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Research paper

Genetic susceptibility to infectious diseases: Current status and future perspectives from genome-wide approaches

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ABSTRACT

Genome-wide association studies (GWASs) have been widely applied to identify genetic factors that affect complex diseases or traits. Presently, the GWAS Catalog includes > 2800 human studies. Of these, only a minority have investigated the susceptibility to infectious diseases or the response to therapies for the treatment or prevention of infections. Despite their limited application in the field, GWASs have provided valuable insights by pinpointing associations to both innate and adaptive immune response loci, as well as novel unexpected risk factors for infection susceptibility. Herein, we discuss some issues and caveats of GWASs for infectious diseases, we review the most recent findings ensuing from these studies, and we provide a brief summary of selected GWASs for infections in non-human mammals. We conclude that, although the general trend in the field of complex traits is to shift from GWAS to next-generation sequencing, important knowledge on infectious disease-related traits can be still gained by GWASs, especially for those conditions that have never been investigated using this approach. We suggest that future studies will benefit from the leveraging of information from the host's and pathogen's genomes, as well as from the exploration of models that incorporate heterogeneity across populations and phenotypes. Interactions within *HLA* genes or among *HLA* variants and polymorphisms located outside the major histocompatibility complex may also play an important role in shaping the susceptibility and response to invading pathogens.

1. General overview

Genome-wide association studies (GWASs) are based on the screening of many genomes to find genetic variants associated with a trait or disease. Both dichotomous and quantitative traits can be analyzed in GWASs, and the genomes can be those of unrelated subjects or derive from samples with familiar structure (e.g., parent-affected child trios). Because GWASs analyze variants distributed throughout the genome, they are unbiased with respect to prior biological knowledge, offering the potential to identify novel variants and genes associated to the trait of interest.

The first small-scale GWAS results were performed in 2005–2006 and investigated age-related macular degeneration, a common disease in elderly populations worldwide (Dewan et al., 2006; Klein et al., 2005). After those early efforts, the Wellcome Trust Case Control Consortium large-scale study in 2007 (Wellcome Trust Case Control Consortium, 2007) gave way to the GWAS era. In recent years, hundreds of GWASs have been published. Their results are stored in a dedicated database, the GWAS Catalog, presently hosted by the EMBL-EBI (https://www.ebi.ac.uk/gwas/) (MacArthur et al., 2017). As of April 24th 2017, the catalog comprised 2880 studies and > 9700 unique variant-trait associations. This figure refers to associations with a p value lower than or equal to 5×10^{-8}, which is usually considered as the threshold for genome-wide significance.

We mined the catalog to obtain a global overview of the application of GWAS in the field of infectious diseases. We classified studies and associations in broad categories depending on the disease or trait they analyzed. The category “infectious disease” was intended in a very broad sense: for instance, it included virus-associated cancers, specific phenotypes associated with infections (e.g., mood disorders in prion

Abbreviations: GWAS, Genome-wide association study; MHC, major histocompatibility complex; HLA, human leukocyte antigen; KIR, Killer-cell immunoglobulin-like receptor; lncRNA, long non-coding RNA; PCA, principal components analysis; LD, linkage disequilibrium; SNP, single nucleotide polymorphism; T2D, Type 2 diabetes; TB, tuberculosis; HCV, hepatitis C virus; HIV-1, Human Immunodeficiency virus type 1; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; eQTL, expression quantitative trait locus; HPV, Human Papillomavirus; VZV, Varicella Zooster virus; IAV, Influenza A virus; PCT, periodontal complex trait; CNV, copy number variant; CJD, Creutzfeldt-Jacob disease; CC, Collaborative Cross; EBOV, Ebola virus; WNV, West Nile virus; PRRSV, porcine reproductive and respiratory syndrome virus

