

Genome Sequencing and Breast Cancer Prevention

Sieh *et al.* _____ **Page 2322**

There is uncertainty about the benefits of using genome-wide sequencing to implement cancer-preventive strategies at the population level, with some projections suggesting little benefit. Sieh and colleagues used data for known breast cancer susceptibility variants to assess the benefits and harms of targeting populations at the highest genomic risk of breast cancer. The authors found that targeting those in the top 25% of the breast cancer risk distribution would include approximately half of all future breast cancer cases. This study indicates that preventive strategies based on genome sequencing will bring greater gains in disease prevention than previously projected.

Prostate Cancer Heritability

Hjelmborg *et al.* _____ **Page 2303**

Prostate cancer is thought to be the most heritable cancer. Hjelmborg and colleagues performed a large prospective study within the Nordic Twin Study of Cancer cohort to examine the heritability of prostate cancer. The cumulative risk for twins whose co-twin was diagnosed with prostate cancer was greater for monozygotic twins than for dizygotic twins across all ages. Genetic differences contributed substantially to variation in both the risk and the liability of developing prostate cancer. These results support that there are significant genetic contributions to the risk of developing prostate cancer.

Receptor-Defined Breast Cancer in South Africa

Dickens *et al.* _____ **Page 2311**

Receptor-defined breast cancer proportions vary across Africa. To evaluate this closely in South Africa, Dickens and colleagues utilized data from South Africa's national cancer registry and from Namibia's cancer hospital to evaluate estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER2) statuses in breast cancer patients. The authors found that the ER⁺/PR⁺HER2⁻ subtype was the most common, followed by the triple-negative subtype, the ER⁺/PR⁺HER2⁺ subtype, and the ER⁻PR⁻HER2⁺ subtype. ER⁺ breast cancer dominates in all Southern African races and improving survival should be achievable through earlier diagnosis and appropriate treatment.

Guanylin as a Colorectal Cancer Biomarker

Wilson *et al.* _____ **Page 2328**

GUCY2C is an intestine-specific tumor suppressor that controls epithelial homeostasis, but the GUCY2C tumor suppressor is universally overexpressed by human colorectal cancer cells. This likely reflects silencing of GUCY2C through loss of its paracrine hormone, guanylin. Wilson and colleagues quantified expression of guanylin mRNA and protein in tumors and normal epithelia from patients with colorectal cancer. Guanylin mRNA was reduced 100- to 1,000-fold in 85% of tumors compared to matched normal adjacent mucosa. Intestinal tumorigenesis may be prevented by oral GUCY2C hormone replacement therapy.

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