

# CSCI2820 Medical Bioinformatics

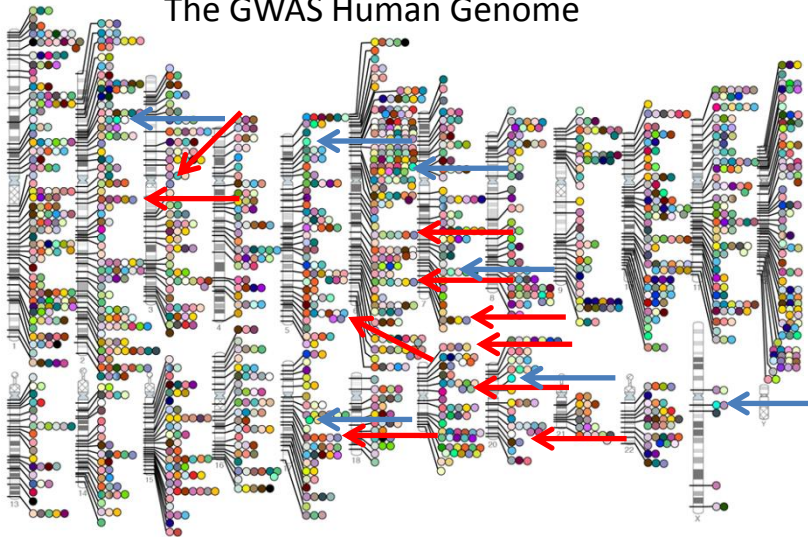
## Genome-wide Association Studies (GWAS)

<http://www.cs.brown.edu/courses/csci2820/>

Prof. Sorin Istrail

Published Genome-Wide Associations through 2011  
1,617 published GWA at  $p \leq 5 \times 10^{-8}$  for 249 traits

