Investigación con muestras de ADN

MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD

CSIC
CONSEJO SUPERIOR DE INVESTIGACIONES CIENTÍFICAS

ipbln
INSTITUTO DE PARASITOLOGÍA Y BIOMEDICINA "LÓPEZ-NEYRA"

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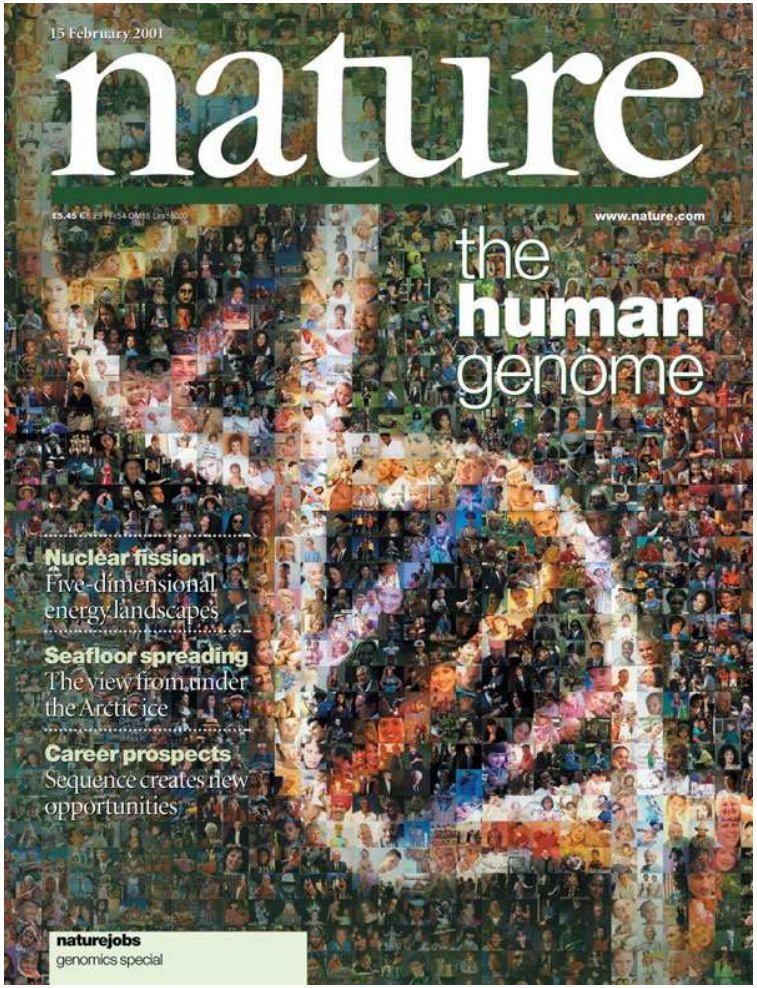
The Human Genome

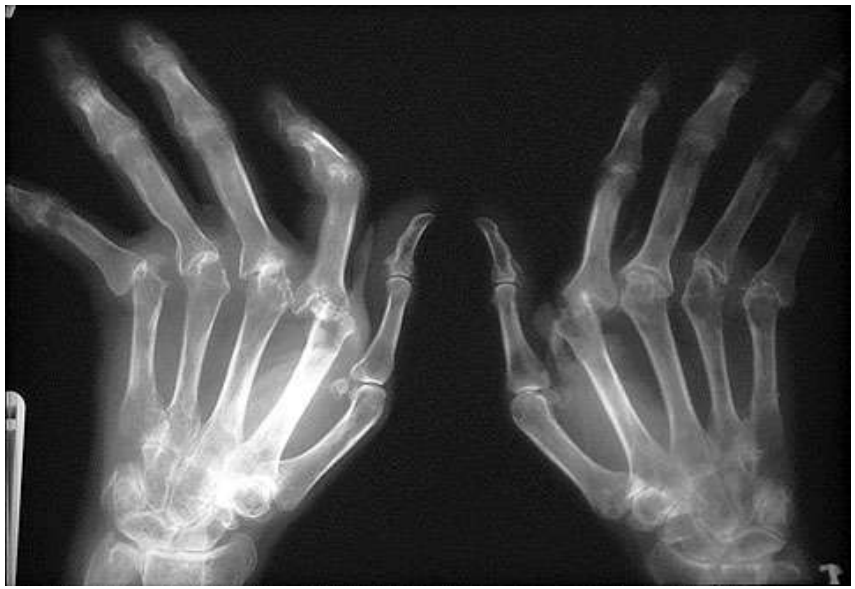


Common Complex Diseases

Autoimmune Diseases can affect several organs

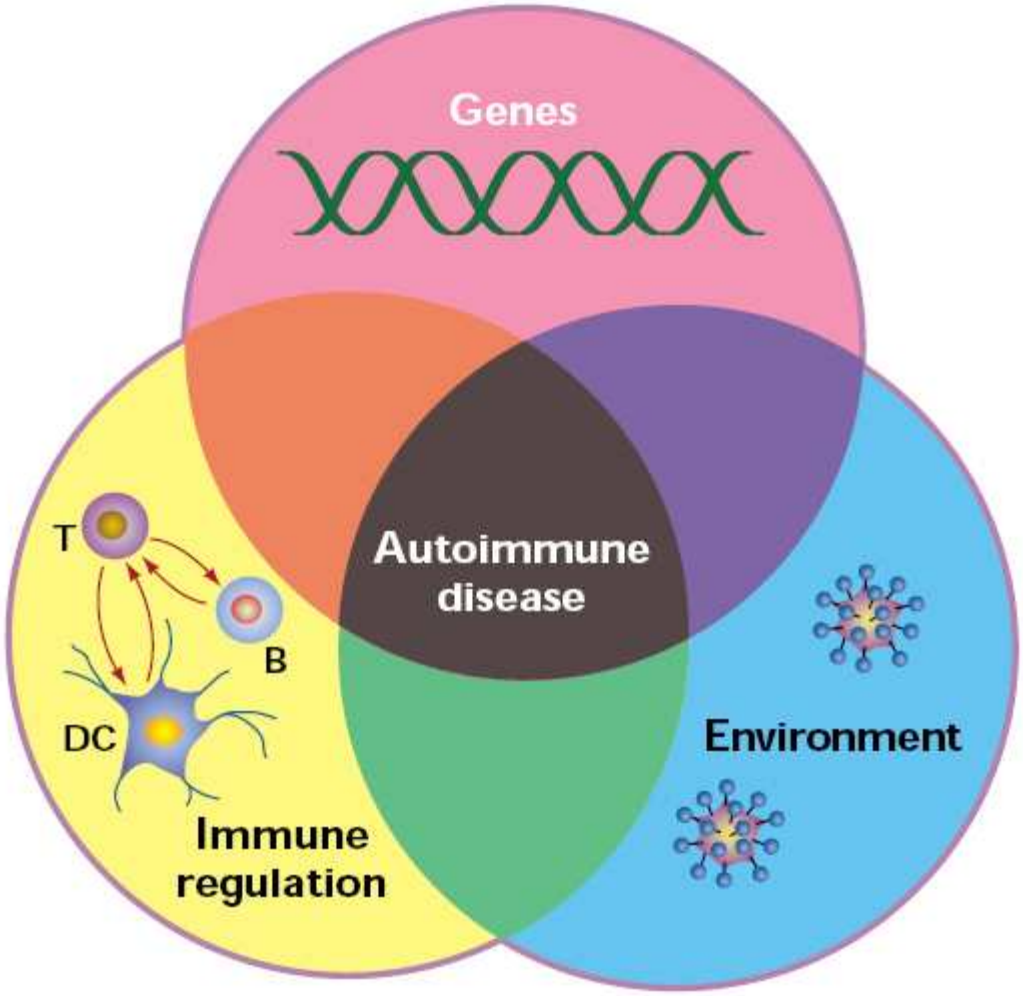
SYSTEMIC

Rheumatoid Arthritis (RA)



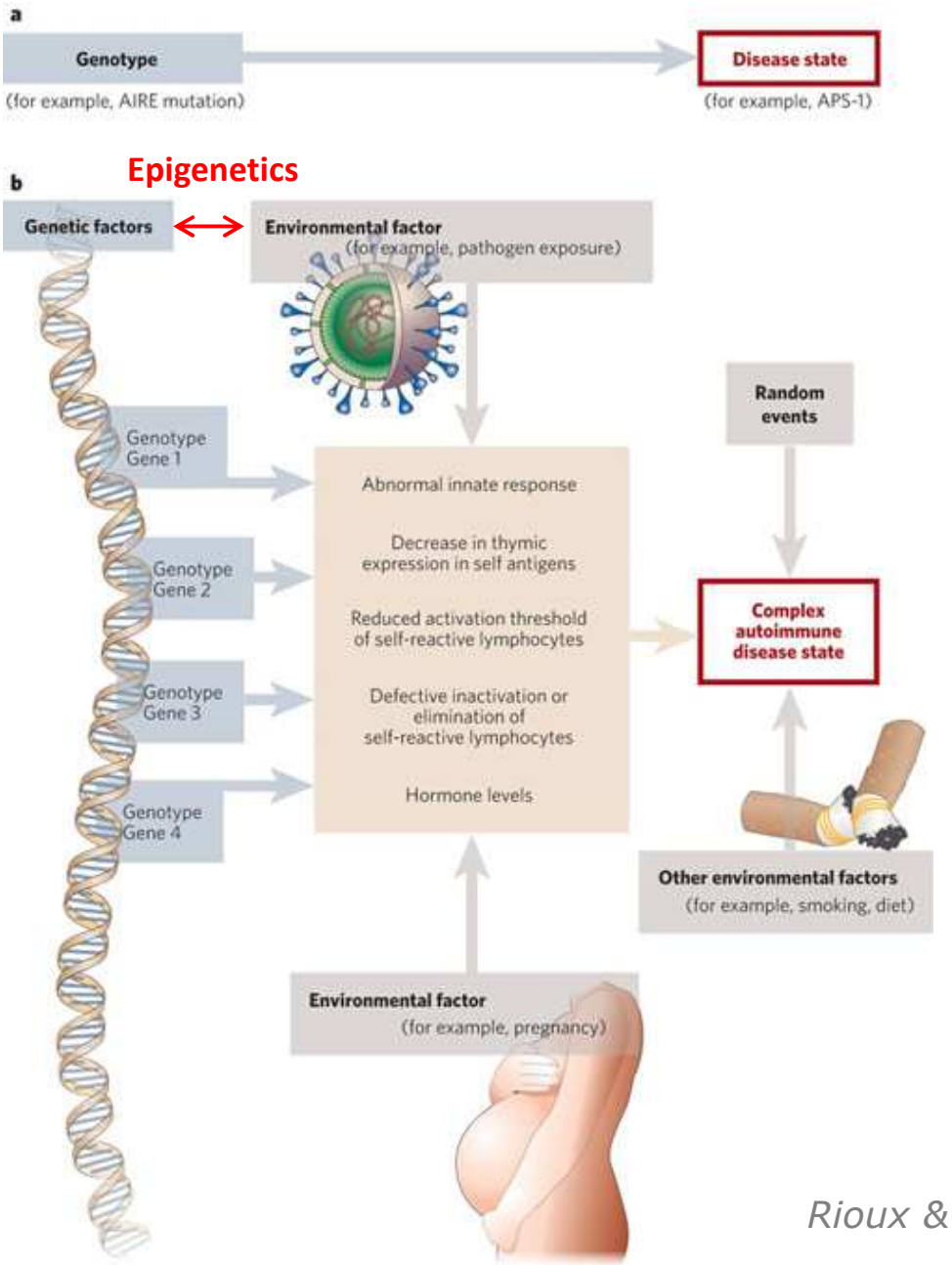
Systemic Sclerosis (SSc) / Scleroderma

Autoimmune Diseases aetiology: unknown



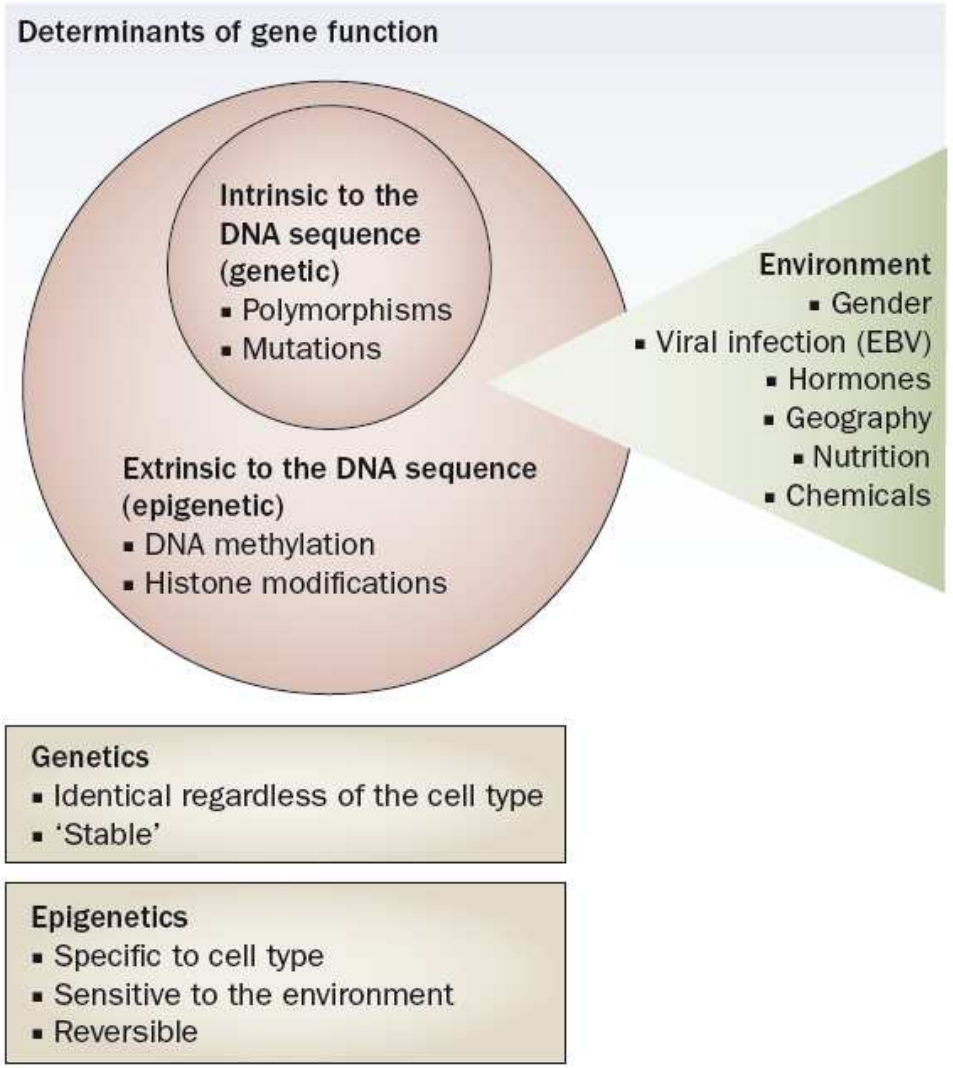
Ermann & Fathman, Nat Immunol, 2001

Autoimmune Diseases aetiology: unknown



Rioux & Abbas, Nature , 2005

GENETICS and EPIGENETICS



Ballestar E, Nat Rev Rheumatol, 2011

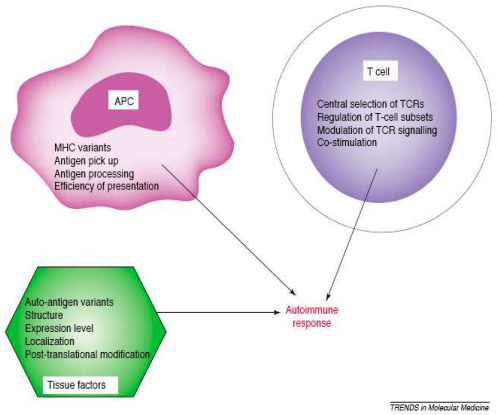
Heritability of Autoimmune Diseases

Genetic heritability for specific autoimmune diseases based on available twin concordance rates and prevalence estimated.

	Genetic heritability
Acute rheumatic fever	0.60 (0.41–0.81)
Ankylosing spondilitis	0.97 (0.92–0.99)
Celiac disease	0.57 (0.32–0.93) if 1/1000 prevalence
	0.87 (0.49–1.00) if 1/91 prevalence
Crohn's disease	1.00 (0.34–1.00)
	0.55 (*)
Multiple sclerosis	0.25 (0–0.88)
	0.76 (0.33–0.88)
Psoriasis	0.66 (0.52–0.77)
Psoriatic arthritis	0.65 (0.22–1.00)
Rheumatoid arthritis	0.68 (0.55–0.79) if ACPA-positive
	0.66 (0.21–0.82) if ACPA-negative
Sarcoidosis	0.66 (0.52–0.80)
Systemic lupus erythematosus	0.66 (*)
Systemic sclerosis	0.55
Type 1 diabetes	0.88 (0.78–0.94)
	0.80 (*)

Why do we study the genetic component of a disease?

