AIBT Associazione Italiana di Immunogenetica e Biologia dei Trapianti
XXX Congresso Nazionale
Napoli, 10/12 ottobre 2024
"The programme of this event has been approved by the EFI Education Committee"

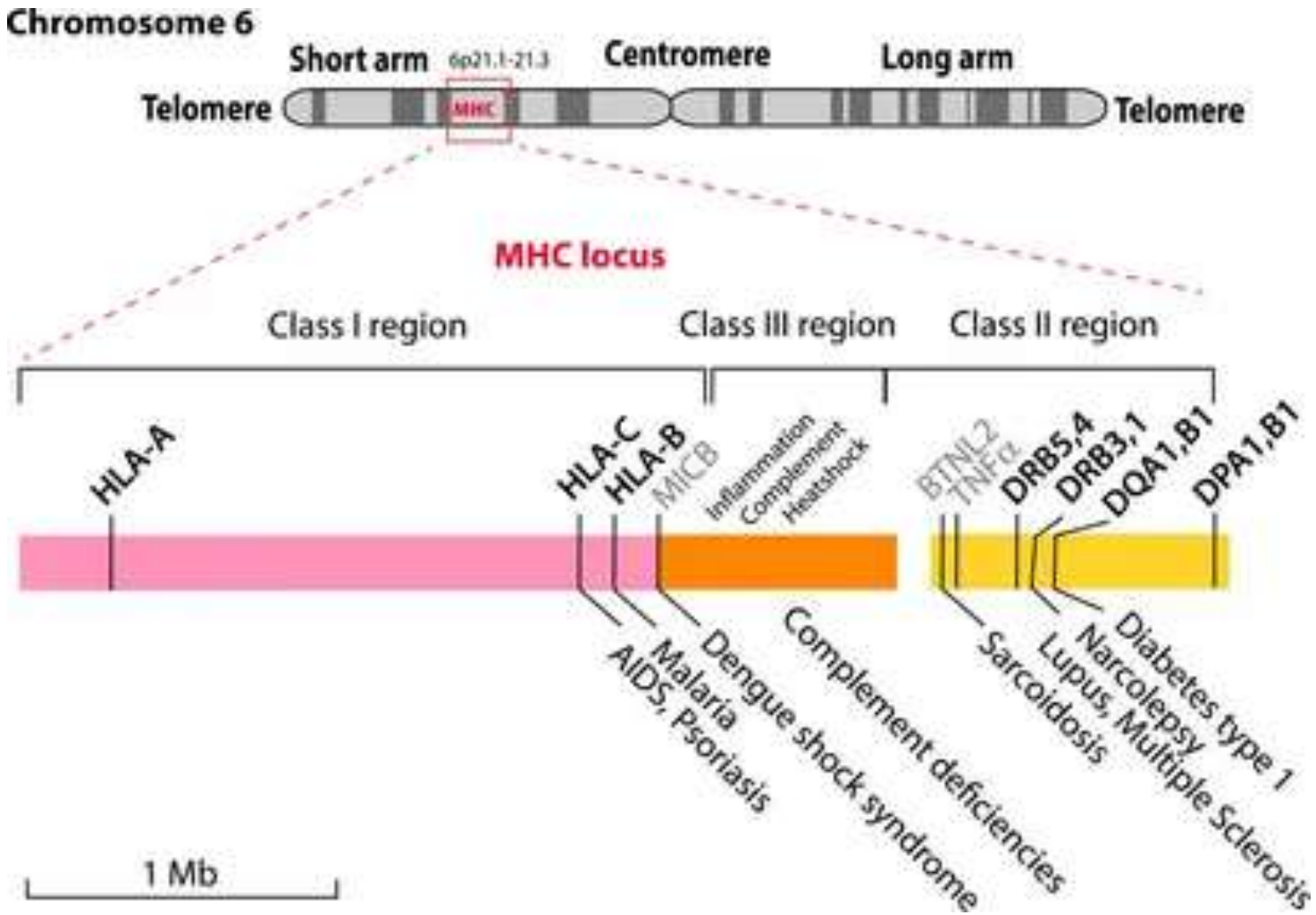
IGB

Dr. Giovanna Del Pozzo

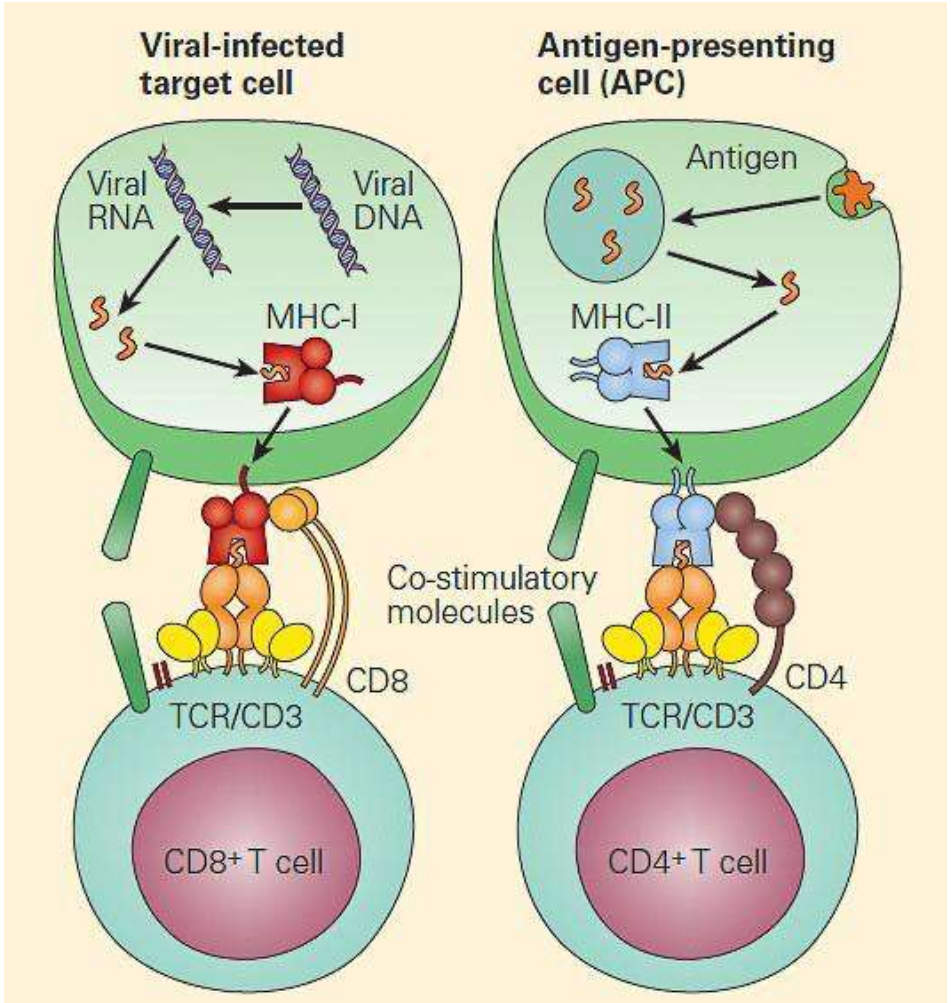
National Research Council of Italy

