SCIENTIFIC SEMINAR

Joseph Lachance

Georgia Institute of Technology

Atlanta, GA

How ascertainment bias and differences in genetic architecture impair the generalizability of polygenic risk scores for cancer

Genome-wide association studies do not always replicate well across populations, limiting the generalizability of polygenic risk scores. This obstacle is due to multiple causes, including ascertainment bias and divergent evolutionary histories. First, I will demonstrate how choice of genotyping technology and study cohort can bias what is known about the genetics of complex diseases. Second, I will explore how different mechanisms of evolutionary change can cause the genetic architectures of complex traits to differ across populations. These mechanisms include founder effects, natural selection, and ancient introgression. Third, I will focus on the population genetics of a known health disparity: elevated rates of prostate cancer in men of African descent. Novel data from Senegal, Ghana, Nigeria, and South Africa reveal that existing polygenic risk scores for prostate cancer perform poorly when they are applied to non-European populations. Lastly, I will share new findings from the MADCaP Network. Undertaking the first pan-African cancer GWAS, we identify fifteen independent disease associations that reach genome-wide significance, four of which are novel. Intriguingly, multiple lead SNPs are private alleles (i.e., they are Africa-specific). We also find that the genetic architecture of prostate cancer differs across Africa, and effect size differences contribute more to this heterogeneity than allele frequency differences. Furthermore, population genetic analyses reveal that prostate cancer associations are largely governed by neutral evolution. Collectively, our findings emphasize the utility of conducting genetic studies on diverse populations.

CIC bioGUNE
MEMBER OF BASQUE RESEARCH & TECHNOLOGY ALLIANCE

EXCELENCIA SEVERO OCHOA

Tuesday
June 27
Atrio 800
12.00H

BRTA
BASQUE RESEARCH & TECHNOLOGY ALLIANCE