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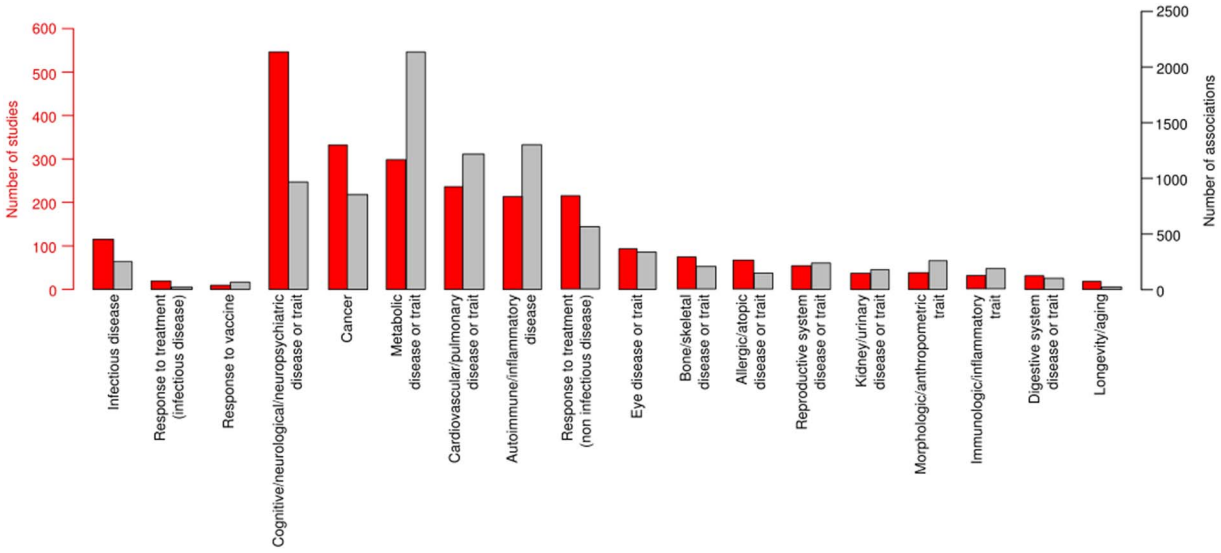

Fig. 1. Bar-plot representation of studies and associations recorded in the GWAS Catalog (as of April 24th, 2017). Bars represent the number of studies (red) or the number of unique SNP-trait associations (gray). Studies were manually categorized based on the diseases or trait they investigated. Only a subset of traits/diseases are shown. Associations were included only if they displayed an association p value $\leq 5 \times 10^{-8}$.

disease), and hematological measurements related to infectious agents (e.g., antibody levels for common infections, cytokine production during septic shock). We also defined categories for response to therapy, by classifying GWAS that analyzed the response to treatments for infectious diseases, non-communicable conditions, and vaccines. Overall, 4%, 0.66%, and 0.31% of all studies in the catalog were classified in the categories “infectious disease”, “response to treatment for infectious disease”, and “response to vaccine”, respectively (Fig. 1). In terms of unique variant-trait associations, percentages were as follows: 2.5% for “infectious disease”, 0.18% for “response to treatment for infectious disease”, and 0.66% for “response to vaccine” (Fig. 1). Based on the relative number of studies and associations, it is clear that some traits/diseases have attracted huge efforts that provided consequent reward (e.g., inflammatory/autoimmune disorders, metabolic traits and phenotypes), whereas others have been deeply investigated with comparatively modest success (e.g., neurologic/neuropsychiatric/cognitive diseases and traits, cancers). The reasons for these differences are manifold and outside the scope of this Review, which focuses on infections and related traits. Based on the percentages given above and on the comparison with other traits, we conclude that, despite the huge burden that infections pose for human health, relatively few GWASs for infectious diseases have been performed and these have attained a moderate success. Apparently, the best performance was obtained by GWASs for response to vaccination, with 9 studies that reported 64 associations. However, most of these associations will require validation, as they derive from a relatively small-scale study with no replication (Kennedy et al., 2012).