Istituto di Genetica e Biofisica , CNR , Napoli

L'espressione dei geni HLA nell'autoimmunità e nel trapianto

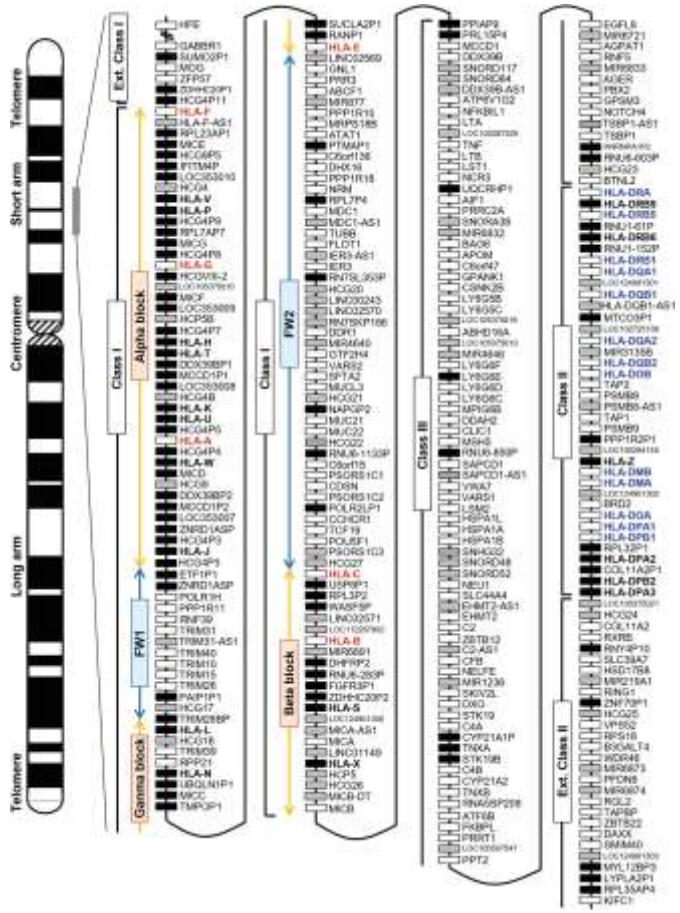


doi: 10.3389/fbinf.2024.1392613


Viral-infected target cell
Antigen-presenting cell (APC)
Viral RNA
Viral DNA
MHC-I
Antigen
MHC-II
Co-stimulatory molecules
CD8
CD4
TCR/CD3
TCR/CD3
CD8+ T cell
CD4+ T cell

