. Results showed the prevalence of metabolic syndrome in the entire study population could be as low as 22% or as high as 39% depending on the definition used. Among Native Hawaiians, the prevalence could be as low as 26.9% or as high as 48.6%. Among all groups in the study, only Native Hawaiians had a significant difference in prevalence depending on which definition was used. The researchers concluded that varying definitions may exacerbate ethnic disparities. More research is needed to identify the best way to define metabolic syndrome.

- Asato CBH, Nelson-Hurwitz DC, Lee T, Grandinetti A. comparative analysis of metabolic syndrome diagnostic criteria and its effects on prevalence in a multiethnic population. *Metab Syndr Relat Disord*. 2021;10.1089/met.2020.0090. doi:10.1089/met.2020.0090

Opportunistic Measurements of Visceral Fat May Improve Assessments of Women's Cardiometabolic Risk

Obesity is generally assessed using body mass index (BMI), which is simple to determine. However, it is thought that intra-abdominal visceral fat (VAT) may be responsible for many obesity-associated health risks. Researchers including John Shepard, PhD, of the UH Cancer Center, investigated whether VAT measurements obtained from abdominal MRIs were assosciated with having metabolic syndrome. The data came from 1860 older adult members of the Multiethnic Cohort (MEC) study, which enrolled individuals of 5 major racial/ethnic groups including African Americans, Native Hawaiians, Japanese Americans, Latinos, and whites. The researchers calculated participants' VAT measurements from MRI image slices taken at 4 different levels across the abdomen. Results showed that for women, total VAT area as well as the VAT measurements from each of the 4 locations had stronger associations with metabolic syndrome than either BMI or total body fat. Among men, Native Hawaiians showed a stronger association between metabolic syndrome and total VAT area than either BMI or total body fat. The researchers concluded that opportunistic screening for elevated VAT area in women may be warranted across multiple ethnic groups.

- Villegas-Valle RC, Lim U, Maskarinec G, et al. Metabolic syndrome screening using visceral adipose tissue (VAT) from opportunistic MRI locations in a multi-ethnic population. *Obes Res Clin Pract*. 2021;S1871-403X(21)00049-1. doi:10.1016/j.orcp.2021.03.007