Sheer numbers, though, are not the only indicator of success. Important results were obtained by GWASs, both by identifying or refining associations in genes that were a priori expected to modulate infection susceptibility and by pointing out unexpected genes and pathways. Herein we discuss some issues associated with GWASs for infectious diseases, we review the most recent findings ensuing from these studies, and we provide a brief summary of selected GWASs in non-human mammals. Table 1 summarizes the results of human studies that detected at least one associated variant at genome-wide significance, whereas a list of all studies is available as Supplementary Table S1.

2. GWAS evolution

GWASs rely on linkage disequilibrium between genotyped SNPs and causal variants (often ungenotyped). The number of variants on the SNP chips that are used for GWASs has increased sensibly since the development of this technology (from ~500,000 in the initial studies to > 4,000,000 in the latest platforms). Moreover, the availability of an increasing number of fully sequenced genomes, together with the development of efficient imputation methods, has definitely expanded the power of GWASs to detect association with variants in the low range of the frequency spectrum (reviewed in (Visscher et al., 2017)). However, the overall power of a GWAS is also critically dependent on the sample size (reviewed in (Visscher et al., 2017) and see below) and in most cases power remains low for variants with a frequency below 1% (reviewed in (Visscher et al., 2017)).

Notably, though, important developments have been achieved in terms of imputation of variants within the Major Histocompatibility Complex (MHC), with clear relevance for the investigation of infectious (and immuno-mediated) diseases. As recently reviewed elsewhere (Matzaraki et al., 2017), the development of large reference panels (at least for Europeans and Asian populations) and the use of advanced imputation methods allowed the fine mapping of human leukocyte antigen (HLA) variants as susceptibility factors for some infectious diseases (e.g., HIV-1, HCV, and HBV infection) and many more autoimmune conditions (Matzaraki et al., 2017).

Recently, an imputation algorithm for typing *KIR* (Killer-cell immunoglobulin-like receptor) gene copy number has also been developed and applied to data from European populations (Vukcevic et al., 2015). However, *KIR* variability extends beyond copy number variation and next-generation sequencing technologies were proposed to allow high-resolution genotyping of *KIR* loci (Maniangou et al., 2017; Norman et al., 2016).

Finally, we mention that in 2009 a SNP chip (Immunochip) providing high coverage of immune-related genes, including *HLA* and *KIR* loci, came into use to fine-map and validate association signals for immune-mediated diseases (Cortes and Brown, 2011). The application of the Immunochip in the field of infectious diseases has been very limited, with the notable exception of a study that investigated the genetic susceptibility to candidaemia and identified three risk variants (Kumar et al., 2014).

3. Issues and caveats of GWASs for infectious diseases and related traits

Some considerations apply to GWASs, whether they investigate

Table 1
Significant associations with infectious diseases (or related traits) in genome-wide association studies.