Better understanding disease pathogenesis



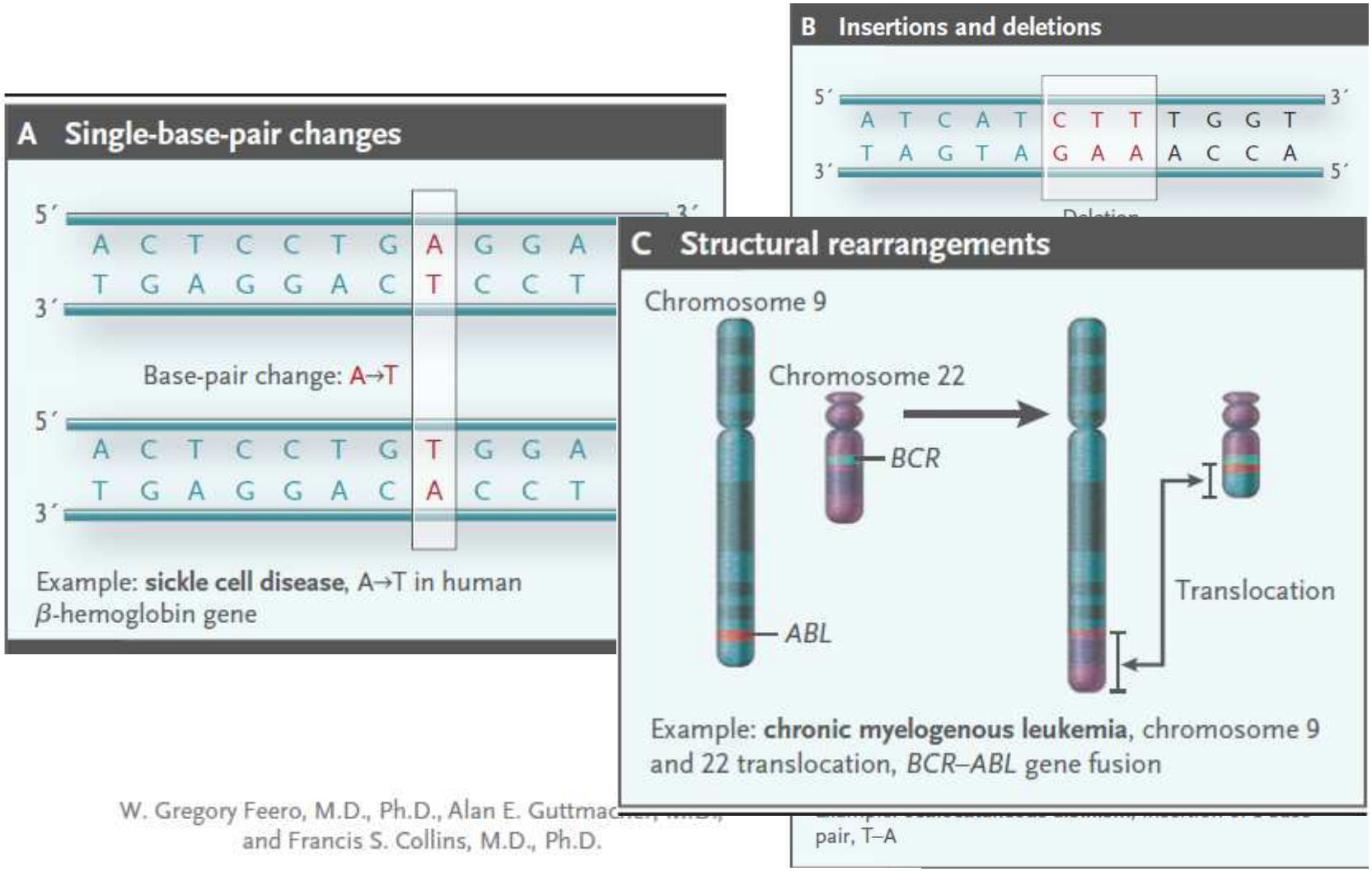
Prognosis / biomarkers

Pharmacogenomics /

Personalized Medicine

New therapeutic targets

Human Genetic Variation

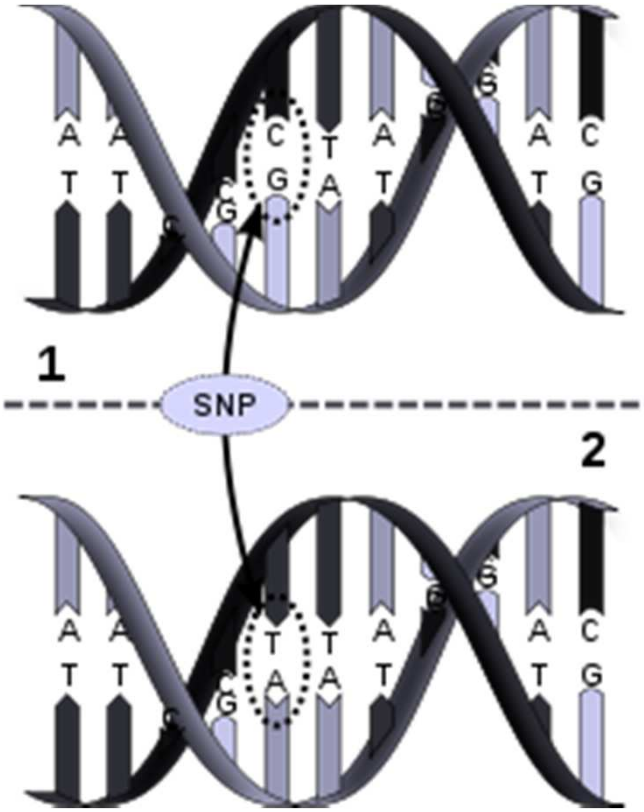


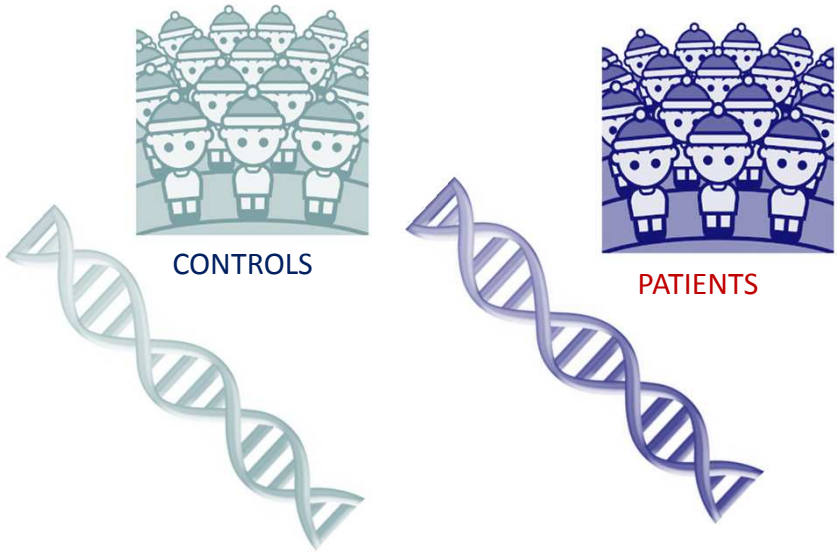
W. Gregory Feero, M.D., Ph.D., Alan E. Guttmacher, M.D., and Francis S. Collins, M.D., Ph.D.

pair, T–A

Genetic Studies in Immune-Mediated Diseases

- **Complex traits affected by common variations.**
- **Single-nucleotide polymorphisms.**
- **Case-control studies.**





Candidate Genes studies

Genome Wide Association studies –GWAs-

- Advances in genotyping technologies
- Reduction in genotyping costs
- HapMap project

Genome-wide association studies (GWAS)

2007: “the year of GWAS”

Hokusai, K. *The Great Wave*

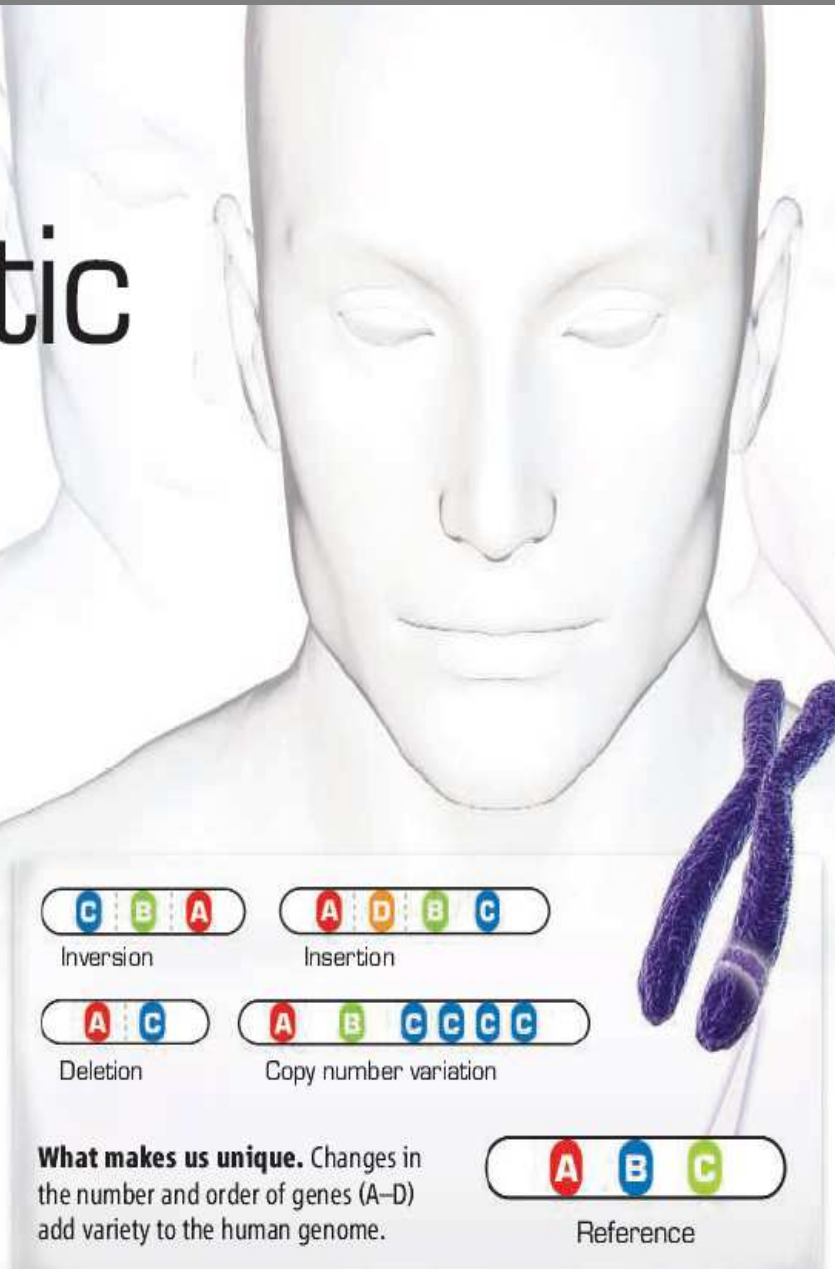
BREAKTHROUGH OF THE YEAR

Human Genetic Variation

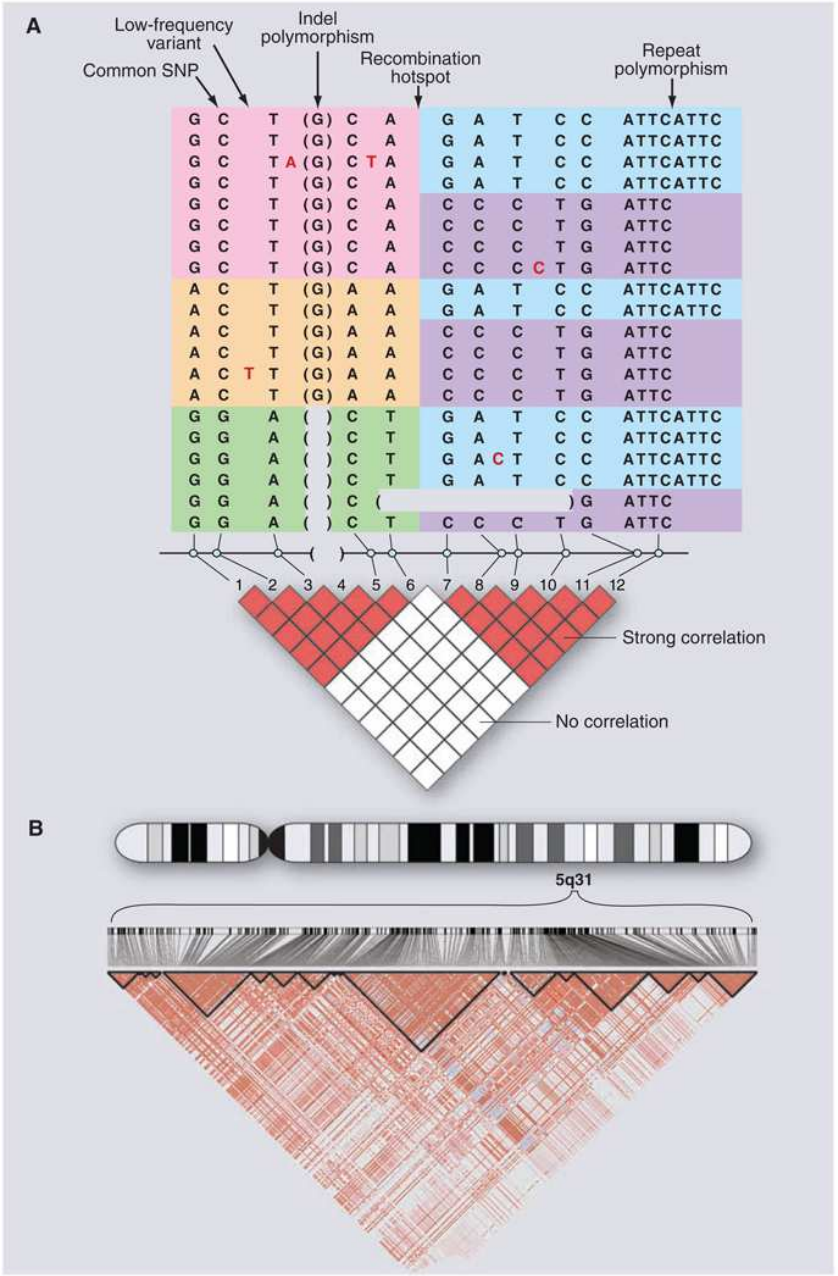
Equipped with faster, cheaper technologies for sequencing DNA and assessing variation in genomes on scales ranging from one to millions of bases, researchers are finding out how truly different we are from one another

THE UNVEILING OF THE HUMAN GENOME ALMOST 7 YEARS AGO cast the first faint light on our complete genetic makeup. Since then, each new genome sequenced and each new individual studied has illuminated our genomic landscape in ever more detail. In 2007, researchers came to appreciate the extent to which our genomes differ from person to person and the implications of this variation for deciphering the genetics of complex diseases and personal traits.

Less than a year ago, the big news was triangulating variation between us and our primate cousins to get a better handle on genetic changes along the evolutionary tree that led to humans. Now, we have moved from asking what in our DNA makes us human to striving to

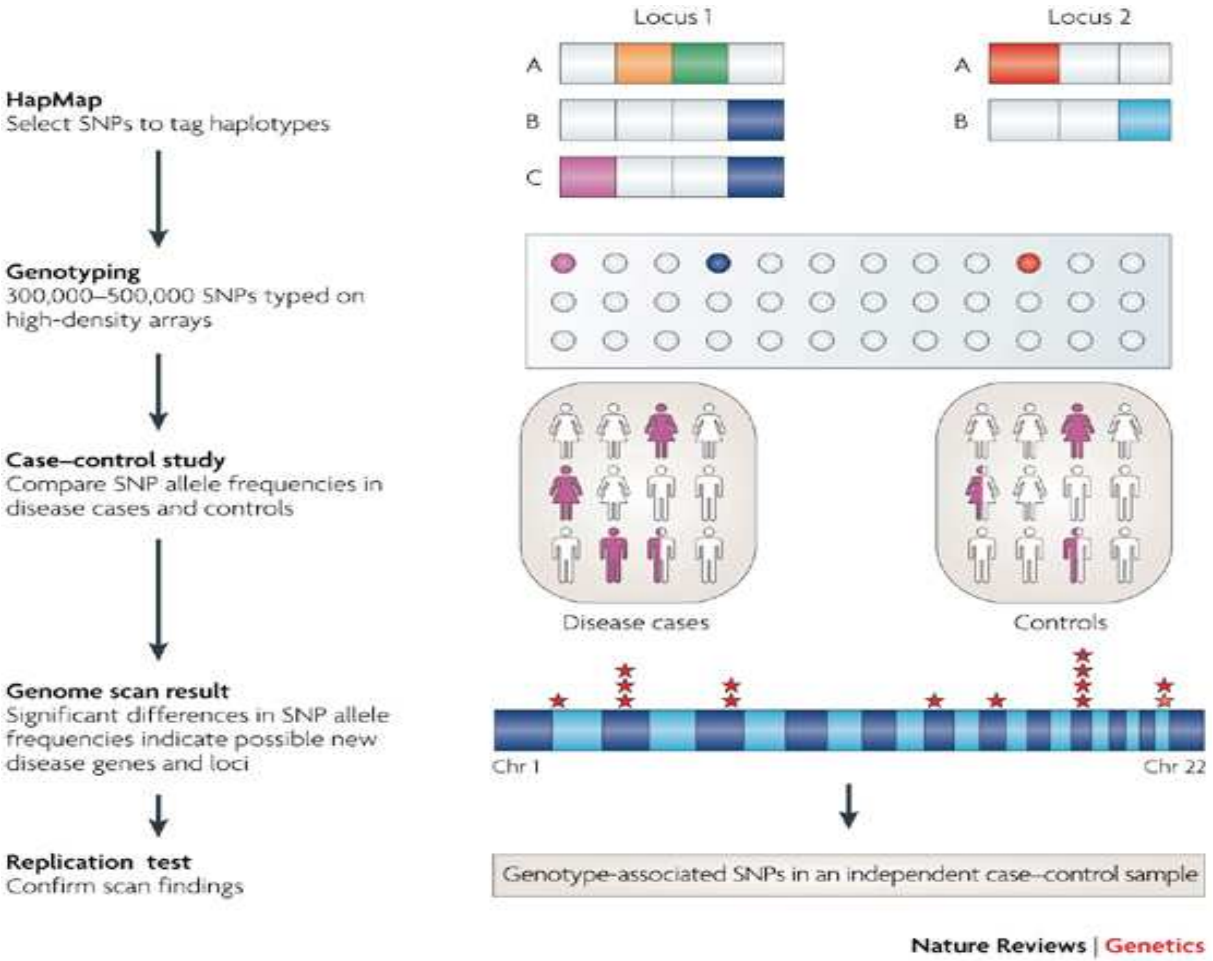


What makes us unique. Changes in the number and order of genes (A–D) add variety to the human genome.