The GWAS Human Genome



- Abdominal aortic aneurysm
- Acute lymphoblastic leukemia
- Adhesion molecules
- Adiponectin levels
- Age-related macular degeneration
- AIDS progression
- Alcohol dependence
- Alopecia areata
- Alzheimer disease
- Amyloid A levels
- Ankyrolytic lateral sclerosis
- Angiotensin-converting enzyme activity
- Ankylosing spondylitis
- Arterial stiffness
- Asparagus anosmia
- Asthma
- Atherosclerosis in HIV
- Axial keratoconus
- Ataxin 3-deficient hyperactivity disorder
- Autism
- Basal cell cancer
- Behcet's disease
- Bipolar disorder
- Biliary stricture
- Birtan
- Bitter taste response
- Birth weight
- Bladder cancer
- Bleomycin sensitivity
- Blond or brown hair
- Blood pressure
- Blue or green eyes
- BMI, waist circumference
- Bone density
- Breast cancer
- Butyrylcholinesterase levels
- C-reactive protein
- Calcium traits
- Cardiac structure/function
- Cardiovascular risk factors
- Carnitine levels
- Carotenoid/cholesterol levels
- Carotid atherosclerosis
- Celiac disease
- Celiac disease and rheumatoid arthritis
- Cerebral atrophy measures
- Chronic lymphocytic leukemia
- Chronic myeloid leukemia
- Cleft lip/palate
- Coffee consumption
- Cognitive function
- Conduct disorder
- Colorectal cancer
- Corneal thickness
- Coronary disease
- Cortical thickness
- Creutzfeldt-Jakob disease
- Crohn's disease
- Crohn's disease and celiac disease
- Cutaneous nevi
- Cystic fibrosis severity
- Dermatitis
- DHEA-s levels
- Diabetic retinopathy
- Dilated cardiomyopathy
- Drug-induced liver injury
- Drug-induced liver injury (immune-mediated)
- Endometrial cancer
- Endometriosis
- Eosinophil count
- Eosinophilic esophagitis
- Epirubicin-induced leukopenia
- Erectile dysfunction and prostate cancer treatment
- Erythrocyte parameters
- Esophageal cancer
- Essential tremor
- Exfoliation glaucoma
- Eye color traits
- F cell distribution
- Fibrinogen levels
- Folate pathway vitamins
- Galactosemia
- Follicular lymphoma
- Fuch's corneal dystrophy
- Freckles and burning
- Gallstones
- Gastric cancer
- Glioma
- Glycemic traits
- Graves disease
- Hair color
- Hair morphology
- Handedness in dyslexia
- HDL cholesterol
- Heart failure
- Heart rate
- Height
- Hemostasis parameters
- Hepatic steatosis
- Hepatitis
- Hepatitis B vaccine response
- Hepatocellular carcinoma
- Hirschsprung's disease
- HIV-1 control
- Hodgkin's lymphoma
- Homocysteine levels
- HPV seropositivity
- Hypospadias
- Idiopathic pulmonary fibrosis
- IFN-related cytopeni
- Iga levels
- Iga levels
- Inflammatory bowel disease
- Insulin-like growth factors
- Intracranial aneurysm
- Iris color
- Iron status markers
- Ischemic stroke
- Juvenile idiopathic arthritis
- Keldoid
- Kidney stones
- LDL cholesterol
- Leprosy
- Leptin receptor levels
- Liver enzymes
- Longevity
- LP (a) levels
- LpPLA(2) activity and mass
- Lung cancer
- Magnesium levels
- Major mood disorders
- Malaria
- Male pattern baldness
- Mammographic density
- Matrix metalloproteinase levels
- MCP-1
- Melanoma
- Menarche & menopause
- Menstruata
- Meningococcal disease
- Metabolic syndrome
- Migraine
- Moyamoya disease
- Multiple sclerosis
- Myeloproliferative neoplasms
- Myopia (pathologic)
- N-glycan levels
- Narcolepsy
- Nasopharyngeal cancer
- Natriuretic peptide levels
- Neuroblastoma
- Nicotine dependence
- Obesity
- Open angle glaucoma
- Open personality
- Optic disc parameters
- Osteoarthritis
- Osteoporosis
- Osteostropis
- Other metabolic traits
- Ovarian cancer
- Ovarian cancer
- Pain
- Paget's disease
- Panic disorder
- Parkinson's disease
- Periodontitis
- Peripheral arterial disease
- Personality dimensions
- Phosphatidylcholine levels
- Phosphorus levels
- Photic sneeze
- Phytosterol levels
- Platelet count
- Polycystic ovary syndrome
- Primary biliary cirrhosis
- Primary sclerosing cholangitis
- PR interval
- Programulin levels
- Progressive supranuclear palsy
- Prostate cancer
- Protein levels
- PSA levels
- Psoriasis
- Psoriatic arthritis
- Pulmonary funct. COPD
- QRS interval
- QT interval
- Quantitative traits
- Recombination rate
- Red vs non-red hair
- Refractive error
- Renal cell carcinoma
- Renal function
- Response to antidepressants
- Response to antipsychotic therapy
- Response to carbamazepine
- Response to clopidogrel therapy
- Response to hepatitis C treat
- Response to interferon beta therapy
- Response to metformin
- Response to statin therapy
- Restless legs syndrome
- Retinal vascular caliber
- Retinal levels
- Rheumatoid arthritis
- Ribavirin-induced anemia
- Schizophrenia
- Serum metabolites
- Smoking behavior
- Speech perception
- Sphingolipid levels
- Statin-induced myopathy
- Stevens-Johnson syndrome
- Stroke
- Sudden cardiac arrest
- Suicide attempts
- Systemic lupus erythematosus
- Systemic sclerosis
- T-tau levels
- Tau AB1-42 levels
- Telomere length
- Testicular germ cell tumor
- Thyroid cancer
- Thyroid volume
- Tooth development
- Total cholesterol
- Trglycerides
- Tuberculosis
- Type 1 diabetes
- Type 2 diabetes
- Ulcerative colitis
- Urate
- Urinary albumin excretion
- Urinary metabolites
- Uterine fibroids
- Venous thrombembolism
- Ventricular conduction
- VEGF levels
- Vertical cup-disc ratio
- Vitamin B12 levels
- Vitamin D insufficiency
- Vitamin E levels
- Vitiligo
- Warfarin dose
- Weight
- White cell count
- White matter hyperintensity
- YKL-40 levels

← Autism marker   ← Multiple Sclerosis Marker

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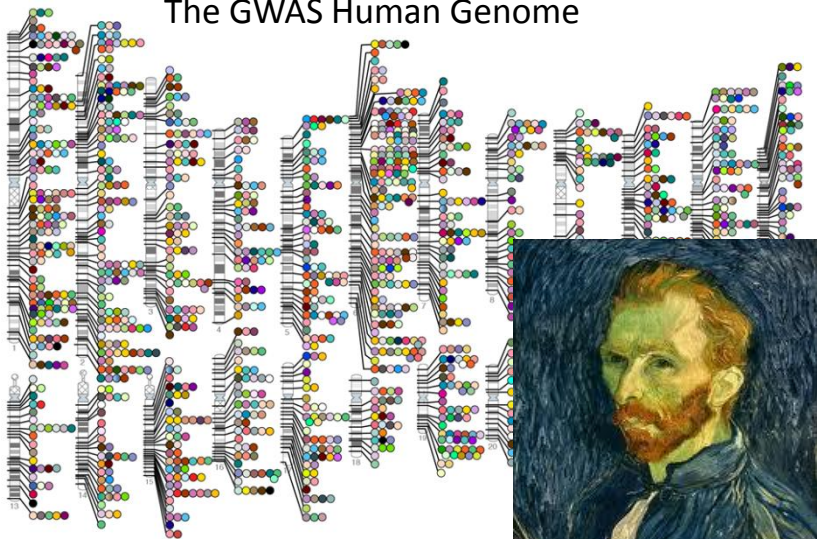
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## Genetic Heterogeneity

The Common Disease Common Variant (CDCV) hypothesis is dead.  
Long live the Common Disease Many Rare Variants hypothesis!