Elevato Polimorfismo
Alta densità genica
Linkage disequilibrium

Malattie autoimmuni **Infezioni** **Trapianti**

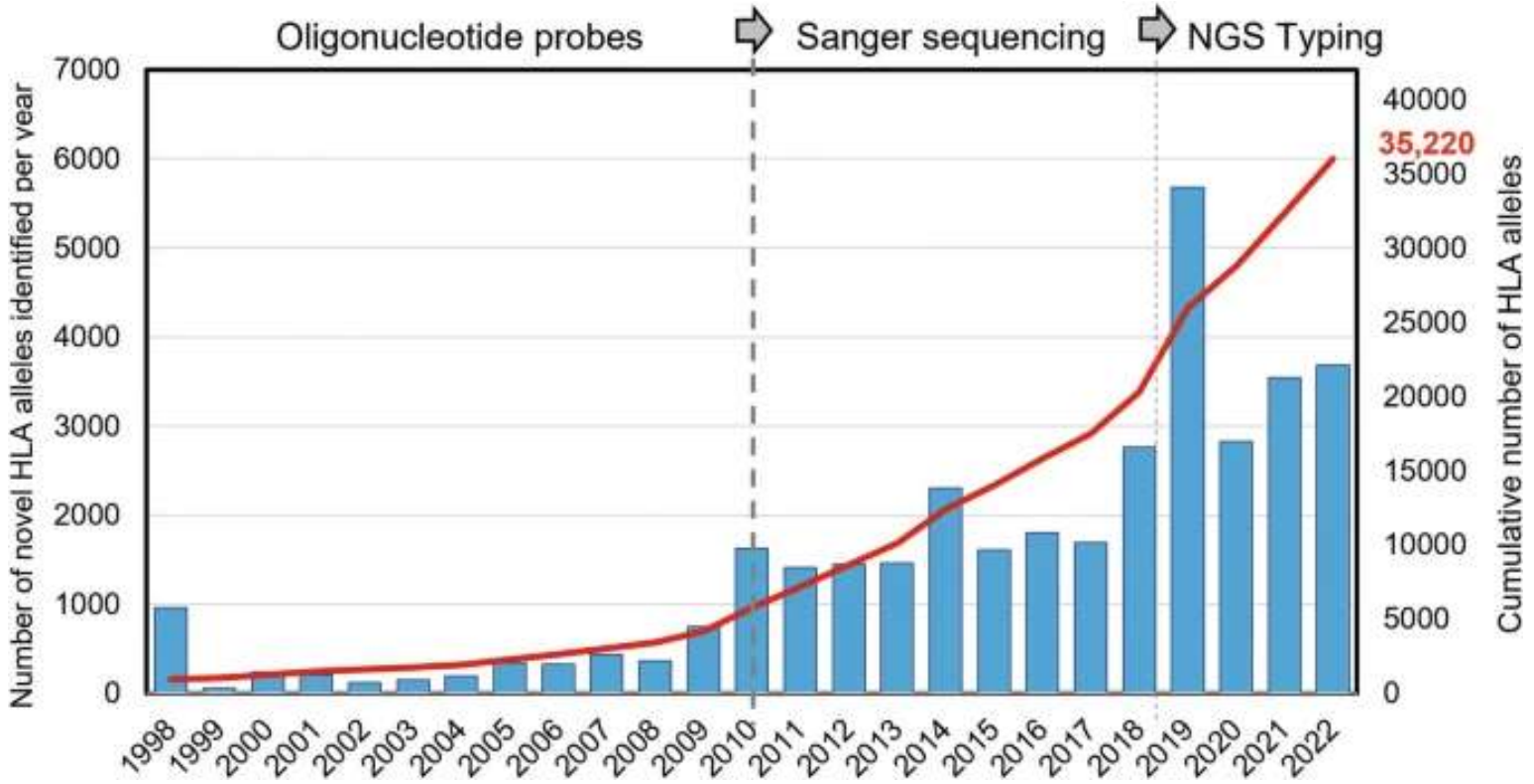


283 loci
144 protein-coding genes
58 ncRNA
81 pseudogenes

IPD-IMGT/HLA databases

GRCh38.p14 (NCBI)