Altshuler & Daly & Lander; Science, 2008

Strategy for GWA studies



- ***Hypothesis free*** **Common variants, > 5%**
- ***Hypothesis generating***

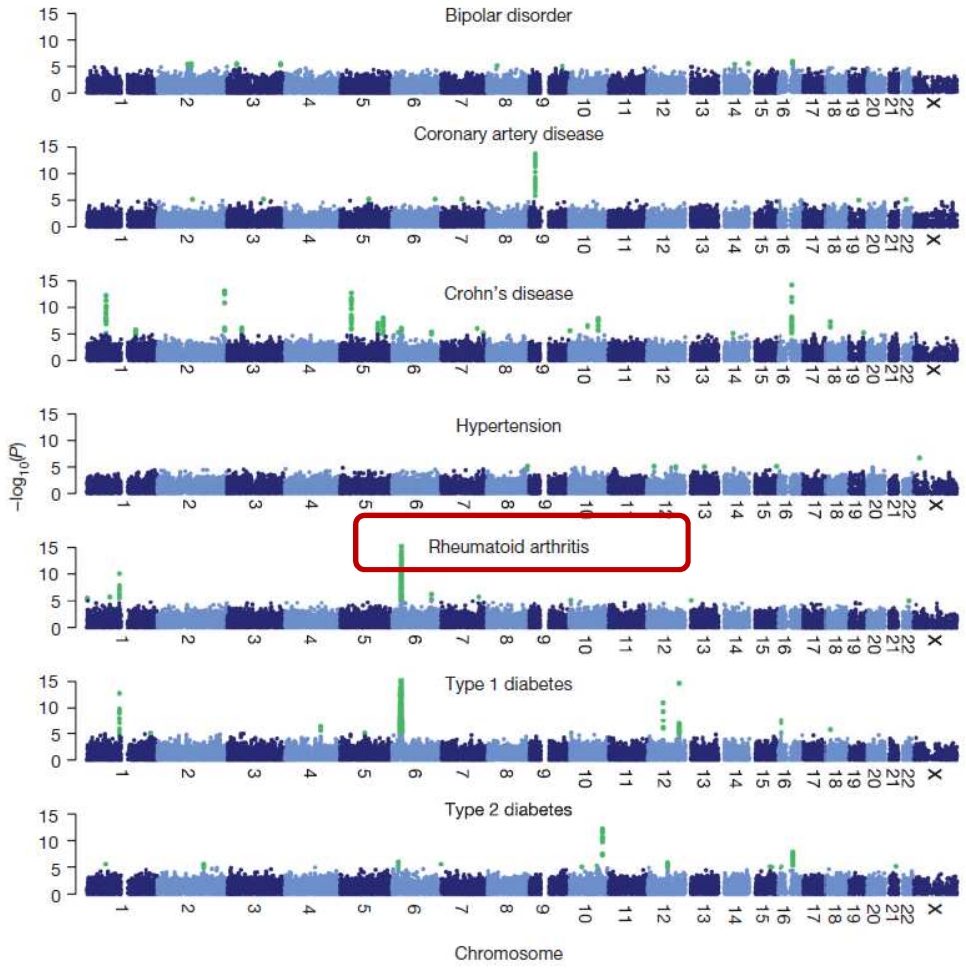
GWAS in Common Complex Diseases

Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls

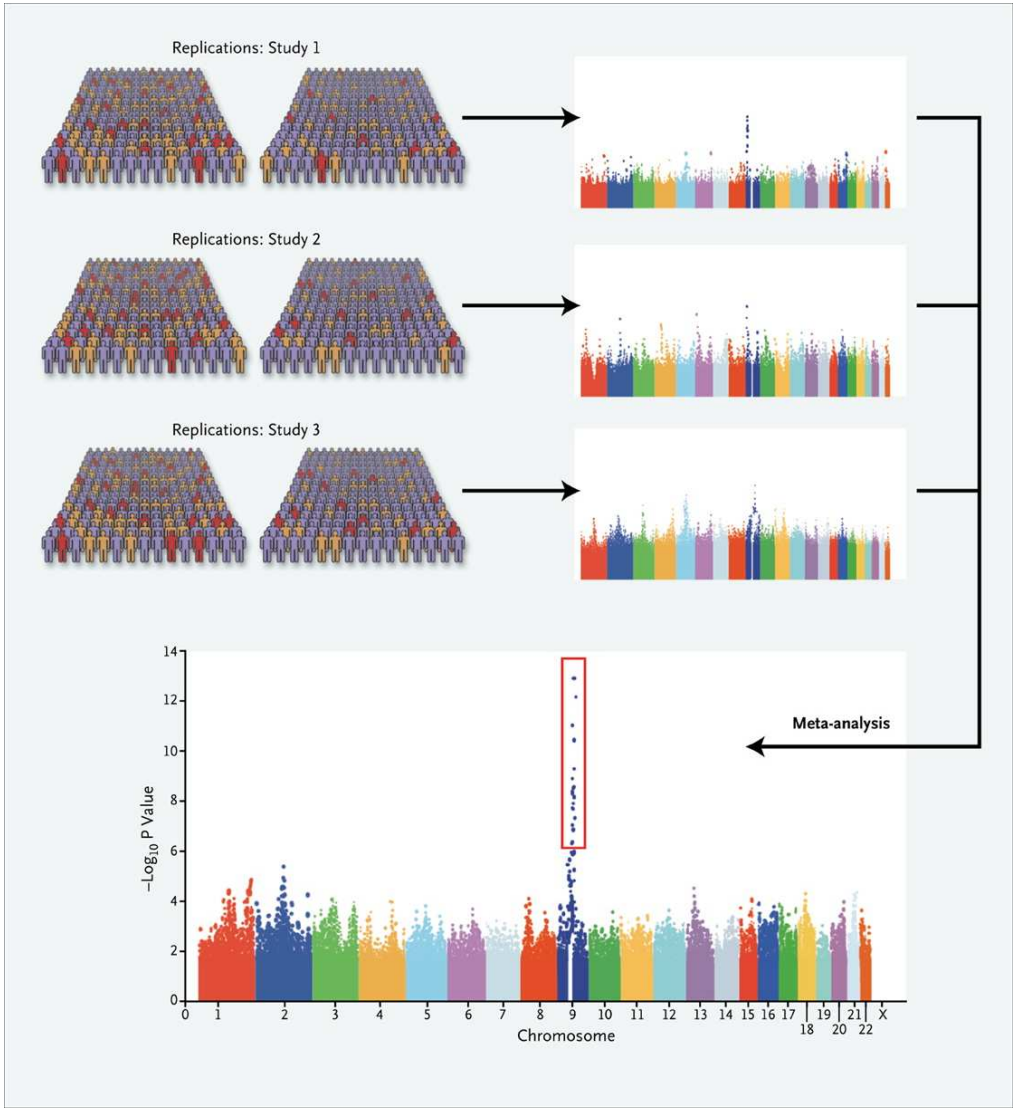
The Wellcome Trust Case Control Consortium*

NATURE|Vol 447|7 June 2007

GWAS significance level (5×10^{-8})

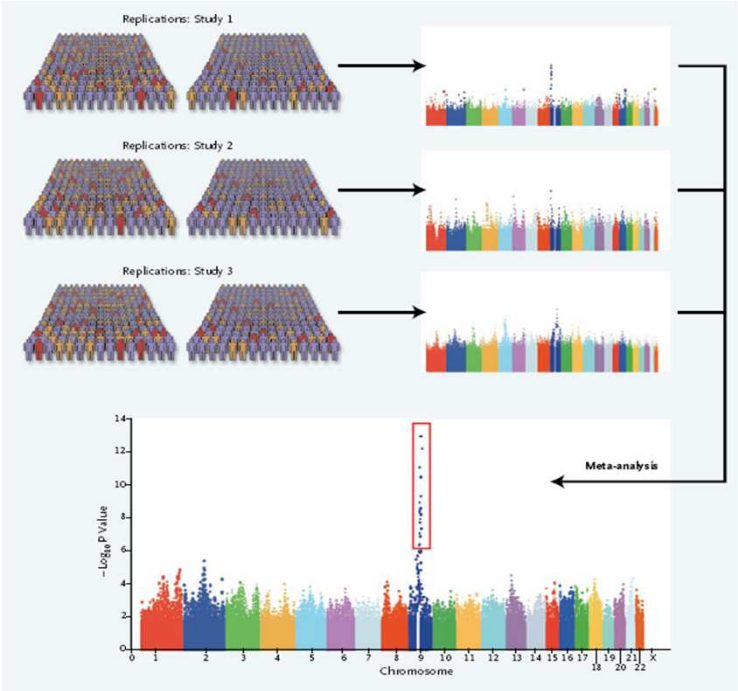


Meta - GWAS



Manolio T, NEJM 2010

meta – GWAS in Rheumatoid Arthritis



- BRASS
- EIRA
- CANADA
- NARAC
- WTCCC

≅ 12.000 RA cases, 30.000 controls

- 7 new RA loci
- 31 confirmed RA loci

Stahl et al., Nat Genet, 2010

Gene discovery in Rheumatoid Arthritis

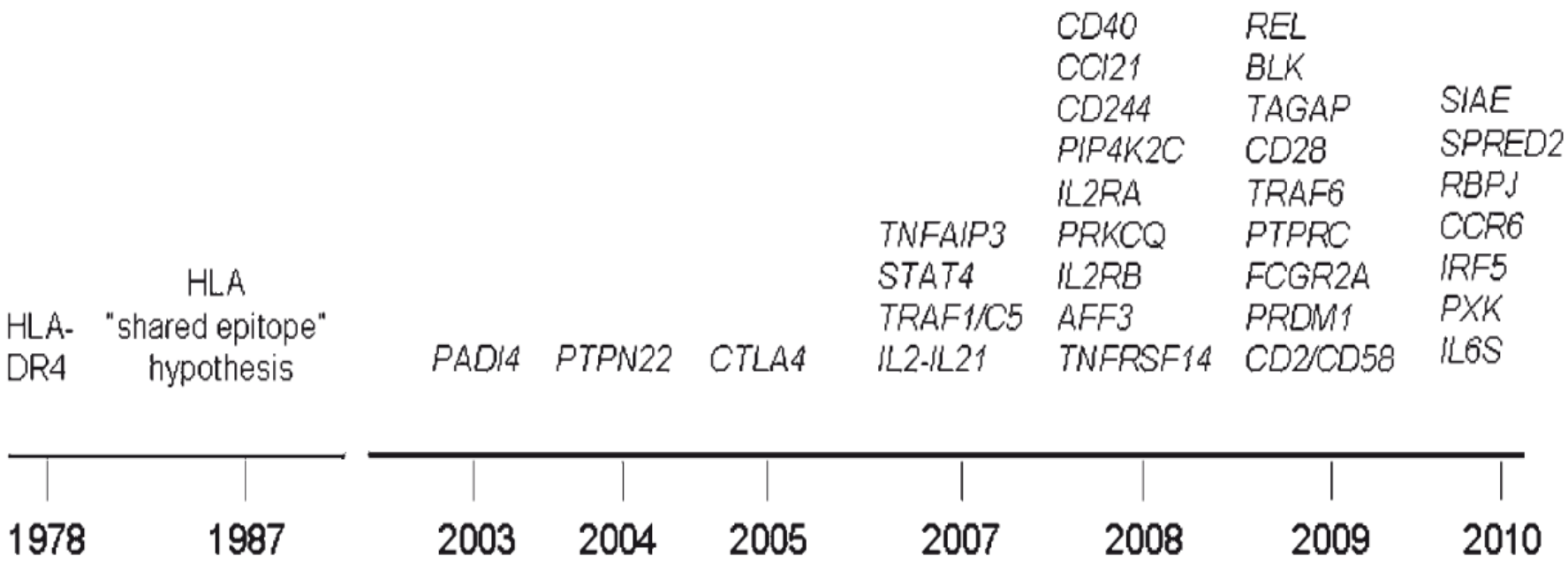
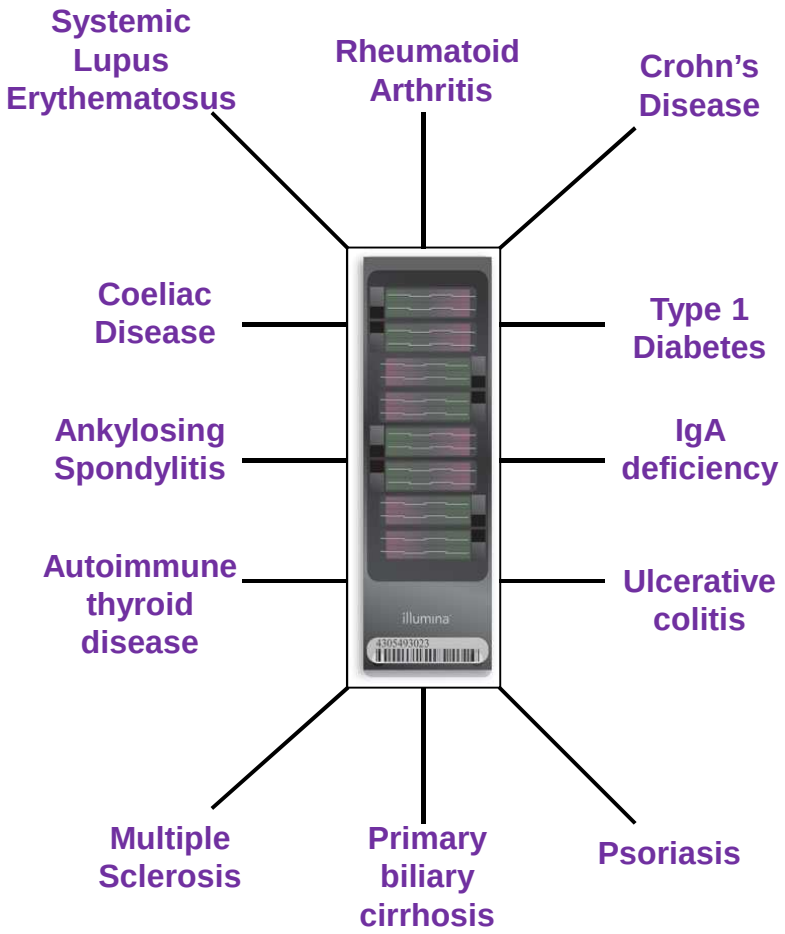


Figure 1 A timeline of gene discovery in rheumatoid arthritis.

Gregersen PK, Bull NYU Hosp Jt Dis., 2010

The Immunochip

Fine-mapping of 186 *loci* previously associated with autoimmune diseases



- Custom Illumina array
- ~180,000 SNPs across ~200 genomic regions
- **Multi disease** project makes identification of overlapping loci feasible

wellcome trust

Immunochip in Rheumatoid Arthritis

High-density genetic mapping identifies new susceptibility loci for rheumatoid arthritis

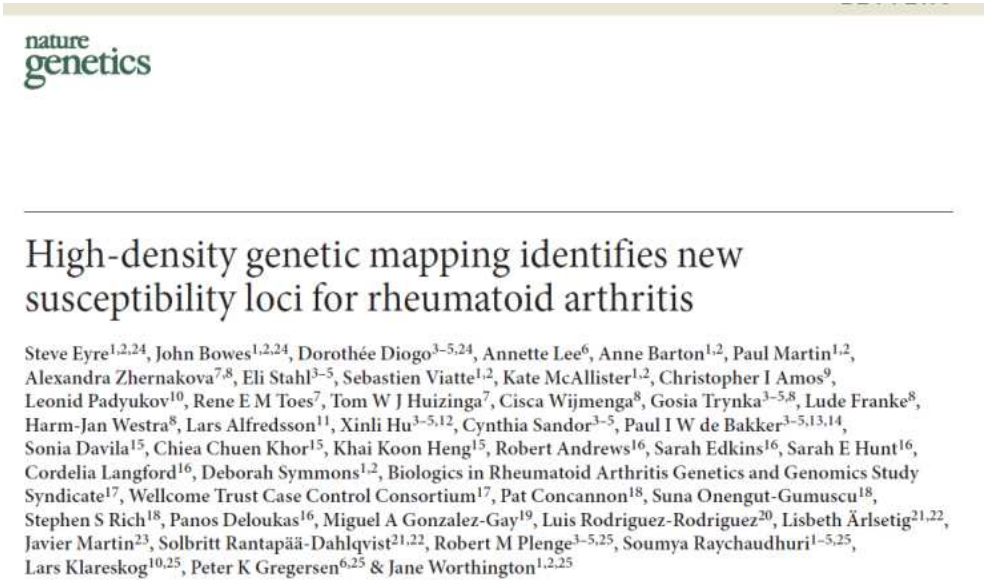
Steve Eyre[1,2,24], John Bowes[1,2,24], Dorothée Diogo[3–5,24], Annette Lee[6], Anne Barton[1,2], Paul Martin[1,2], Alexandra Zhernakova[7,8], Eli Stahl[3–5], Sebastien Viatte[1,2], Kate McAllister[1,2], Christopher I Amos[9], Leonid Padyukov[10], Rene E M Toes[7], Tom W J Huizinga[7], Cisca Wijmenga[8], Gosia Trynka[3–5,8], Lude Franke[8], Harm-Jan Westra[8], Lars Alfredsson[11], Xinli Hu[3–5,12], Cynthia Sandor[3–5], Paul I W de Bakker[3–5,13,14], Sonia Davila[15], Chiea Chuen Khor[15], Khai Koon Heng[15], Robert Andrews[16], Sarah Edkins[16], Sarah E Hunt[16], Cordelia Langford[16], Deborah Symmons[1,2], Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate[17], Wellcome Trust Case Control Consortium[17], Pat Concannon[18], Suna Onengut-Gumuscu[18], Stephen S Rich[18], Panos Deloukas[16], Miguel A Gonzalez-Gay[19], Luis Rodriguez-Rodriguez[20], Lisbeth Ärlsetig[21,22], Javier Martin[23], Solbritt Rantapää-Dahlqvist[21,22], Robert M Plenge[3–5,25], Soumya Raychaudhuri[1–5,25], Lars Klareskog[10,25], Peter K Gregersen[6,25] & Jane Worthington[1,2,25]