The CDCV 's classical drawing metaphor as "Needles in the Haystack," with few needles with a common look in a large haystack, needs to be replaced now with a van Gogh-like drawing, with many needles each differently looking and private to areas in the large haystack.

Vincent

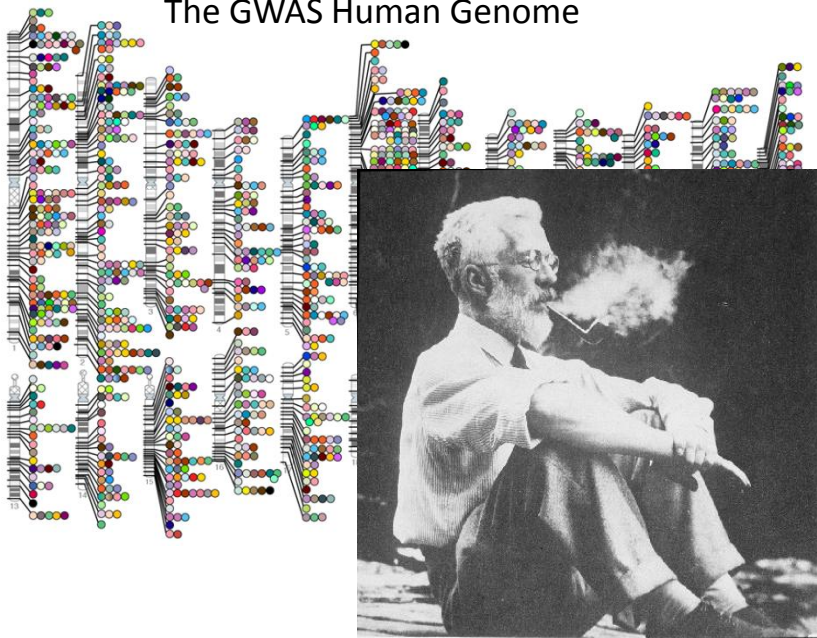
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## The Missing Heritability Puzzle

Additivity of alleles? Just a convenient approximation, friendly to “heritability” measured as a correlation coefficient.

Ronald

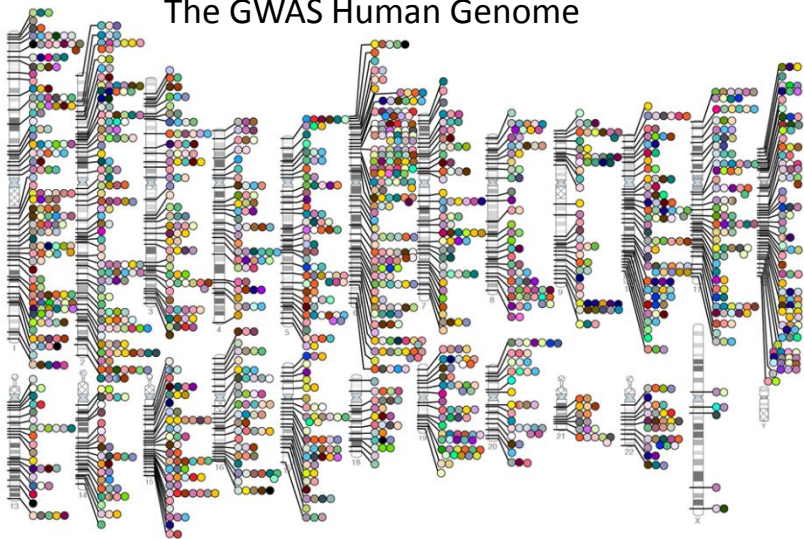
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## Topics include

- haplotype phasing, linkage disequilibrium, tagging SNPs, identical by descent (IBD), pedigrees, trios
- coalescent theory, Polya urn game, Ewens sampling lemma, genome-wide graph theory algorithms
- the genetic heterogeneity problem, the missing heritability problem
- statistical models of disease, association tests and multiple hypothesis testing
- autism, multiple sclerosis, type 2 diabetes