https://doi.org/10.1007/978-981-99-9781-7_16

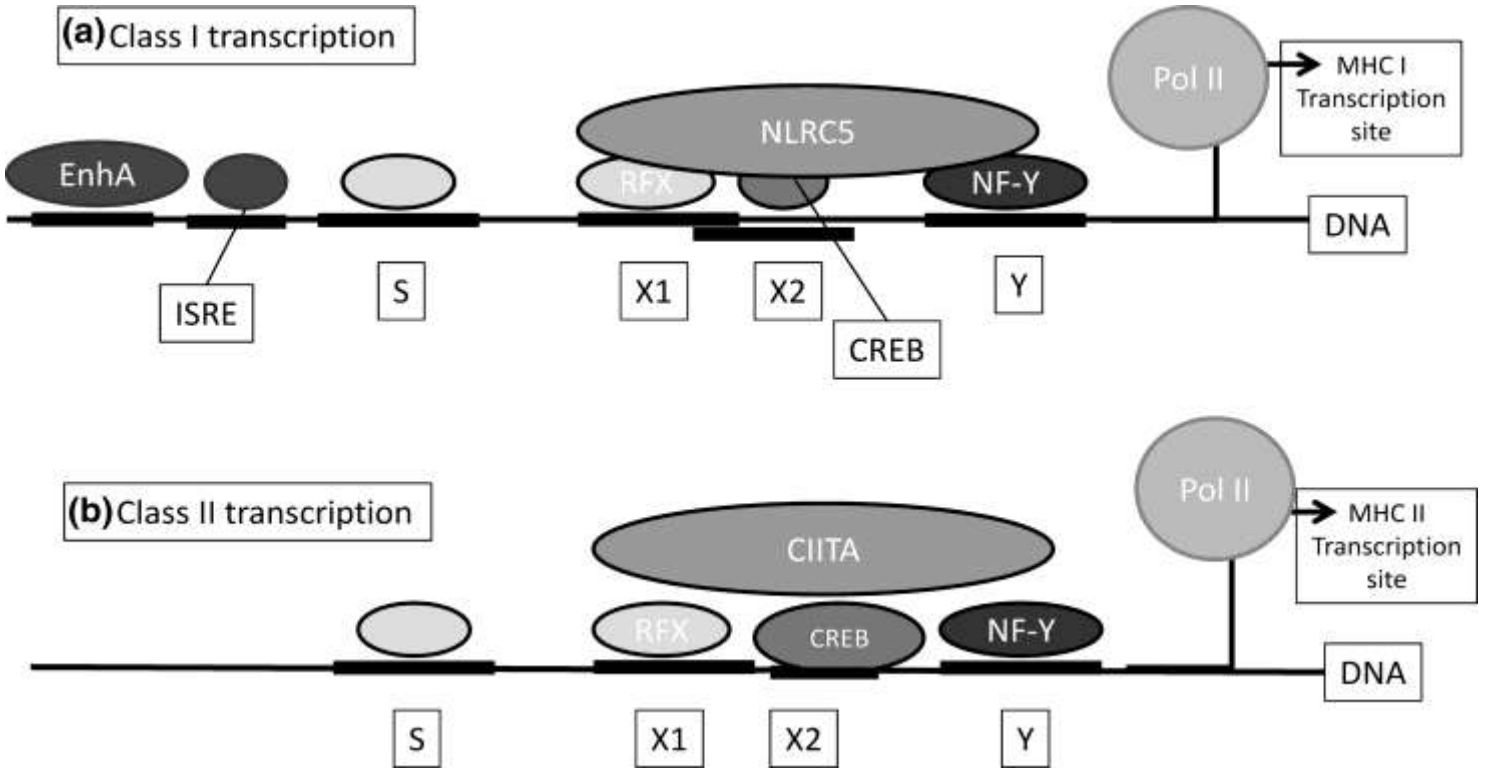


Locus	Number of alleles	Number of amino acid sequences	Null allele number
HLA-A	7644	4450 (58.2%)	404 (5.3%)
HLA-B	9097	5471 (60.1%)	325 (3.6%)
HLA-C	7609	4218 (55.4%)	344 (4.5%)
HLA-DRB1	3389	2203 (65.0%)	119 (3.5%)
HLA-DQB1	2330	1455 (62.4%)	109 (4.7%)
HLA-DPB1	2221	1321 (59.5%)	121 (5.4%)
Total (including other loci)	35,220		1552 (4.4%)

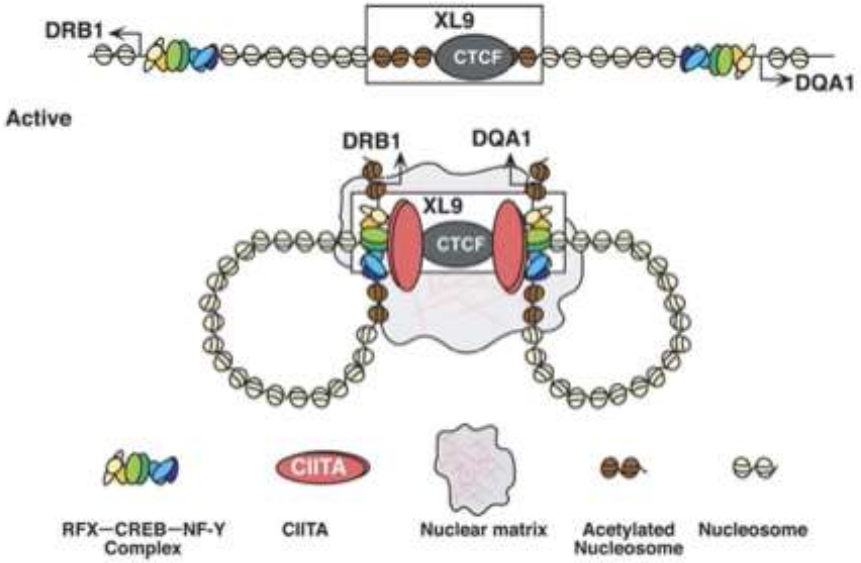
https://doi.org/10.1007/978-981-99-9781-7_16