Table 1 Sample collections

		Cases				Controls	
	Collection	All	Female (%)	ACPA+	ACPA−	All	Female (%)
Immunochip	UK	3,870	74	2,406	1,000	8,430	53
	Swedish EIRA	2,762	70	1,762	987	1,940	73
	United States	2,536	75	1,803	593	2,134	65
	Dutch	648	66	330	301	2,004	42
	Swedish Umea	852	70	524	242	963	69
	Spanish	807	74	397	216	399	65
	TOTAL	11,475	73	7,222	3,339	15,870	57

Eyre et al, Nat Genet, 2012

Gene discovery in Rheumatoid Arthritis



nature genetics

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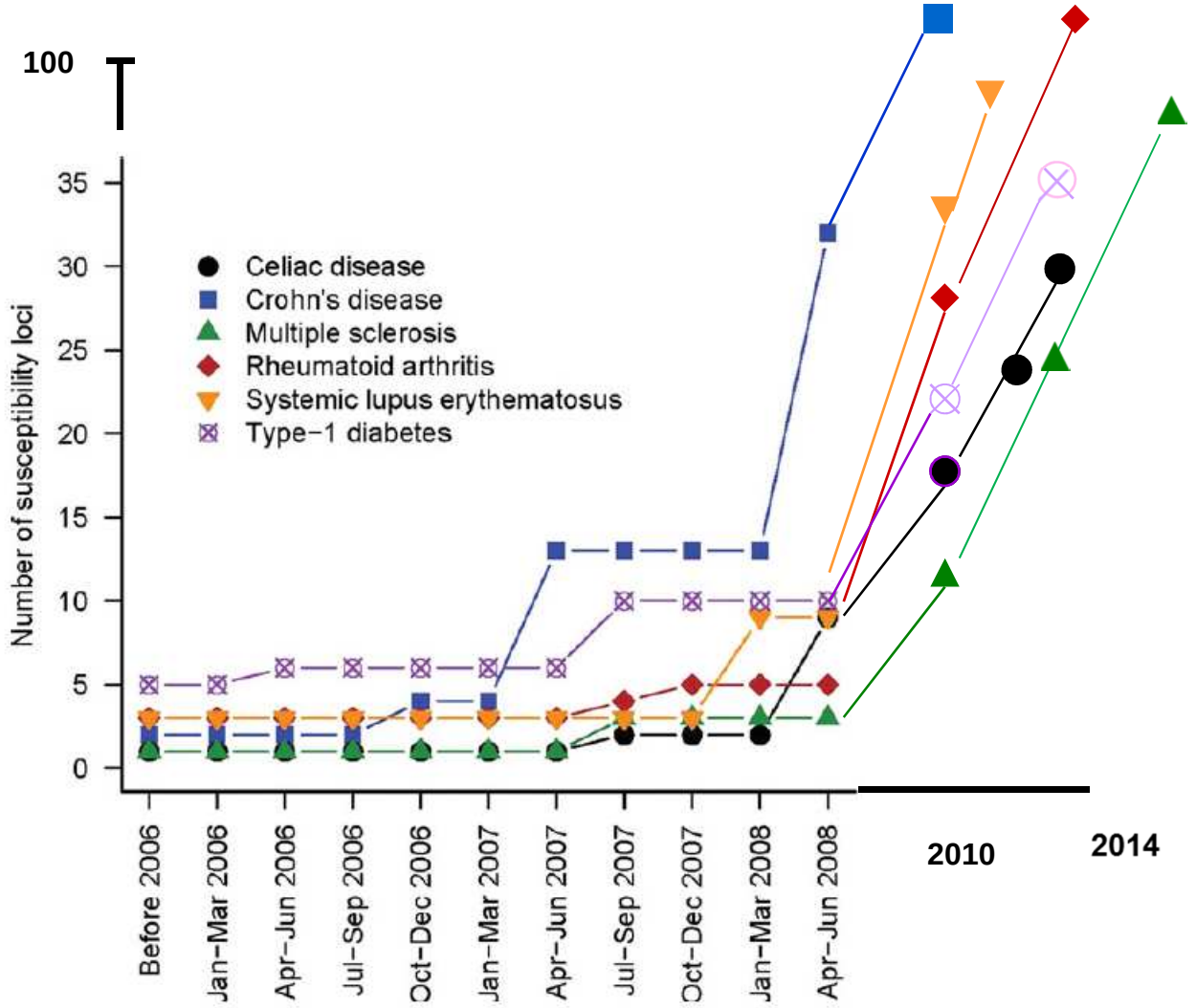
1978	2004	2007	2008	2009	2010	2012
HLA-DRB1	*PTPN22*	*TNFAIP3* *STAT4* *TRAF1* *IL2 / IL21*	*CD40* *CCL21* *TNFRSF14* *IL2RB* *CTLA4* *PRKCQ* *KIF5A* *IL2RA* *AFF3*	*REL* *BLK* *TAGAP* *CD28* *TRAF6* *PTPRC* *FCGR2A* *PRDM1* *CD2-CD58*	*ANKRD55* *SPRED2* *C5orf30* *RBPJ* *CCR6* *IRF5* *PXK*	*TYK2* *IRAK1* *TLE* *RASGRP* *1* *PADI4* *IL6R* *IRF8* *ARID5B* *RUNX1* *IKZF3* *POU3F1* *RCAN1* *CD5* *GATA3* *PTPN2* *BACH2* *RAD51L1*

Genome wide association studies, replication studies and meta-analyses have been used to identify over **46 RA susceptibility loci** at genome-wide significance ($p<5x10^{-8}$).

GWAs in Autoimmune Diseases



Modified from Lettre & Rioux, HMG, 2008

GWAs in Systemic Sclerosis

LETTERS

nature genetics

Genome-wide association study of systemic sclerosis identifies *CD247* as a new susceptibility locus

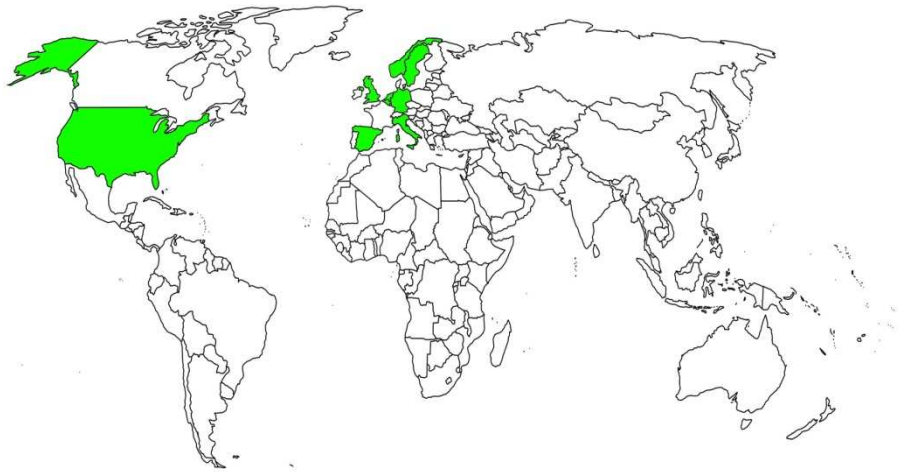
Timothy R D J Radstake[1,38], Olga Gorlova[2,38], Blanca Rueda[3,38], Jose-Ezequiel Martin[3,38], Behrooz Z Alizadeh[4], Rogelio Palomino-Morales[3], Marieke J Coenen[5], Madelon C Vonk[1], Alexandre E Voskuyl[6], Annemie J Schuerwegh[7], Jasper C Broen[1], Piet L C M van Riel[1], Ruben van 't Slot[4], Annet Italiaander[4], Roel A Ophoff[4,8], Gabriela Riemekasten[9], Nico Hunzelmann[10], Carmen P Simeon[11], Norberto Ortego-Centeno[12], Miguel A González-Gay[13], María F González-Escribano[14], Spanish Scleroderma Group[37], Paolo Airo[15], Jaap van Laar[16], Ariane Herrick[17], Jane Worthington[17], Roger Hesselstrand[18], Vanessa Smith[19], Filip de Keyser[19], Fredric Houssiau[20], Meng May Chee[21], Rajan Madhok[21], Paul Shiels[21], Rene Westhovens[22], Alexander Kreuter[23], Hans Kiener[24], Elfride de Baere[25], Torsten Witte[26], Leonid Padykov[27], Lars Klareskog[27], Lorenzo Beretta[28], Rafaella Scorza[28], Benedicte A Lie[29], Anna-Maria Hoffmann-Vold[30], Patricia Carreira[13,31], John Varga[32], Monique Hinchcliff[32], Peter K Gregersen[33], Annette T Lee[33], Jun Ying[2], Younghun Han[2], Shih-Feng Weng[2], Christopher I Amos[2], Fredrick M Wigley[34], Laura Hummers[34], J Lee Nelson[35], Sandeep K Agarwal[36], Shervin Assassi[36], Pravitt Gourh[36], Filemon K Tan[36], Bobby P C Koeleman[4,38], Frank C Arnett[36,38], Javier Martin[3,38] & Maureen D Mayes[36,38]

