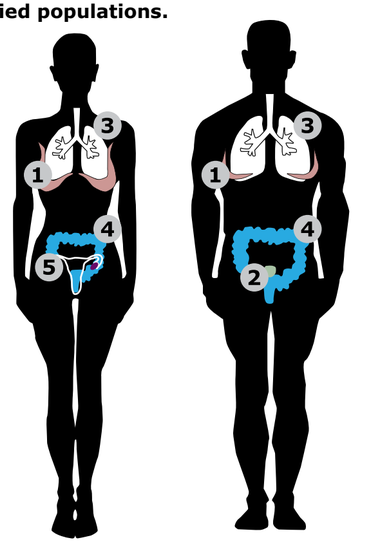
GAME-ON

THE GENETIC ASSOCIATIONS AND MECHANISMS IN ONCOLOGY (GAME-ON) INITIATIVE

The 2000s saw an explosion of population-scale genome-wide association studies (GWAS). Seeing a need to accelerate and coordinate post-GWAS research to advance our understanding of the genetic architecture of cancer, NCI spearheaded the GAME-ON initiative.

This initiative, focused on five cancer types, brought together genetic epidemiologists and biologists, along with other disciplines, to build a cross-discipline collaboration to empower rapid replication of GWAS results and additional discovery, particularly in understudied populations.

FIVE CANCER SITES



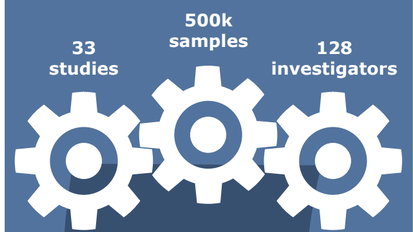
1. BREAST
2. PROSTATE
3. LUNG
4. COLORECTAL
5. OVARIAN

GAME-ON HAS MADE SIGNIFICANT CONTRIBUTIONS IN MULTIPLE DOMAINS

LEVERAGING EXISTING DATA & INFRASTRUCTURE

The GAME-ON initiative pooled genotyping data from several existing studies, giving rise to some of the largest collections of cancer genomic risk data.

Pooling data on this large scale (33 studies; 500,000 samples, and 128 investigators) empowered both the replication of previous findings and the discovery of new risk loci.



300+ new cancer predisposition variants discovered

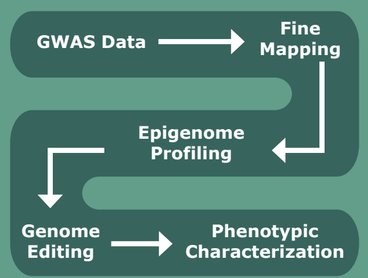
More than 400 publications

Collaborations across more than 350 institutions, 60 countries and multiple research areas

COLLABORATION ACROSS DISCIPLINES

As a cross-disciplinary initiative, GAME-ON built teams with expertise in genetics, epidemiology and biology.

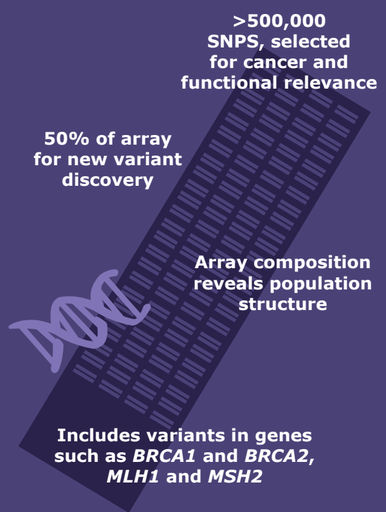
Biologists and genetic epidemiologists worked closely to develop a framework for efficient determination of how variants affect cancer risk. The CAUSEL (Characterization of Alleles USing Editing of Loci) pipeline incorporates genetic, bioinformatic, and lab-based approaches to provide a methodical approach to functional analysis of genetic variants identified in any GWAS, not only cancer GWAS.



SCIENTIFIC DISCOVERY & RESOURCES

GAME-ON investigators have generated more than 420 publications.

OncoArray is a powerful, comprehensive, high-density array for pan-cancer studies that has led to the discovery of hundreds of new cancer predisposition variants.



FunciSNP is an R/ bioconductor tool that integrates functional non-coding data sets with genetic association studies to identify candidate regulatory SNPs.

UNDERSTUDIED POPULATIONS

GAME-ON included ~200,000 samples from previously understudied populations, which helped find cancer risk variants across and unique to different populations.

The large and diverse sample size of the GAME-ON consortium allows for greater scientific examination of rare cancer subgroups/subtypes.

40% of samples are from African, Asian, and Hispanic backgrounds.

Another ~300,000 samples from European populations were included in the GAME-ON initiative, creating a sample size of nearly 500,000 people.

~200k samples from understudied populations

~300k samples from European populations

DATA SHARING

The discoveries and products of the GAME-ON initiative highlight the value of data sharing amongst studies.

Many investigators have already leveraged these data to formulate new hypotheses and have been funded by NIH grants.

Cancer Site	dbGap Accession No.
BREAST	PHS 001263 PHS 001483 PHS 001265 PHS 001321 PHS 001088
COLON	PHS 001499
LUNG	PHS 000877 PHS 000876 PHS 001273
ORAL	PHS 001202
OVARY	PHS 001131 PHS 001132 PHS 001133 PHS 001142 PHS 001150 PHS 001882
PROSTATE	PHS 001125 PHS 001120 PHS 001081 PHS 001391

To access this data, visit NIH's Database of Genotypes and Phenotypes (dbGaP) at www.ncbi.nlm.nih.gov/gap.

Visit: www.epi.grants.cancer.gov/gameon