Cell line	AH/CEH	MHC class II type	HLA-A	HLA-B	HLA-C	HLA-DRB3,4,5	HLA-DRB1	HLA-DQA1	HLA-DQB1
APD	60.X	DR3	A*01:01:01	B*40:01:01	C*06:02:01	DRB3*02:02:01	DRB1 *03,*11,*12,*13 or *14	DQA1*01:03:01	DQB1*06:03:01
COX	8.1	DR3	A*01:01:01	B*08:01:01	C*07:01:01	DRB3*01:01:02	DRB1 *03,*11,*12,*13 or *14	DQA1*05:01:01	DQB1*02:01:01
DBB	57.x	DR4	A*02:01:01	B*57:01:01	C*06:02:01	DRB4*01:03:01	DRB1 *04 , *09 or *07	DQA1*02:01:01	DQB1*03:03:02
KAS116	51	DR1	A*24:02:01	B*51:01:01	C*12:03:01		DRB1 *01 or *10	DQA1*01:01:01	DQB1*05:01:01
MANN	44.2/44.3	DR4	A*29:02:01	B*44:03:01	C*16:01:01	DRB4*01:01:01	DRB1 *04 , *09 or *07	DQA1*02:01:01	DQB1*02:02:01
PGF	7.1	DR2	A*03:01:01	B*07:02:01	C*07:02:01	DRB5*01:01:01	DRB1 *15 or *16 ,	DQA1*01:02:01	DQB1*06:02:01
QBL	18.2	DR3	A*26:01:01	B*18:01:01	C*05:01:01	DRB3*02:02:01	DRB1 *03,*11,*12,*13 or *14	DQA1*05:01:01	DQB1*02:01:01
SSTO	44.x	DR4	A*32:01:01	B*44:02:01	C*05:01:01	DRB4*01:03:01	DRB1 *04 , *09 or *07	DQA1*03:01:01	DQB1*03:05:01

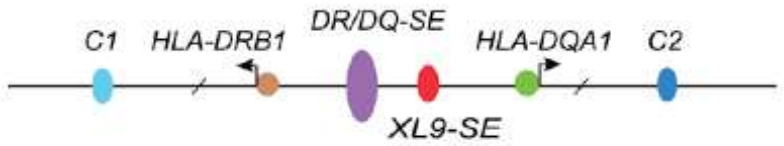
Sartoris and Del Pozzo, 2024



DOI: 10.1111/iji.12443



J Exp Med. 2008. doi:10.1084/jem.20071843



J Exp Med 2020doi.org/10.1084/jem.20190668

COX (HLA-A1-B8-Cw7-DR3) : Type 1 diabetes, systemic lupus erythematosus and myasthenia gravis.

PGF (A3-B7-Cw7-DR15) :protection from type 1 diabetes and susceptibility to multiple sclerosis and systemic lupus erythematosus)

QBL (A26-B18-Cw5-DR3-DQ2) (associated with type 1 diabetes and Graves' disease)

L'analisi del trascrittoma dei tre aplotipi ha dimostrato differenze nell'espressione dei geni, aplotipo-specifiche riconducibili variazioni della trascrizione e a meccanismi di splicing alternativo

http://www.genome.org/cgi/doi/10.1101/gr.116681.110.

G3 Genes | Genomes | Genetics

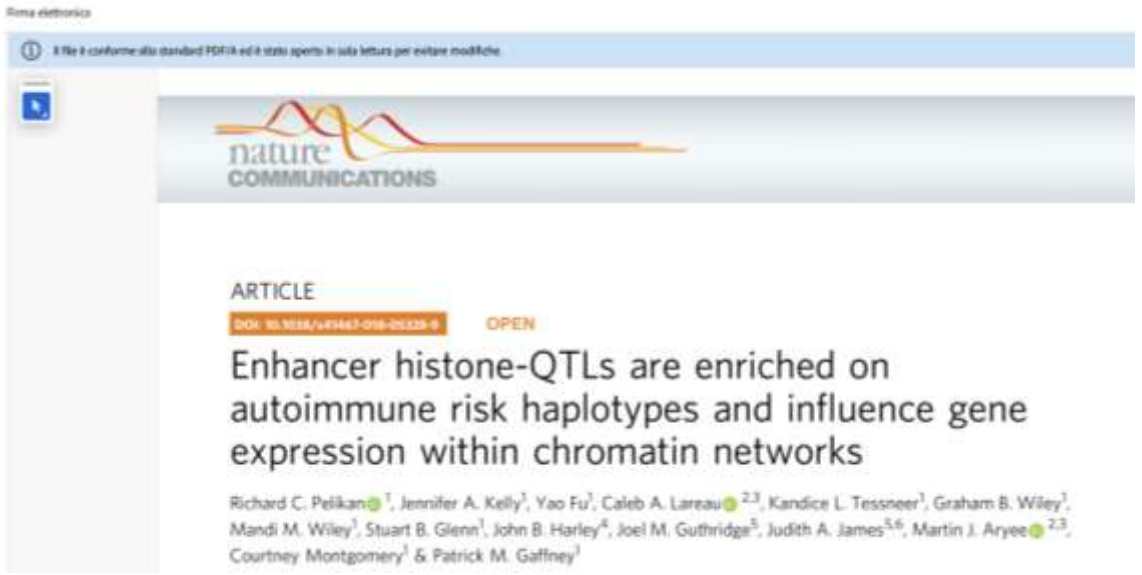
INVESTIGATION

Unique Allelic eQTL Clusters in Human MHC Haplotypes

Tze Hau Lam,* Meixin Shen,* Matthew Zirui Tay,† and Ee Chee Ren*,‡,1
*Singapore Immunology Network, A*STAR, Singapore 138648, †Department of Molecular Genetics and Microbiology, Duke University, Durham, North Carolina 27710, and ‡Department of Microbiology and Immunology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore 117597
ORCID ID: 0000-0001-5039-2207 (E.C.R.)