Subjects

GWAS analysis

2,296 SSc patients
5,171 Controls

1486/3477
364/384
270/671
176/639



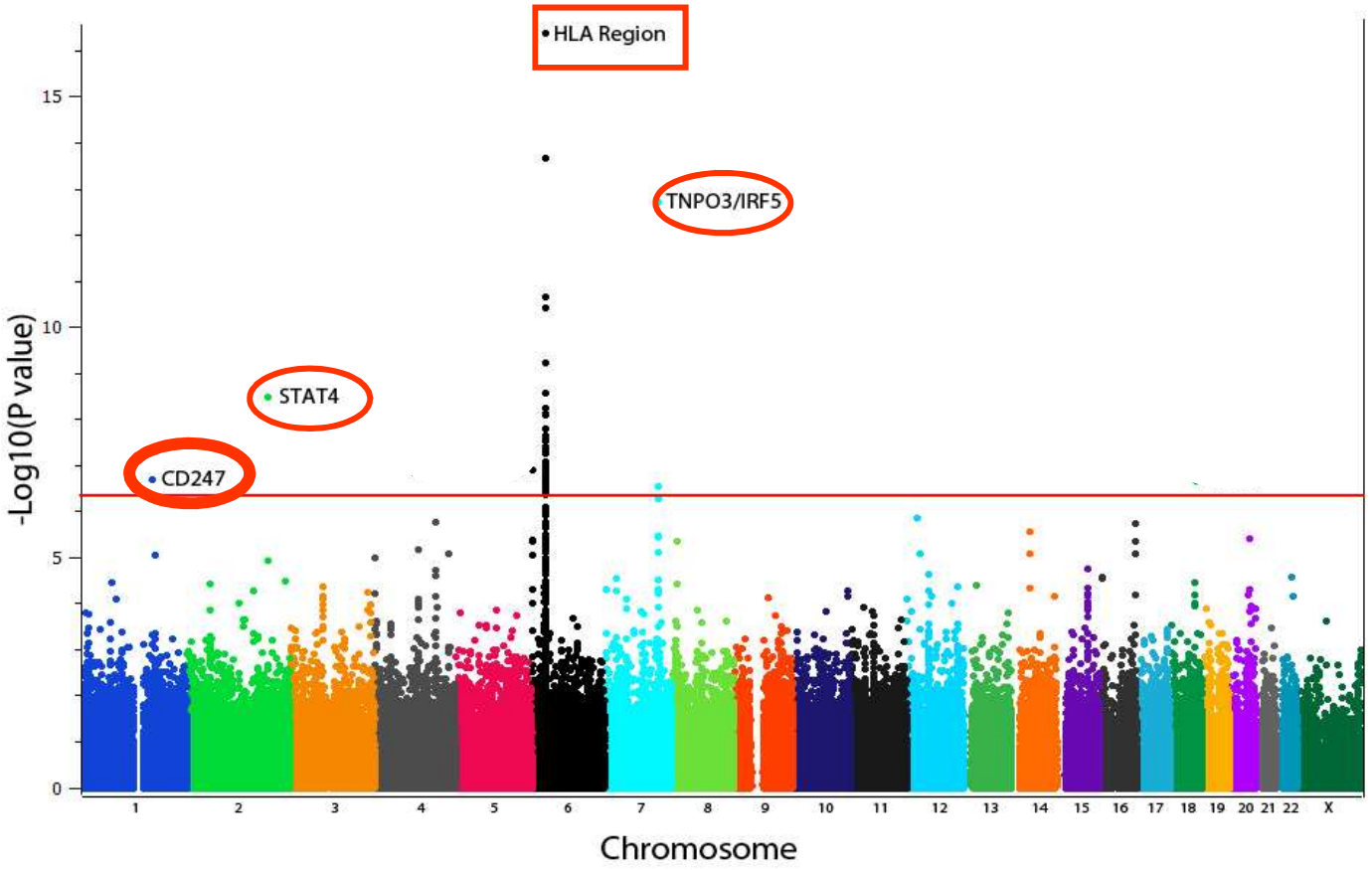
Replication phase

3,175 SSc patients
4,971 healthy controls
from **9** countries

Total

5,471 SSc patients
10,142 controls

GWAs in Systemic Sclerosis



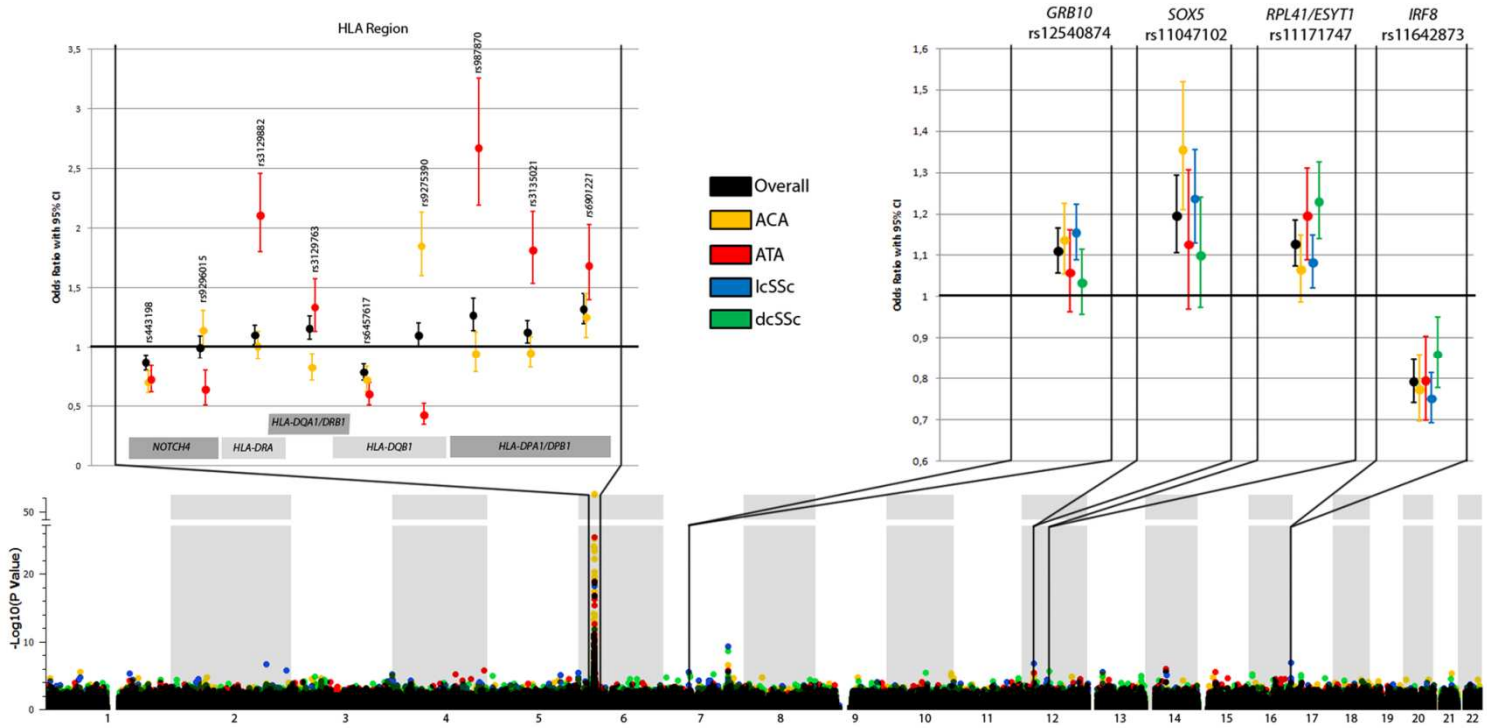
Radstake et al., Nat Genet, 2010

OPEN ACCESS Freely available online PLoS GENETICS

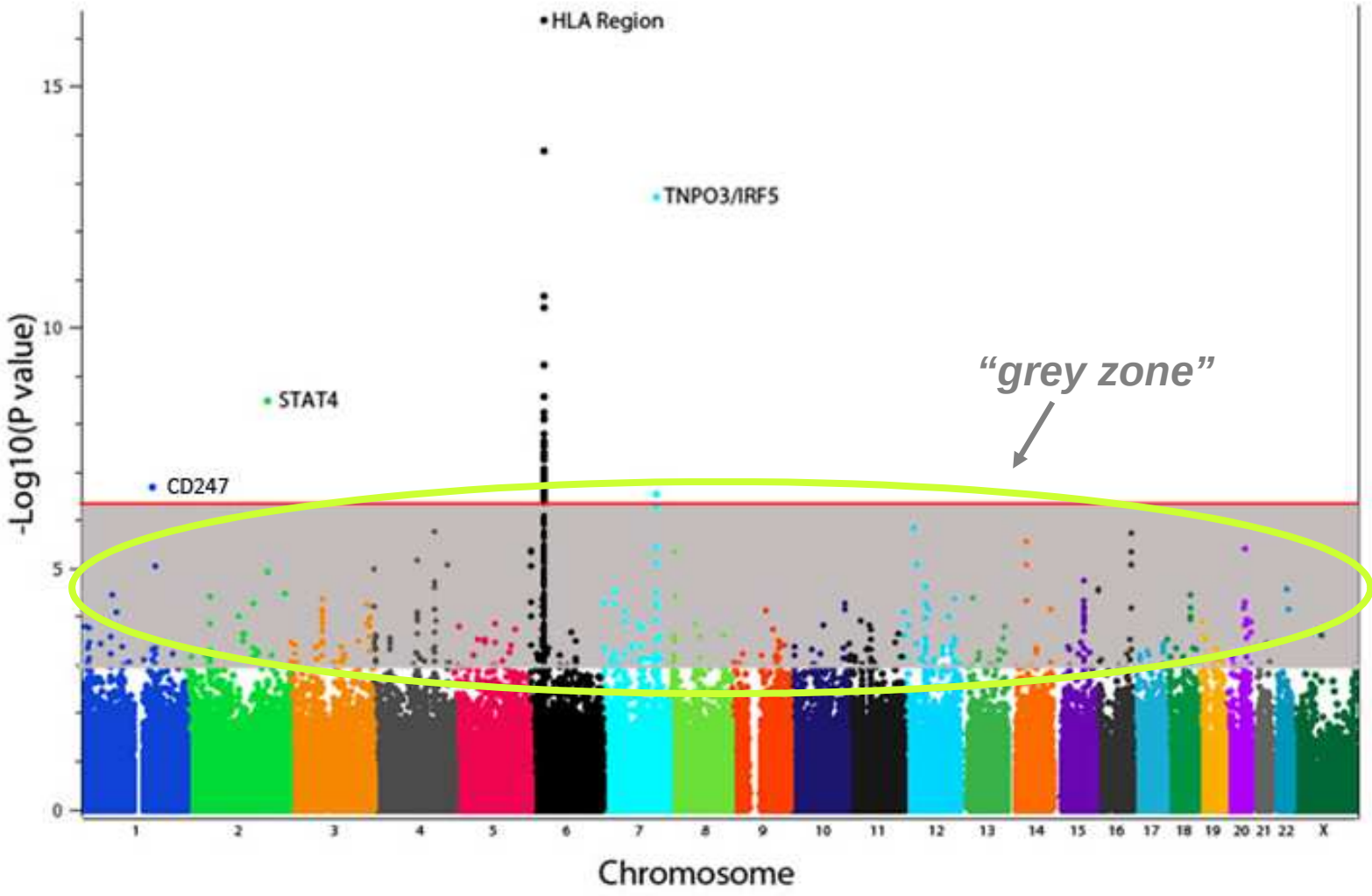
Identification of Novel Genetic Markers Associated with Clinical Phenotypes of Systemic Sclerosis through a Genome-Wide Association Strategy

Olga Gorlova[1☯*], Jose-Ezequiel Martin[2☯], Blanca Rueda[2☯], Bobby P. C. Koeleman[3☯], Jun Ying[1], Maria Teruel[2], Lina-Marcela Diaz-Gallo[2], Jasper C. Broen[4], Madelon C. Vonk[4], Carmen P. Simeon[5], Behrooz Z. Alizadeh[6], Marieke J. H. Coenen[7], Alexandre E. Voskuyl[8], Annemie J. Schuerwegh[9], Piet L. C. M. van Riel[4], Marie Vanthuyne[10], Ruben van 't Slot[3], Annet Italiaander[3], Roel A. Ophoff[3], Nicolas Hunzelmann[11], Vicente Fonollosa[5], Norberto Ortego-Centeno[12], Miguel A. González-Gay[13], Francisco J. García-Hernández[14], María F. González-Escribano[15], Paolo Airo[16], Jacob van Laar[17], Jane Worthington[18], Roger Hesselstrand[19], Vanessa Smith[20], Filip de Keyser[20], Fredric Houssiau[10], Meng May Chee[21], Rajan Madhok[21], Paul G. Shiels[22], Rene Westhovens[23], Alexander Kreuter[24], Elfride de Baere[25], Torsten Witte[26], Leonid Padyukov[27], Annika Nordin[27], Raffaella Scorza[28], Claudio Lunardi[29], Benedicte A. Lie[30], Anna-Maria Hoffmann-Vold[31], Øyvind Palm[31], Paloma García de la Peña[32], Patricia Carreira[33], Spanish Scleroderma Group[¤], John Varga[34], Monique Hinchcliff[34], Annette T. Lee[35], Pravitt Gourh[36], Christopher I. Amos[1], Frederick M. Wigley[37], Laura K. Hummers[38], J. Hummers[37], J. Lee Nelson[38], Gabriella Riemekasten[39], Ariane Herrick[18], Lorenzo Beretta[28], Carmen Fonseca[40], Christopher P. Denton[40], Peter K. Gregersen[35], Sandeep Agarwal[36], Shervin Assassi[36], Filemon K. Tan[36], Frank C. Arnett[36¶], Timothy R. D. J. Radstake[4¶], Maureen D. Mayes[36¶], Javier Martin[2¶*]

July 2011 | Volume 7 | Issue 7 | e1002178



Follow-up GWA studies



Radstake et al., Nat Genet, 2010

Human Molecular Genetics, 2012, Vol. 21, No. 12 **2825–2835**
doi:10.1093/hmg/dds099
Advance Access published on March 9, 2012

Identification of *CSK* as a systemic sclerosis genetic risk factor through Genome Wide Association Study follow-up

Jose-Ezequiel Martin[1,*], Jasper C. Broen[2], F. David Carmona[1], Maria Teruel[1], Carmen P. Simeon[3], Madelon C. Vonk[2], Ruben van 't Slot[4], Luis Rodriguez-Rodriguez[5], Esther Vicente[6], Vicente Fonollosa[3], Norberto Ortego-Centeno[7], Miguel A. González-Gay[8], Francisco J. García-Hernández[9], Paloma García de la Peña[10], Patricia Carreira[11], Spanish Scleroderma Group[†], Alexandre E. Voskuyl[12], Annemie J. Schuerwegh[13], Piet L.C.M. van Riel[2], Alexander Kreuter[14], Torsten Witte[15], Gabriella Riemekasten[16], Paolo Airo[17], Raffaella Scorza[18], Claudio Lunardi[19], Nicolas Hunzelmann[20], Jörg H.W. Distler[21], Lorenzo Beretta[18], Jacob van Laar[22], Meng May Chee[23], Jane Worthington[24], Ariane Herrick[24], Christopher Denton[25], Filemon K. Tan[26], Frank C. Arnett[26], Shervin Assassi[26], Carmen Fonseca[25], Maureen D. Mayes[26], Timothy R.D.J. Radstake[2,‡], Bobby P.C. Koeleman[4,‡] and Javier Martin[1,‡]

Immunochip in Scleroderma

ARTICLE

Immunochip Analysis Identifies Multiple Susceptibility Loci for Systemic Sclerosis

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The American Journal of Human Genetics *94*, 47–61, January 2, 2014

The study cohorts

- DISCOVERY: **1,833 SSc / 3,466 controls**


- VALIDATION: **4,017 SSc / 5,935 controls**

North America  

Europe       

- **TOTAL**: **5,850 SSc**

9,401 Controls

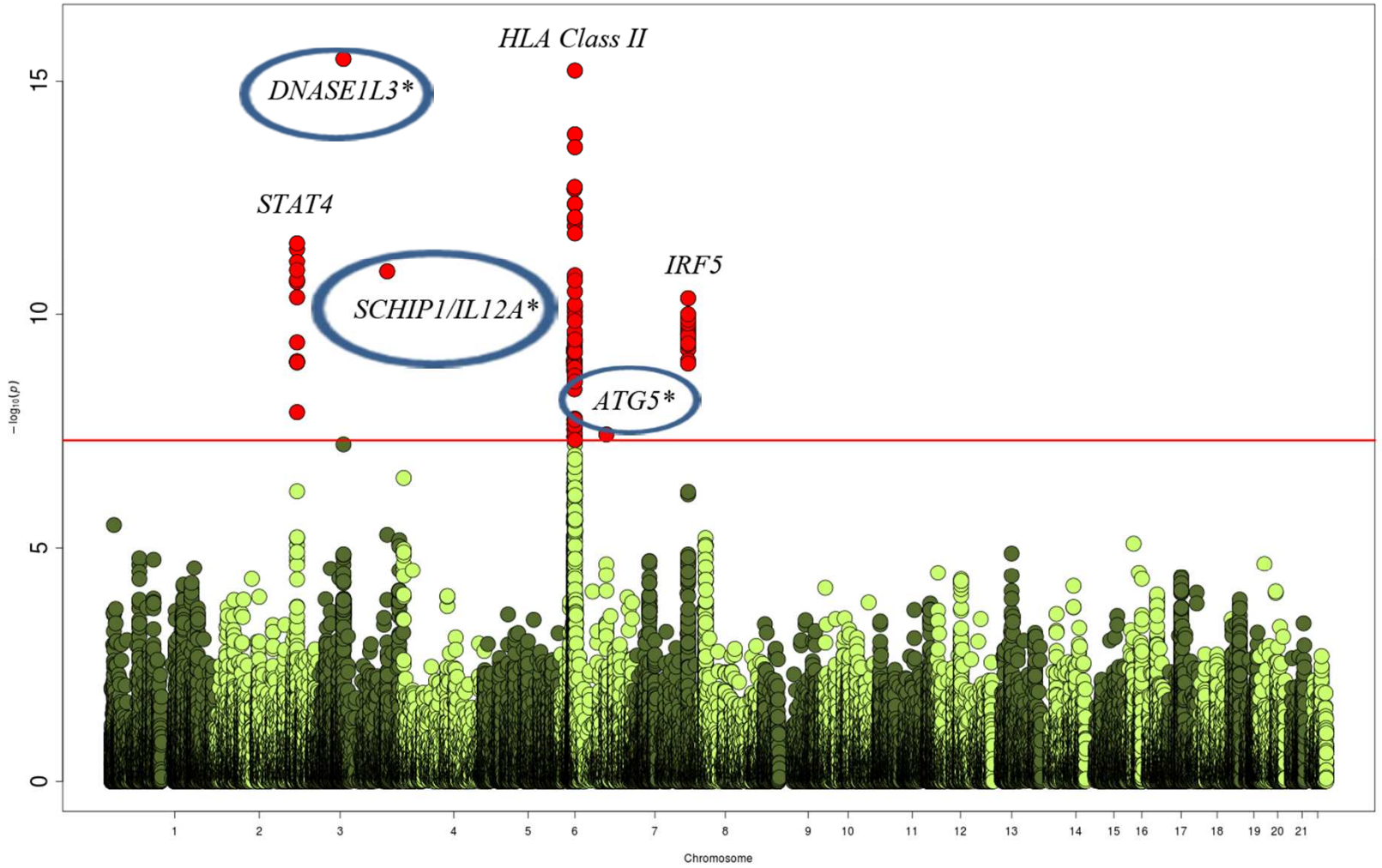
The study cohorts

Número
Calidad
Distribución geográfica
Características: sexo, edad
Ético-Legal

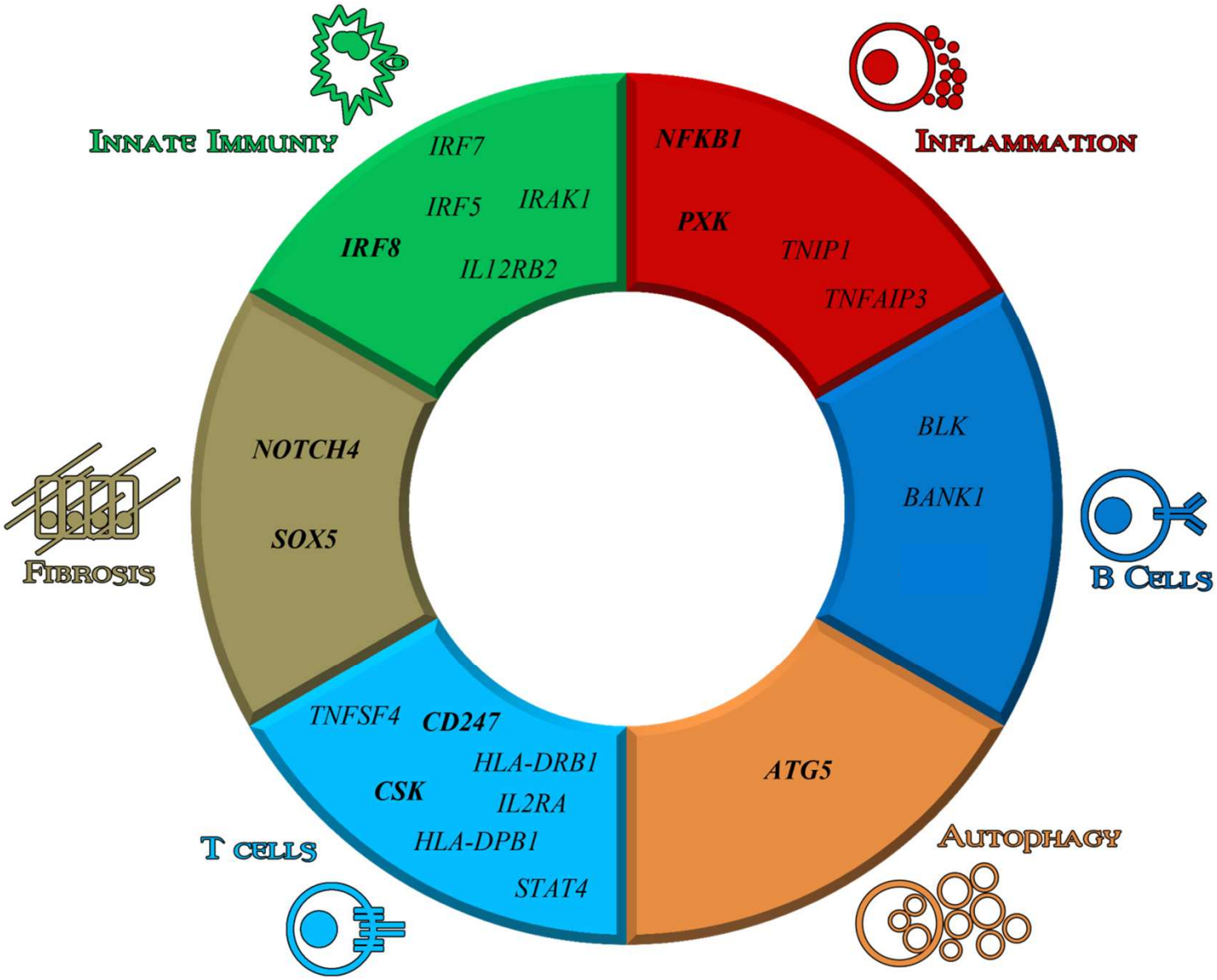
The study cohorts

Combined Discovery & Validation Sets ANALYSIS

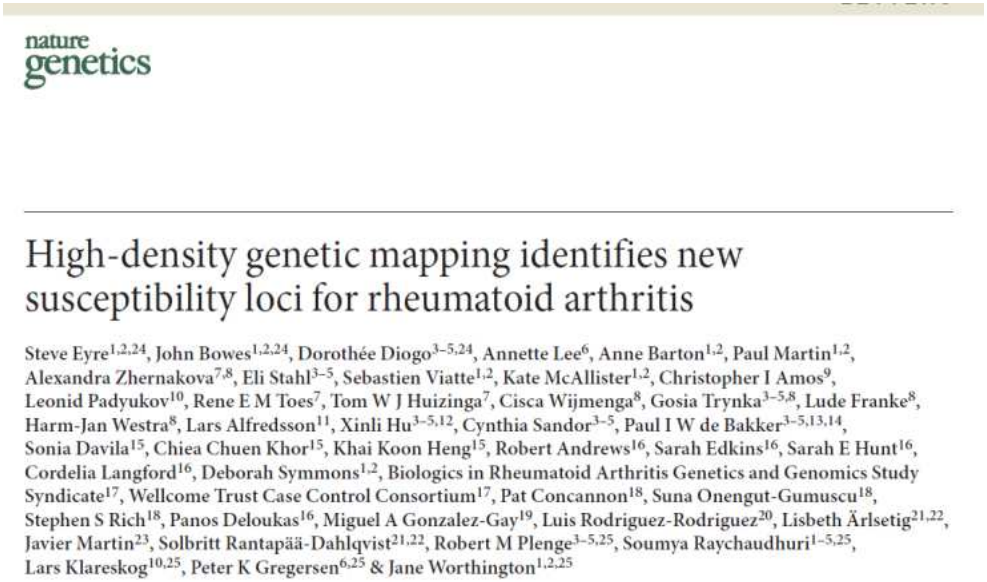
- Variants showing **a genome-wide level of significant association ($p < 5x\ 10^{-8}$)** were considered as **confirmed.**



Pathways of SSc associated genes



Gene discovery in Rheumatoid Arthritis



nature genetics

High-density genetic mapping identifies new susceptibility loci for rheumatoid arthritis

Steve Eyre[1,2,24], John Bowes[1,2,24], Dorothée Diogo[3–5,24], Annette Lee[6], Anne Barton[1,2], Paul Martin[1,2], Alexandra Zhernakova[7,8], Eli Stahl[3–5], Sebastien Viatte[1,2], Kate McAllister[1,2], Christopher I Amos[9], Leonid Padyukov[10], Rene E M Toes[7], Tom W J Huizinga[7], Cisca Wijmenga[8], Gosia Trynka[3–5,8], Lude Franke[8], Harm-Jan Westra[8], Lars Alfredsson[11], Xinli Hu[3–5,12], Cynthia Sandor[3–5], Paul I W de Bakker[3–5,13,14], Sonia Davila[15], Chiea Chuen Khor[15], Khai Koon Heng[15], Robert Andrews[16], Sarah Edkins[16], Sarah E Hunt[16], Cordelia Langford[16], Deborah Symmons[1,2], Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate[17], Wellcome Trust Case Control Consortium[17], Pat Concannon[18], Suna Onengut-Gumuscu[18], Stephen S Rich[18], Panos Deloukas[16], Miguel A Gonzalez-Gay[19], Luis Rodriguez-Rodriguez[20], Lisbeth Ärlsetig[21,22], Javier Martin[23], Solbritt Rantapää-Dahlqvist[21,22], Robert M Plenge[3–5,25], Soumya Raychaudhuri[1–5,25], Lars Klareskog[10,25], Peter K Gregersen[6,25] & Jane Worthington[1,2,25]

1978	2004	2007	2008	2009	2010	2012
HLA-DRB1	*PTPN22*	*TNFAIP3* *STAT4* *TRAF1* *IL2 / IL21*	*CD40* *CCL21* *TNFRSF14* *IL2RB* *CTLA4* *PRKCQ* *KIF5A* *IL2RA* *AFF3*	*REL* *BLK* *TAGAP* *CD28* *TRAF6* *PTPRC* *FCGR2A* *PRDM1* *CD2-CD58*	*ANKRD55* *SPRED2* *C5orf30* *RBPJ* *CCR6* *IRF5* *PXK*	*TYK2* *IRAK1* *TLE* *RASGRP* *1* *PADI4* *IL6R* *IRF8* *ARID5B* *RUNX1* *IKZF3* *POU3F1* *RCAN1* *CD5* *GATA3* *PTPN2* *BACH2* *RAD51L1*

Genome wide association studies, replication studies and meta-analyses have been used to identify over **46 RA susceptibility loci** at genome-wide significance ($p<5x10^{-8}$).

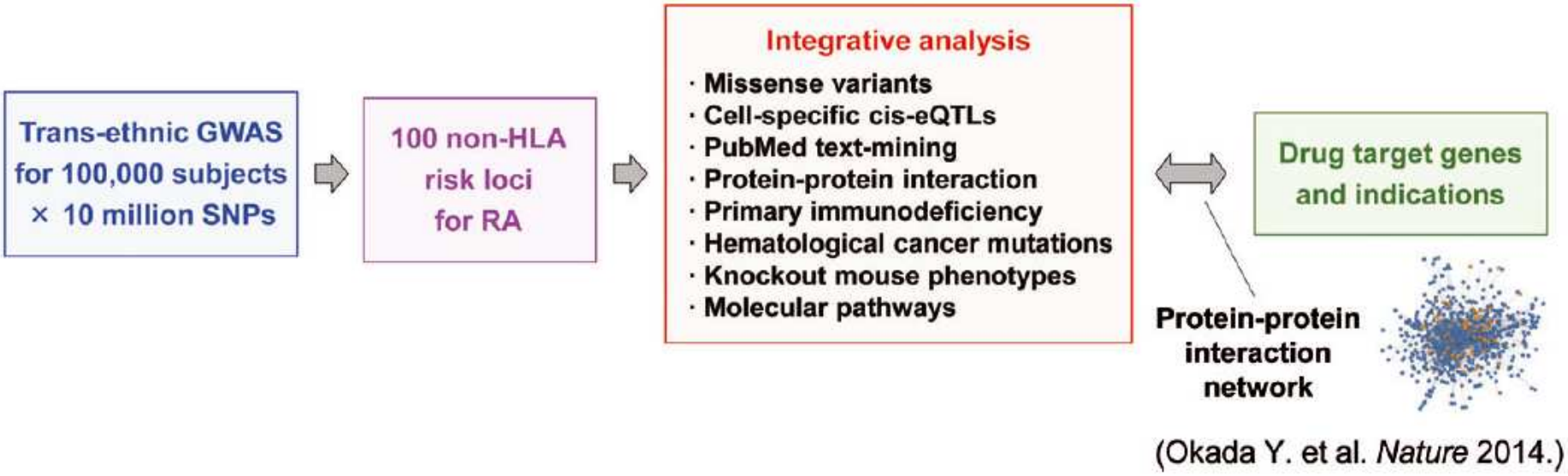
LETTER 376 | NATURE | VOL 506 | 20 FEBRUARY 2014

doi:10.1038/nature12873

Genetics of rheumatoid arthritis contributes to biology and drug discovery

A genome-wide association study meta-analysis in a total of 100,000 subjects of European and Asian ancestries (29,880 RA cases and 73,758 controls), by evaluating 10 million single-nucleotide polymorphisms. We discovered 42 novel RA risk loci at a genome-wide level of significance, bringing the total to **101 genes.**

Genetics of rheumatoid arthritis contributes to biology and drug discovery

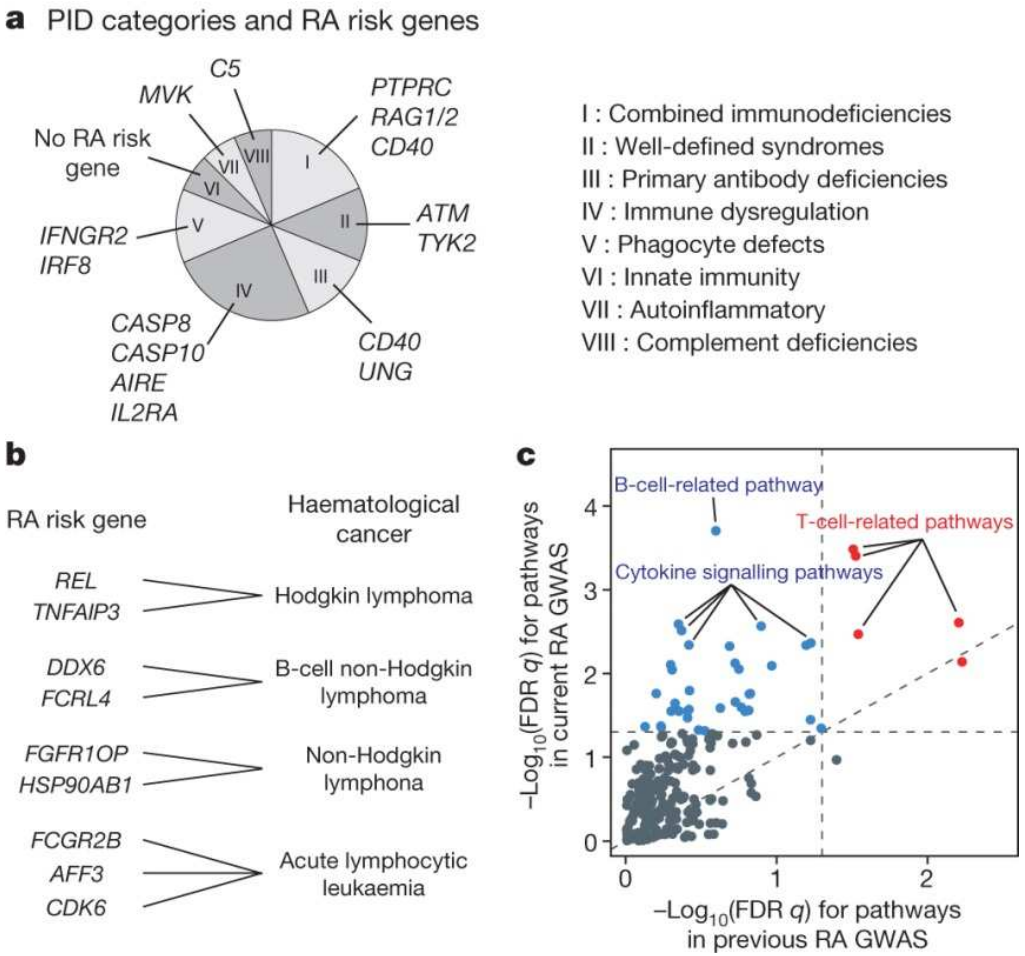


(Okada Y. et al. *Nature* 2014.)

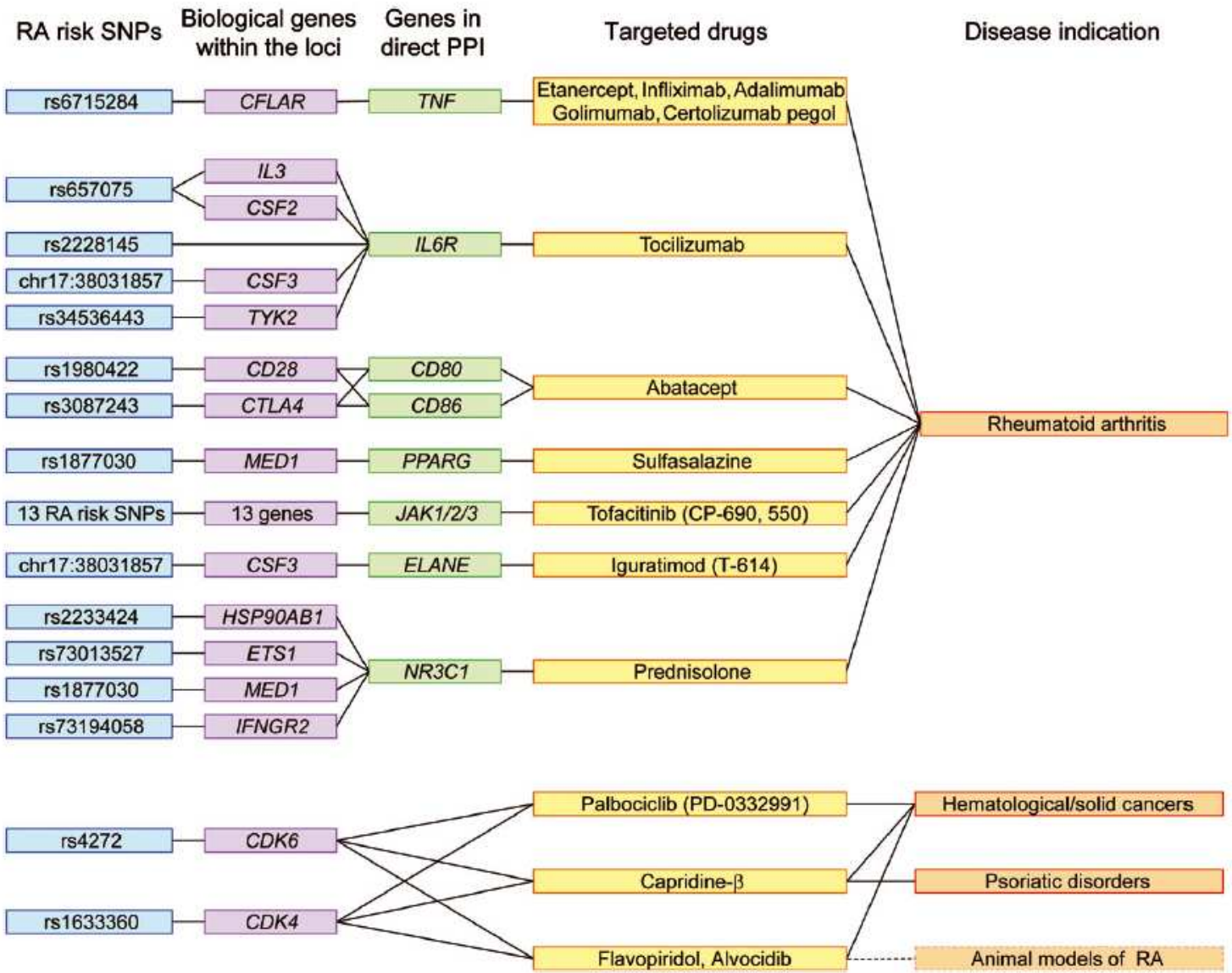
Okada Y, Clin Genet, 2014

Genetics of rheumatoid arthritis contributes to biology and drug discovery

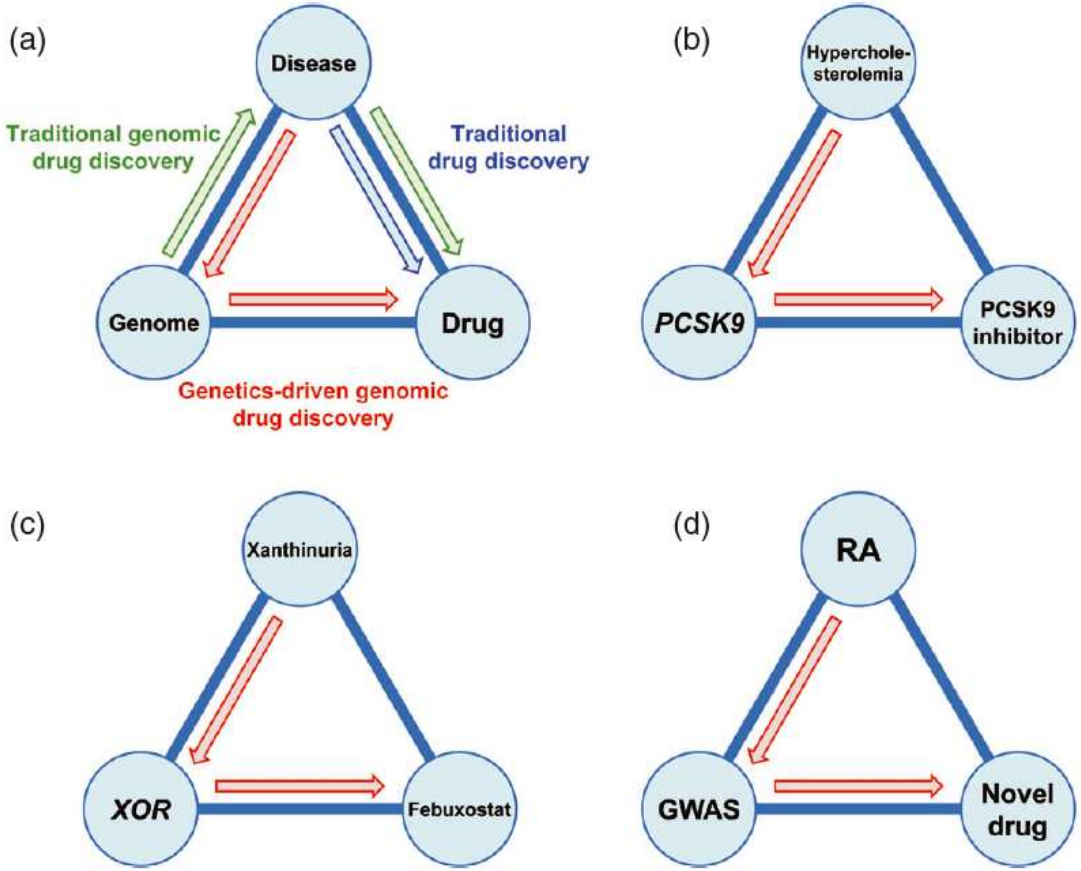
Overlap of RA risk loci with PID genes, haematological cancer somatic mutations and molecular pathways.



Connection of biological RA risk genes to drug targets.