Esperimenti di RNA-Seq su linee B-LCL omozigoti per i tre aplotipi
A2-B46-DR9 **A33-B58-DR3** **A1-B8-DR3**
dimostrano l'espressione differenziale di alcuni alleli in aplotpi distinti

eQTL SNP segregano in base all'aplotipo, in LD anche a distanza di 350 Kb e hanno effetti regolatori aplotipo-specifici



nature COMMUNICATIONS

ARTICLE

OPEN

Enhancer histone-QTLs are enriched on autoimmune risk haplotypes and influence gene expression within chromatin networks

Richard C. Pelikan, Jennifer A. Kelly, Yao Fu, Caleb A. Lareau, Kandice L. Tessneer, Graham B. Wiley, Mandi M. Wiley, Stuart B. Glenn, John B. Harley, Joel M. Guthridge, Judith A. James, Martin J. Aryee, Courtney Montgomery & Patrick M. Gaffney

Analisi dell'architettura epigenomica di linee B-LCL omozigoti con aplotipo HLA-DR3 and HLA-DR15, associati con SLE hanno permesso l'identificazione di *histone quantitative trait loci hQTLs*, varianti che determinano una espressione allelica differenziale attraverso modificazioni post traduzionali degli istoni a livello di enhancer

DOI: 10.1038/s41467-018-05328-9 |

frontiers in Immunology

Capturing Differential Allele-Level Expression and Genotypes of All Classical HLA Loci and Haplotypes by a New Capture RNA-Seq Method

Fumiko Yamamoto, Shingo Suzuki, Akiko Mizutani, Atsuko Shigenari, Sayaka Ito, Yoshie Kametani, Shunichi Kato, Marcelo Fernandez-Viña, Makoto Murata, Soloko Morishima, Yasuo Morishima, Masafumi Tanaka, Jerzy K. Kulski, Soiamak Bahram and Takashi Shiina

> PLoS Genet. 2022 Jun 6;18(6):e1010212. doi: 10.1371/journal.pgen.1010212. eCollection 2022 Jun.

Regulation of HLA class I expression by non-coding gene variations

Florence Sellens [1], Halit Ongen [2], Guillaume Rey [2], Stéphane Buhler [1], Zuleika Calderon Sollet [1], Emmanouil Dermitzakis [2], Jean Villard [1]

> PLoS Genet. 2019 Apr 22;15(4):e1008091. doi: 10.1371/journal.pgen.1008091. eCollection 2019 Apr.

Expression estimation and eQTL mapping for HLA genes with a personalized pipeline

Vitor R C Aguiar [1], Jônatas César [1], Olivier Delaneau [2], Emmanouil T Dermitzakis [2], Diogo Meyer [1]

> Front Immunol. 2021 Feb 25;12:629059. doi: 10.3389/fimmu.2021.629059. eCollection 2021.

HLA RNA Sequencing With Unique Molecular Identifiers Reveals High Allele-Specific Variability in mRNA Expression

Tiira Johansson [1 2], Dawit A Yohannes [1], Satu Koskela [2], Jukka Partanen [2], Päivi Saavalainen [1 2]

Clinical Trial > Proc Natl Acad Sci U S A. 2013 Dec 17;110(51):20705-10.
doi: 10.1073/pnas.1312237110. Epub 2013 Nov 18.

Genetic interplay between HLA-C and MIR148A in HIV control and Crohn disease

Smita Kulkarni [1], Ying Qi, Colm O'hUigin, Florencia Pereyra, Veron Ramsuran, Paul McLaren, Jacques Fellay, George Nelson, Haoyan Chen, Wilson Liao, Sara Bass, Richard Apps, Xiaojiang Gao, Yuko Yuki, Alexandra Lied, Anuradha Ganesan, Peter W Hunt, Steven G Deeks, Steven Wolinsky, Bruce D Walker, Mary Carrington

rs67384697G>T in 3'UTR of HLA-C

> Nat Genet. 2009 Dec;41(12):1290-4. doi: 10.1038/ng.486.

HLA-C cell surface expression and control of HIV/AIDS correlate with a variant upstream of HLA-C

Rasmi Thomas [1], Richard Apps, Ying Qi, Xiaojiang Gao, Victoria Male, Colm O'hUigin, Geraldine O'Connor, Dongliang Ge, Jacques Fellay, Jeffrey N Martin, Joseph Margolick, James J Goedert, Susan Buchbinder, Gregory D Kirk, Maureen P Martin, Amalio Telenti, Steven G Deeks, Bruce D Walker, David Goldstein, Daniel W McVicar, Ashley Moffett, Mary Carrington

rs9264942T>C 35 Kb upstream HLA-C

Elevata espressione di geni / alleli

HLA-B27 associato a ankylosing spondylitis

HLA-A*02:01 gene associato autoimmune vitiligo

HLA-B*39:06, HLA-A*24:02, HLA-B*18 associato aT1D

> Proc Natl Acad Sci U S A. 2016 Feb 2;113(5):1363-8. doi: 10.1073/pnas.1523482113. Epub 2016 Jan 19.