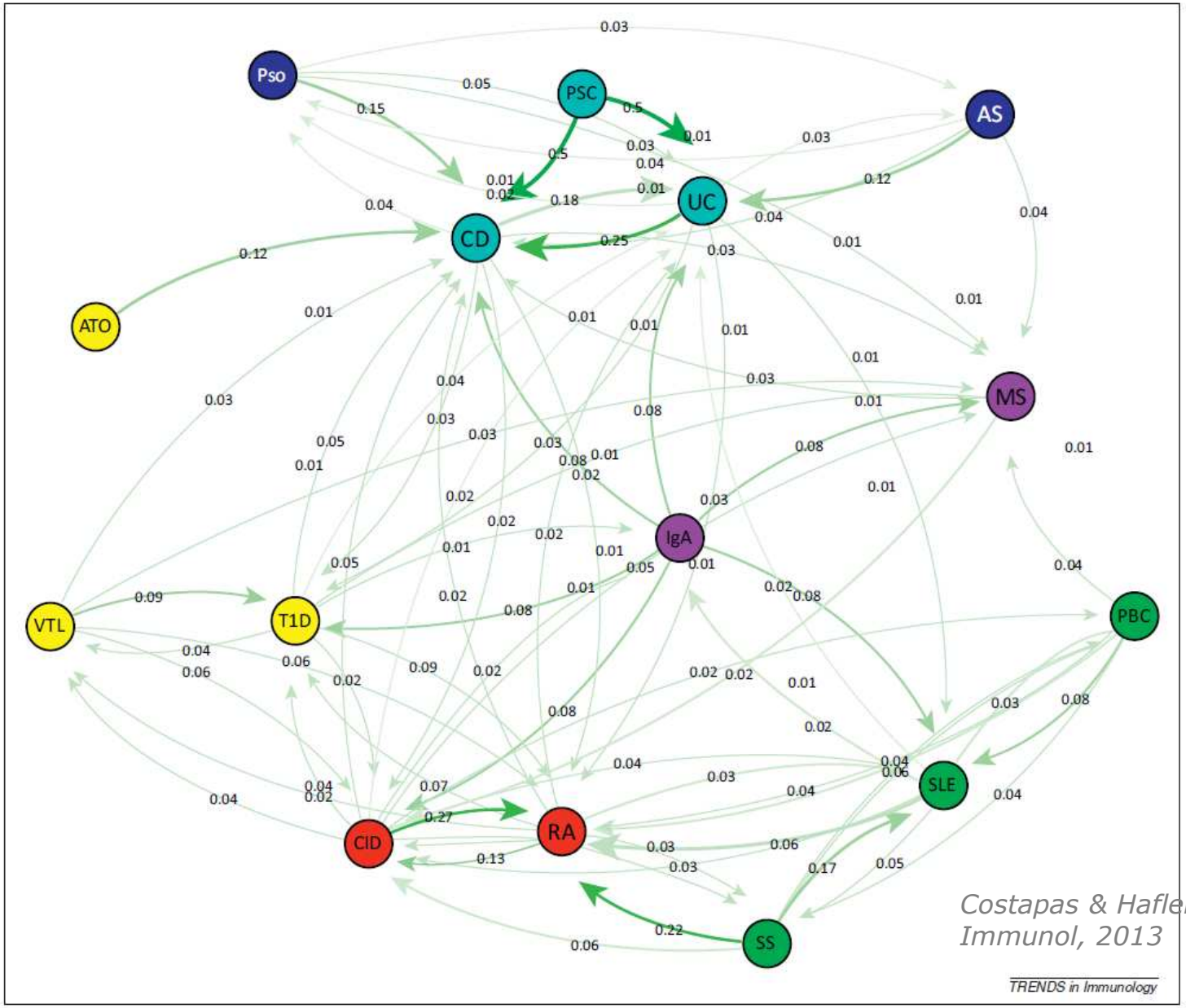


A new model of genomic drug discovery



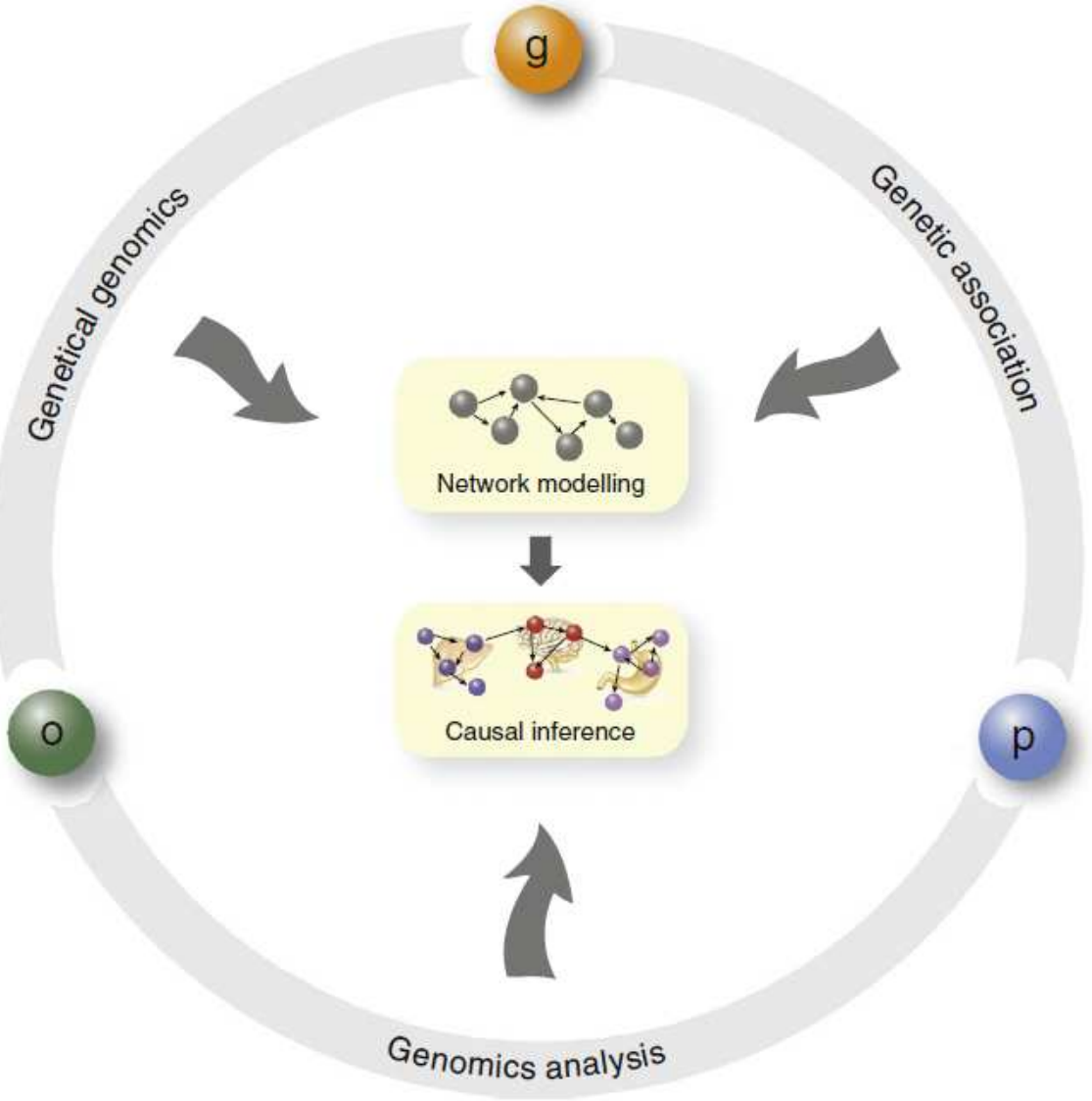
Okada Y, Clin Genet, 2014

Shared genetic in Autoimmunity



Costapas & Hafler, Trend Immunol, 2013

System Genetics: From GWAS to disease pathways



Van der Sijde MR, Ng A, Fu J; BBA, 2014

Genomic Medicine

TRANSLATIONAL GENETICS

Bringing genome-wide association findings into clinical use

Teri A. Manolio

NATURE REVIEWS | GENETICS VOLUME 14 | AUGUST 2013 | 549

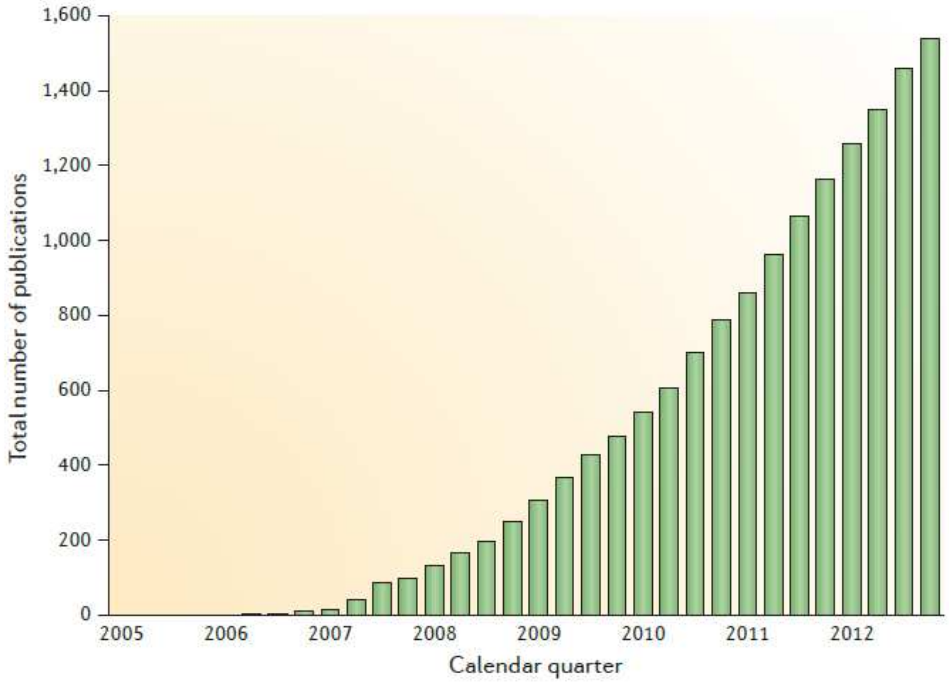


Figure 1 | **Pace of genome-wide association study publications since 2005.** The pace of genome-wide association study (GWAS) publications has increased dramatically over 7 years and shows no signs of slowing. The figure is based on data from the US National Human Genome Research Institute Catalog of Published Genome-Wide Association Studies.

Genomic Medicine

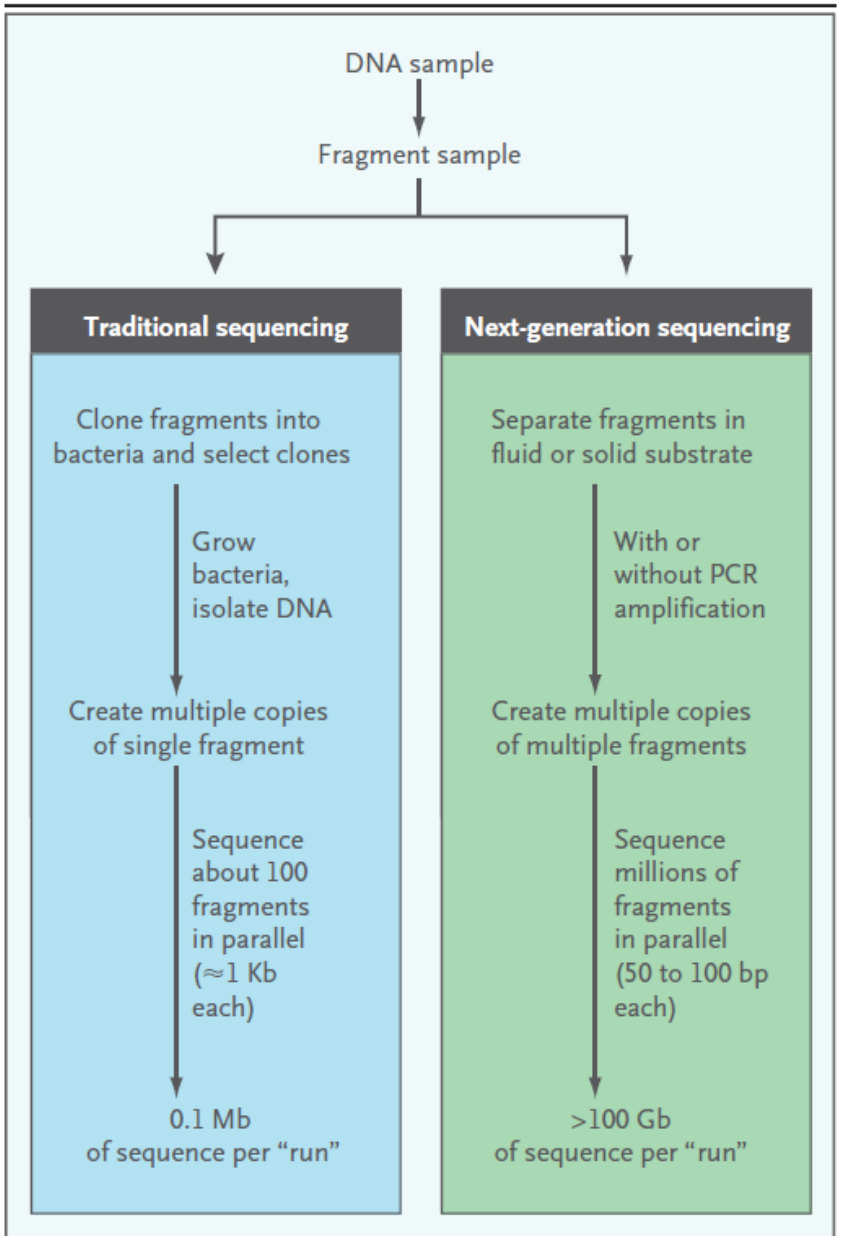
Table 1 | **Characteristics of GWAS findings that make them readily translatable to clinical care**

Application	Key characteristics	Example
Risk prediction	Heritability is high	T1DM loci
	Large proportion of heritability is explained	
	Genotyping can be targeted to high-risk group (such as that defined by positive family history)	
	Genotyping scores substantially increase predictive value	
	Early detection is important	
	Preventive strategies are available	
Disease subtyping or classification	Clinical syndrome has multiple subtypes with varying prognosis or response to treatment aetiologies	*CRP* (or *HNF1A* typing) for MODY
	Subtypes are not readily discernible by clinical examination	
	Compared to other indicators, assay of biomarker (genetic or non-genetic) is easier, cheaper, more available, more reliable and more sensitive	
	Subtyping affects treatment selection	
	Subtyping identifies increased risk in family members	
Drug development	Loss of function variants have a useful biological effect	*ITPA* variants and ribavirin toxicity
Drug toxicity	Variants are common	*SLCO1B1* variants and statins
	Effect sizes are large	
	Alternative drugs or increased monitoring are available	

CRP, C-reactive protein; GWAS, genome-wide association study; *HNF1A*, HNF1 homeobox A; *ITPA*, inosine triphosphatase; MODY, maturity-onset diabetes of the young; *SLCO1B1*, solute carrier organic anion transporter family member 1B1; T1DM, type 1 diabetes mellitus.

Manolio T, Nat Rev Genet, 2013

Next Generation Sequencing



W. Gregory Feero, M.D., Ph.D., Alan E. Guttmacher, M.D., and Francis S. Collins, M.D., Ph.D.

N ENGL J MED 362;21 NEJM.ORG MAY 27, 2010

Genomic Medicine

Review

Cell PRESS

How next-generation sequencing is transforming complex disease genetics

Helena Kilpinen[1,2] and Jeffrey C. Barrett[3]

[1] Department of Genetic Medicine and Development, University of Geneva Medical School, Geneva 1211, Switzerland
[2] Swiss Institute of Bioinformatics, Geneva 1211, Switzerland
[3] Human Genetics Department, Wellcome Trust Sanger Institute, Hinxton, CB10 1HH, UK

Trends in Genetics January 2013, Vol. 29, No. 1

Table 1. Relative computational resources required for processing and storing GWAS or NGS data for 800 'Phase I' samples in the 1000 Genomes Project

	Analysis data storage (Gb)	Raw data storage (Gb)	Processing time (CPU-days)
GWAS	50	4	715
NGS	50	50 000	20 000

Genomic Medicine

How next-generation sequencing is transforming complex disease genetics

Helena Kilpinen[1,2] **and Jeffrey C. Barrett**[3]

[1] Department of Genetic Medicine and Development, University of Geneva Medical School, Geneva 1211, Switzerland
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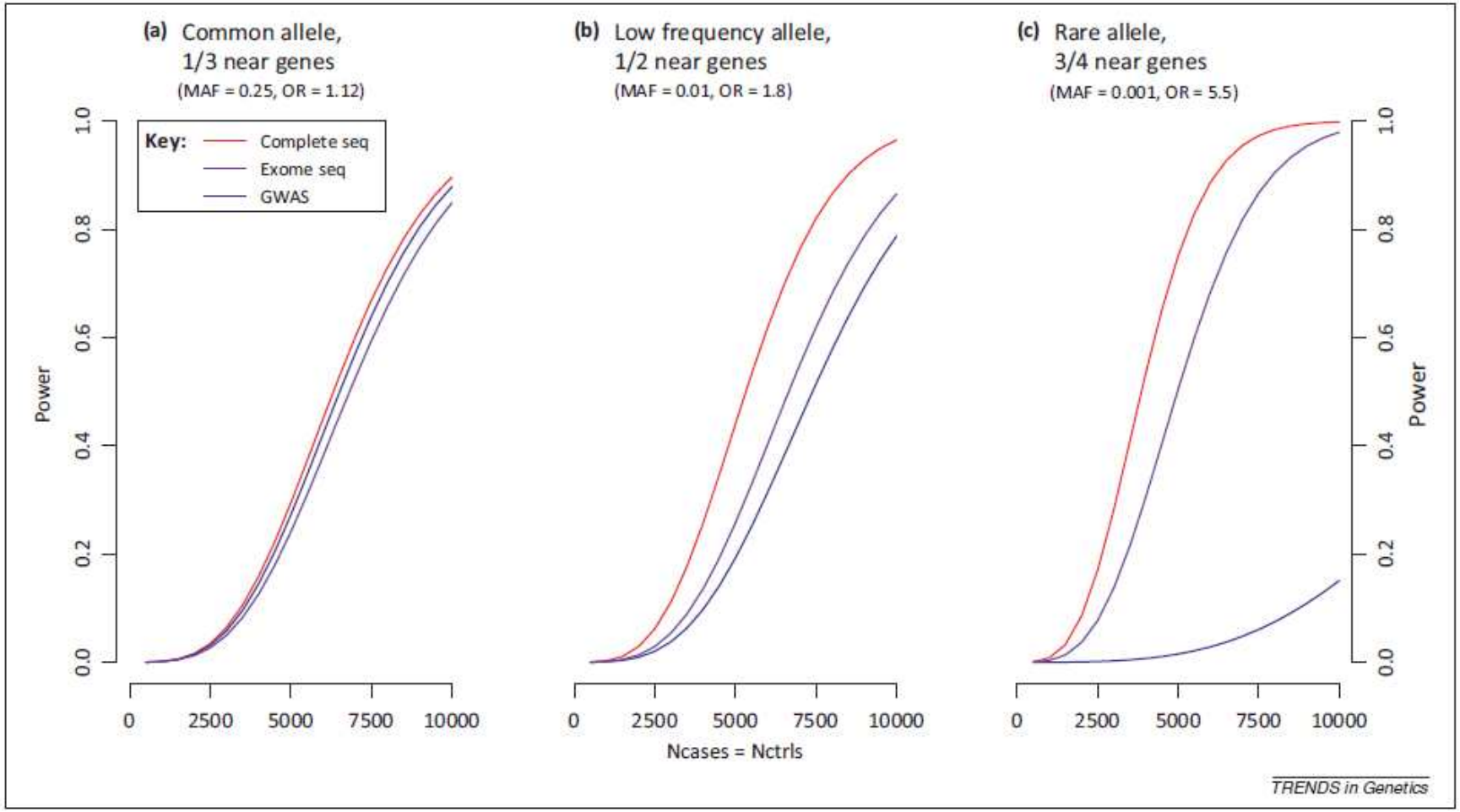
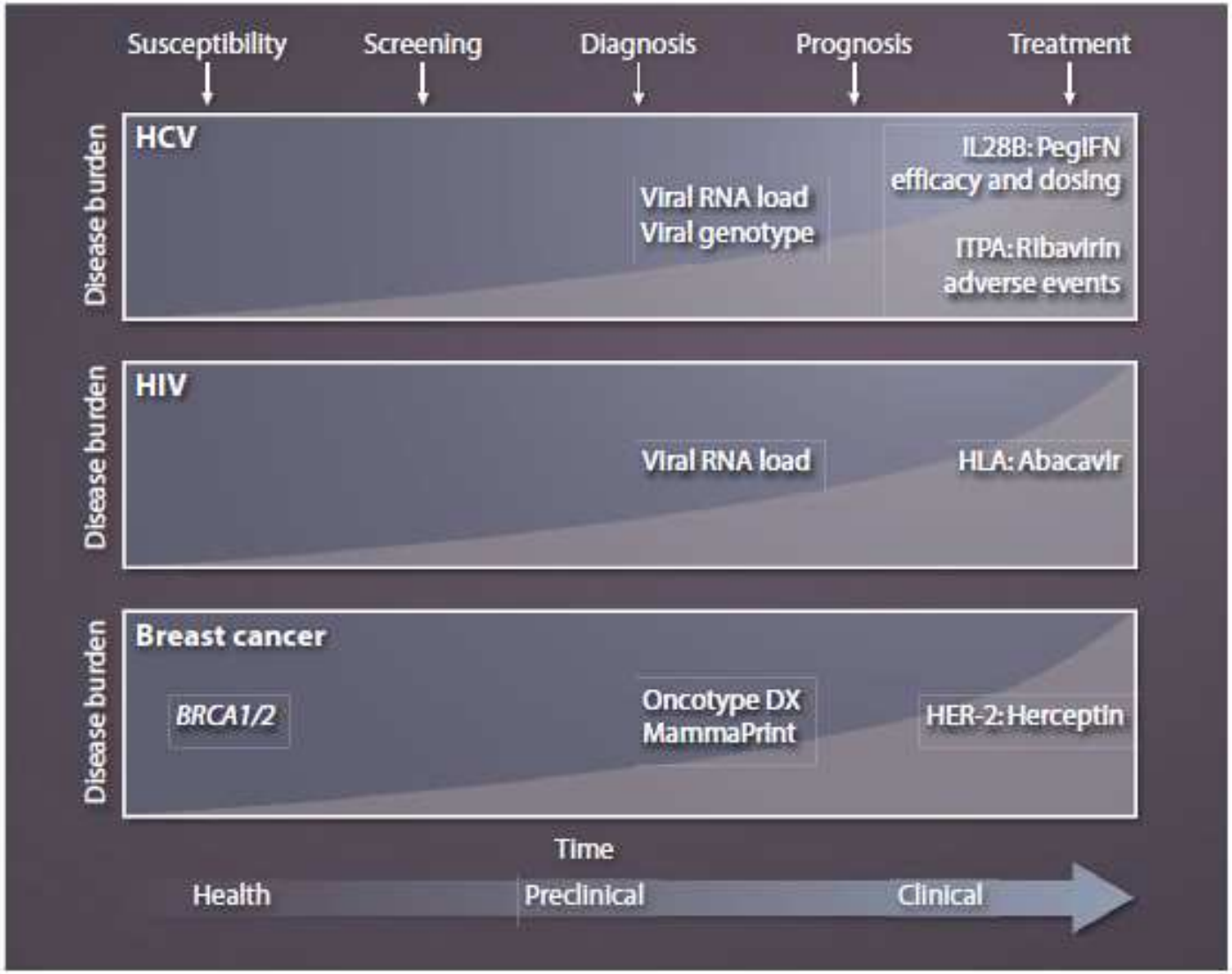
Trends in Genetics January 2013, Vol. 29, No. 1

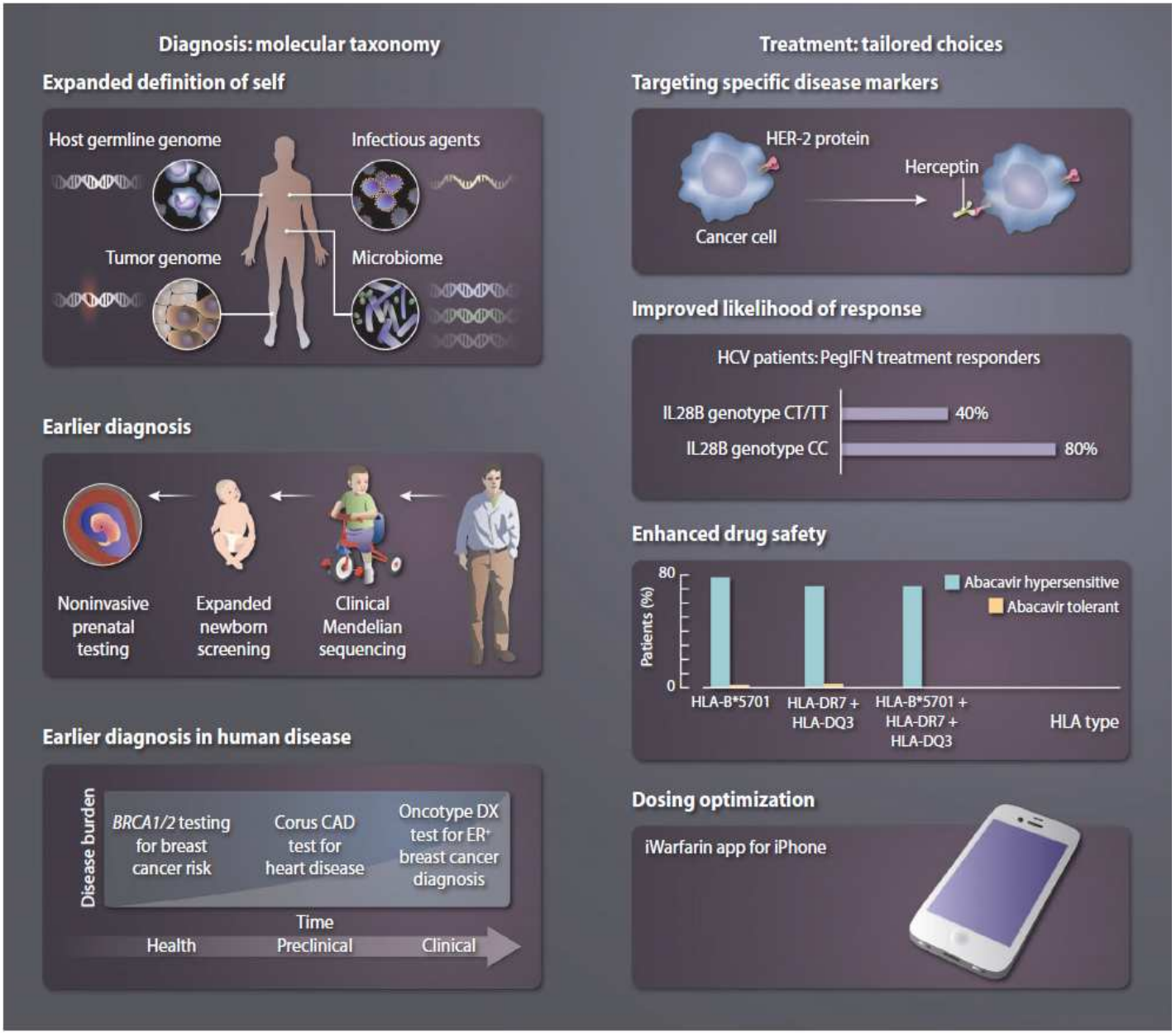


Genomic Medicine



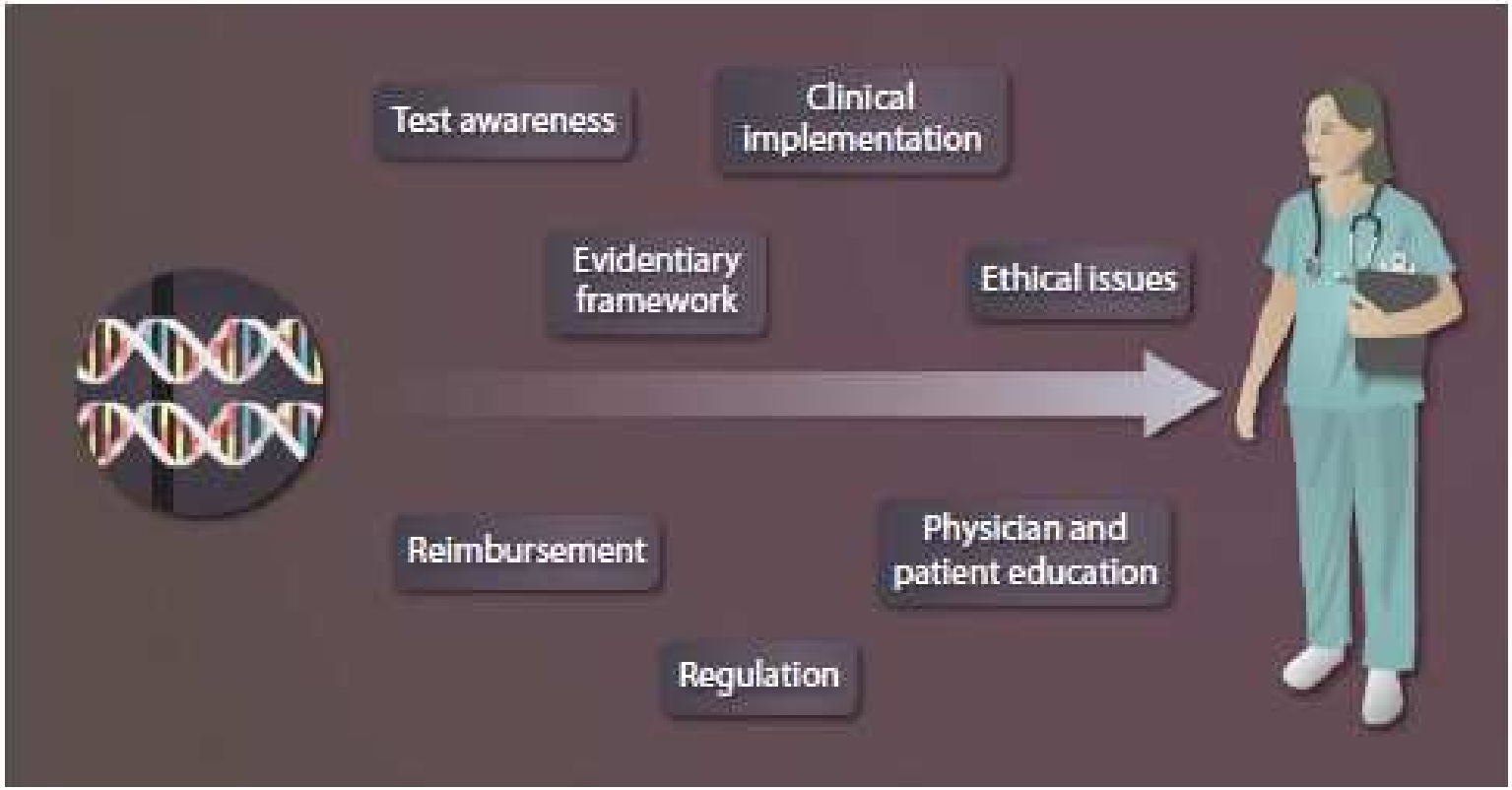
MacCarthy JJ, McLeod HL, Ginsburg GS, ScienceTrasnlationalMedicine, 2013

Genomic Medicine



MacCarthy JJ, McLeod HL, Ginsburg GS, ScienceTrasnlationalMedicine, 2013

Genomic Medicine



MacCarthy JJ, McLeod HL, Ginsburg GS, ScienceTrasnlationalMedicine, 2013

From Gen to Function

Leading Edge
Previews

Cell

FOXO in the Hole: Leveraging GWAS for Outcome and Function

Peter K. Gregersen[1,*] and Nataly Manjarrez-Orduño[1]
[1]The Robert S. Boas Center for Genomics and Human Genetics, The Feinstein Institute for Medical Research, 350 Community Drive, Manhasset, NY 11030, USA

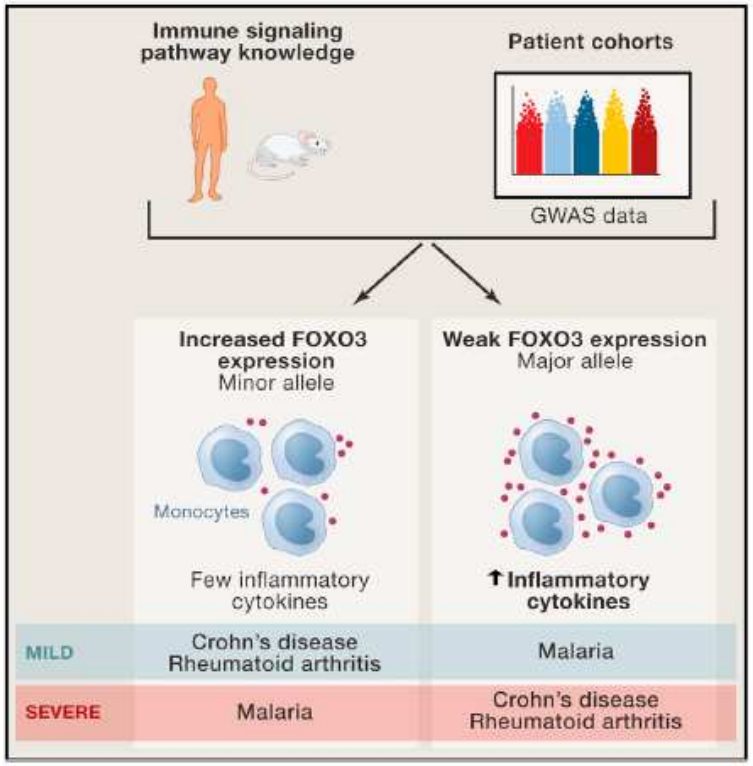


Figure 1. The Identification of FOXO3 as a Marker of Disease Outcomes

Cell *155*, September 26, 2013

It is important to emphasize that all of these functional studies were carried out in human cells by taking advantage of the Cambridge Bioresource. This is an invaluable collection of healthy volunteers who can be recalled for functional studies on the basis of their genotype, and this resource supported some of the first functional studies of GWAS associations in autoimmunity (Dendrou et al., 2009). Without this population resource, a convincing connection between FOXO3 genotype and phenotype would be difficult to establish, because studies of Crohn's patients would be confounded by disease activity and therapy, and

functional studies in cell lines may not reflect the situation in native cells.

From Bio-Bank to Data-Bank

Vast stores of DNA samples and data have been produced by the increasing pace of genetic sequencing.

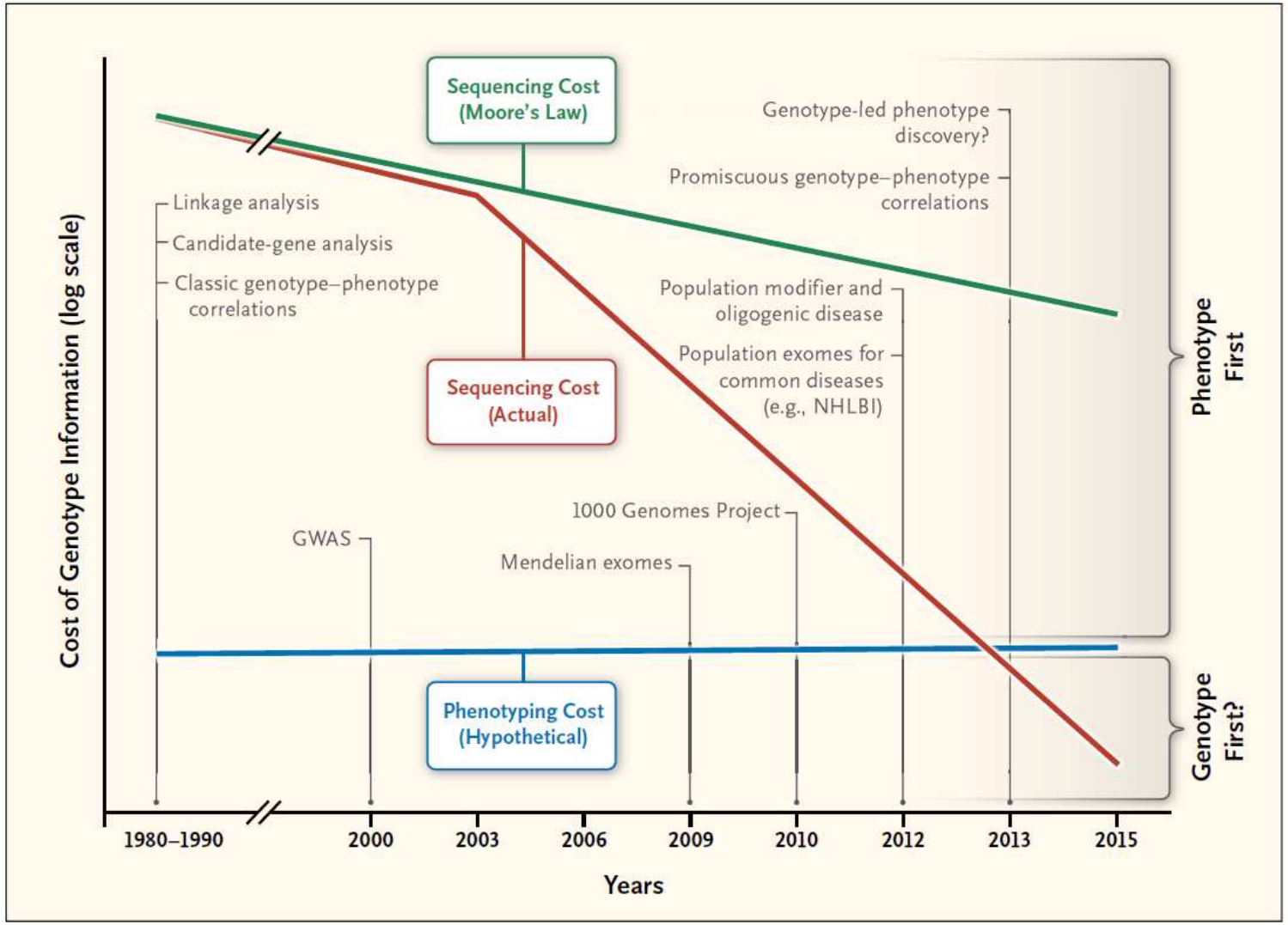
GENOMICS

Giant gene banks take on disease

Researchers bring together troves of DNA sequences in the hope of teasing out links between traits and genetic variants.


obrigado
Dank U
Merci
mahalo
Köszi
спасибо
Grazie
Thank you
mauruuru
Takk
Gracias
Dziękuję
Děkuju
danke
Kiitos

Genotype-Phenotype Correlation



The Decreasing Cost of Genotype Information.

Lu JT, Campeu PM, Lee BH; NEJM, 2104