MHC class II super-enhancer increases surface expression of HLA-DR and HLA-DQ and affects cytokine production in autoimmune vitiligo

Giulio Cavalli [1], Masahiro Hayashi [2], Ying Jin [3], Daniel Yorgov [4], Stephanie A Santorico [5], Cherie Holcomb [6], Melinda Rastrou [6], Henry Erlich [6], Isak W Tengesdal [7], Lorenzo Dagna [8], C Preston Neff [7], Brent E Palmer [7], Richard A Spritz [3], Charles A Dinarello [9]

J Autoimmun. 2016 Jun:70:63-72. doi: 10.1016/j.jaut.2016.03.016. Epub 2016 Apr 12.

HLA-DQ2.5 genes associated with celiac disease risk are preferentially expressed with respect to non-predisposing HLA genes: Implication for anti-gluten T cell response

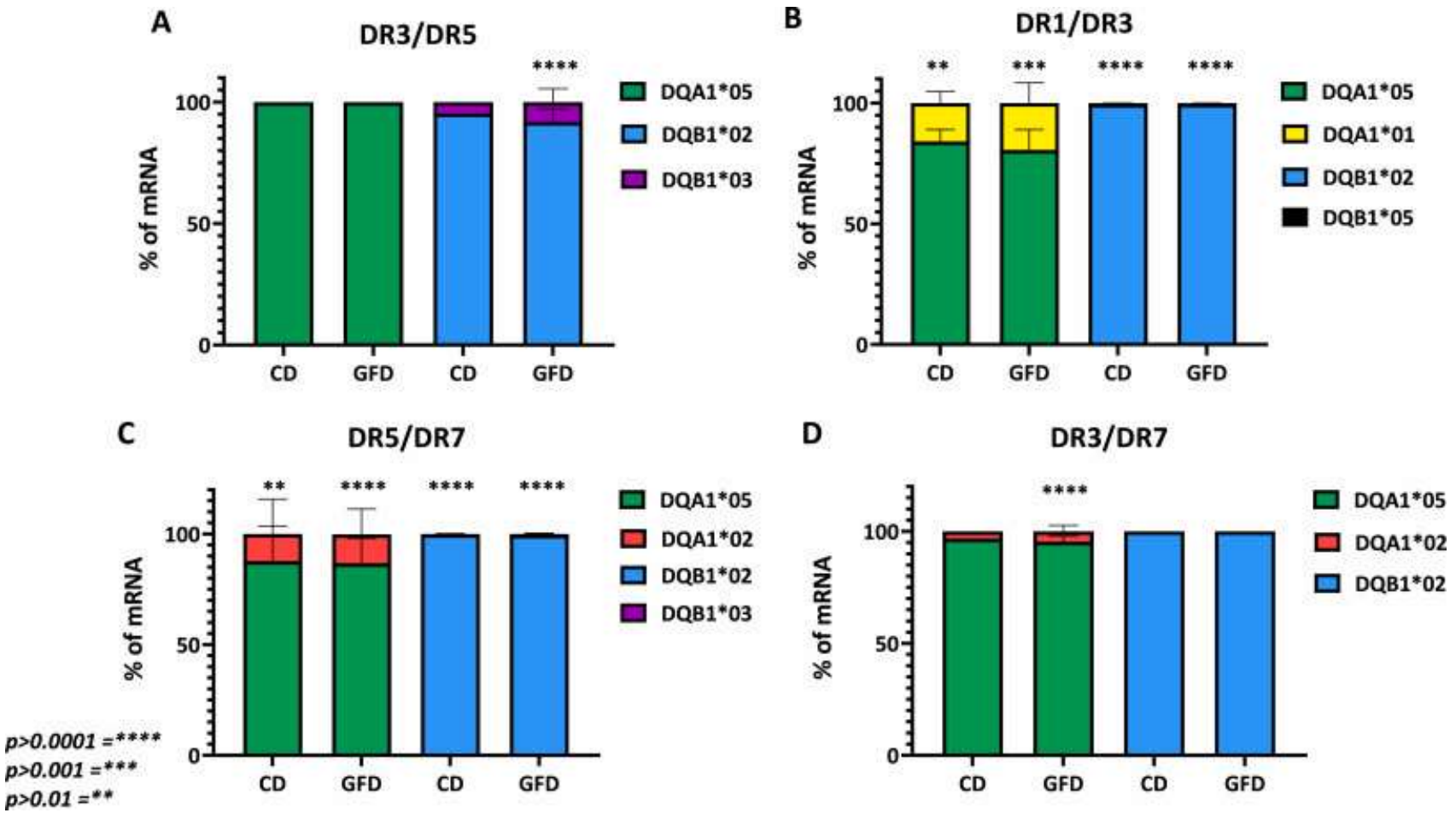
Laura Pisapia [1], Alessandra Camarca [2], Stefania Picascia [3], Virginia Bassi [2], Pasquale Barba [1], Giovanna Del Pozzo [4], Carmen Gianfrani [5]

Sci Rep. 2020 Oct 14;10(1):17227. doi: 10.1038/s41598-020-73907-2.

Differential expression of predisposing HLA-DQ2.5 alleles in DR5/DR7 celiac disease patients affects the pathological immune response to gluten

Laura Pisapia [1], Stefania Picascia [2], Federica Farina [1], Pasquale Barba [1], Carmen Gianfrani [2], vanna Del Pozzo [3]

Gli alleli HLA-DQA1*05 e DQB1*02 codificano la molecola HLA-DQ2.5 che presenta i peptidi della gliadina nella malattia celiaca



Del Pozzo , 2021

> Cells. 2019 Jul 19;8(7):751. doi: 10.3390/cells8070751.

HLA-DQA1 and HLA-DQB1 Alleles, Conferring Susceptibility to Celiac Disease and Type 1 Diabetes, are More Expressed Than Non-Predisposing Alleles and are Coordinately Regulated

Federica Farina [1], Stefania Picascia [2], Laura Pisapia [1], Pasquale Barba [1], Serena Vitale [2], Adriana Franzese [3], Enza Mozzillo [3], Carmen Gianfrani [2], Giovanna Del Pozzo G [4]

HLA-DQA1*03 /DQB1*03

> Int J Immunogenet. 2019 Dec;46(6):479-484. doi: 10.1111/iji.12450. Epub 2019 Jul 17.

The HLA-DRB1 risk alleles for multiple sclerosis are differentially expressed in blood cells of patients from Southern Italy

Laura Pisapia [1], Ilaria Cerillo [2], Federica Farina [1], Arianna Zimbardo [1], Pasquale Barba [1], Giuseppe Orefice [3], Carmen Gianfrani [4], Maria Strazzullo [1], Giovanna Del Pozzo [1]

HLA-DRB1*11 e DRB1*13

> Blood. 2014 Dec 18;124(26):3996-4003. doi: 10.1182/blood-2014-09-599969. Epub 2014 Oct 16.

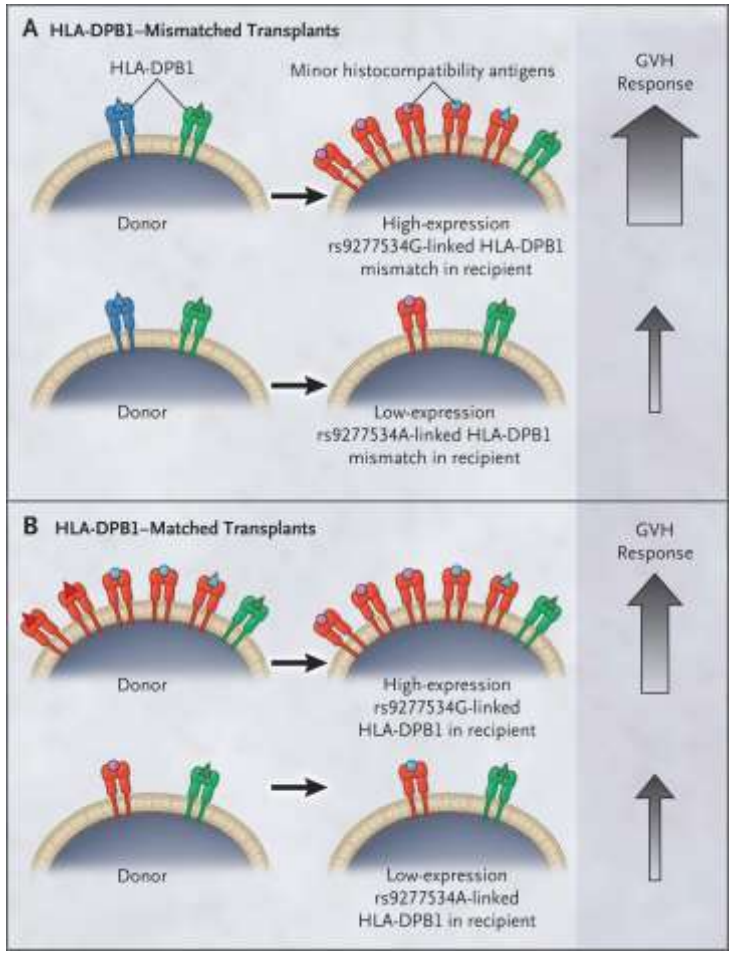
HLA-C expression levels define permissible mismatches in hematopoietic cell transplantation

Effie W Petersdorf [1], Theodore A Gooley [2], Mari Malkki [2], Andrea P Bacigalupo [3], Anne Cesbron [4], Ernette Du Toit [5], Gerhard Ehninger [6], Torstein Egeland [7], Gottfried F Fischer [8], Thibaut Gervais [9], Michael D Haagenson [10], Mary M Horowitz [11], Katharine Hsu [12], Pavel Jindra [13], Alejandro Madrigal [14], Machteld Oudshoorn [15], Olle Ringdén [16], Marlis L Schroeder [17], Stephen R Spellman [10], Jean-Marie Tiercy [18], Andrea Velardi [19], Campbell S Witt [20], Colm O'Huigin [21], Richard Apps [22], Mary Carrington [22]; International Histocompatibility Working Group in Hematopoietic Cell Transplantation

> N Engl J Med. 2015 Aug 13;373(7):599-609. doi: 10.1056/NEJMoa1500140.

High HLA-DP Expression and Graft-versus-Host Disease

Effie W Petersdorf [1], Mari Malkki, Colm O'hUigin, Mary Carrington, Ted Gooley, Michael D Haagenson, Mary M Horowitz, Stephen R Spellman, Tao Wang, Philip Stevenson



Thank you for attention