Pathogen/disease	Year	Population	Associated loci	Trait description	References
GWAS for infectious diseases					
Viruses					
Dengue virus	2011	Asian ancestry Vietnam	*MICB*, *PLCE1*	Dengue shock syndrome (DSS) susceptibility	(Khor et al., 2011)
Diarrhoeal disease	2016	European ancestry *Discovery:* Netherlands, UK, Spain, Germany *Replication:* Norway, UK, U.S., Germany, Netherland, Spain	*NTN5*, *SEC1P*, *FUT2*	Susceptibility to diarrhoeal disease in young children (1 and 2 years)	(Bustamante et al., 2016)
Epstein-Barr virus (EBV)	2013	Hispanic ancestry *Discovery:* Mexico *Replication:* Mexico	*HLA-DRB1*, *HLA-DQB1*	EBV seroreactivity measured by Epstein-Barr virus nuclear antigen 1 (anti-EBNA-1) titer	(Rubicz et al., 2013)
Hepatitis B virus (HBV)	2009	Asian ancestry *Discovery:* Japan *Replication:* Japan and Thailand	*HLA-DPB1*	Chronic hepatitis B (CHB) susceptibility	(Kamatani et al., 2009)
	2010	Asian ancestry *Discovery:* China *Replication:* China	*UBE4B*, *KIF1B*, *PGD*	HBV-related hepatocellular carcinoma (HCC) susceptibility	(Zhang et al., 2010)
	2011	Asian ancestry *Discovery:* Japan *Replication:* Japan	*HLA-DPA1*, *HLA-DPB1*, *HLA-DQB1*, *HLA-DQB2*	CHB susceptibility	(Mbarek et al., 2011)
	2011	Asian ancestry China	*GRIN2A*	HBV progression	(Liu et al., 2011)
	2012	Asian ancestry *Discovery:* Japan *Replication:* Japan and Korea	*HLA-DPA1*, *HLA-DPB1*	HBV clearance	(Nishida et al., 2012)
	2012	Asian ancestry *Discovery:* China *Replication:* China	*GRIK1*, *HLA-DRB1*, *HLA-DQA1*	HBV-related HCC	(Li et al., 2012)
	2013	Asian ancestry *Discovery:* China *Replication:* China	*STAT4*, *HLA-DQ*	HBV-related HCC	(Jiang et al., 2013)
	2013	Asian ancestry *Discovery:* Korea *Replication:* Korea	*HLA-DP*, *HLA-DQ*, *EHMT2*, *TCF19*	CHB susceptibility	(Kim et al., 2013)
	2013	Asian ancestry *Discovery:* China *Replication:* China	*HLA-DQB2*, *HLA-C*, *UBE2L3*	CHB susceptibility	(Hu et al., 2013)
	2014	Asian ancestry *Discovery:* China *Replication:* China	*HLA-DQA2*, *HLA-DQB2*, *HLA-DPB1*, *HLA-DPA3*	CHB in males	(Chang et al., 2014)
	2015	Asian ancestry *Discovery:* China *Replication:* China	*HLA-C*, *CFB*, *NOTCH4*, *HLA-DOA*, *CD40*, *HLA-DQB1*, *HLA-DQB2*, *HLA-DPA1*, *HLA-DPB1*	CHB susceptibility	(Jiang et al., 2015)
	2016	Asian ancestry *Discovery:* China *Replication:* China	rs7000921 (locus 8p21.3)	CHB susceptibility	(Li et al., 2016)
	2017[a]	Asian ancestry *Discovery:* China *Replication:* China	*HLA-DR*	HCV-related acute-on-chronic liver failure (ACLF) susceptibility	(Tan et al., 2017)
Hepatitis C virus (HCV)	2010	European ancestry Germany, Switzerland	*IFNL2* (previously known as *IL28A*), *IFNL3/IFNL4*, *IFNL1* (previously known as *IL29*)	Chronic hepatitis C (CHC) susceptibility	(Rauch et al., 2010)
	2011	Asian ancestry *Discovery:* Japan *Replication:* Japan	*HLA-DQ*, *HLA-DR*, *MICA*	HCV-related HCC	(Kumar et al., 2011)
	2011	Asian ancestry *Discovery:* Japan *Replication:* Japan	*DEPDC5*	HCV-related HCC	(Miki et al., 2011)
	2012	European ancestry *Discovery:* France, Switzerland *Replication:* France, Germany, Italy, UK, U.S., Australia	*RNF7*, *MERTK*	Liver fibrosis progression related to HCV infection	(Patin et al., 2012)
	2013	Asian ancestry *Discovery:* Japan *Replication:* Japan	*C6orf10*, *BTNL2*, *BTNL2-HLA-DRA*	CHC-induced liver cirrhosis (LC)	(Urabe et al., 2013)
	2013	European, African and Afro-Caribbean ancestry *Discovery:* Austria, France, Germany, Greece, UK, U.S. *Replication:* U.S., Egypt	*IFNL4*, *HLA-DQ*	Spontaneous resolution of HCV infection	(Duggal et al., 2013)
	2013		*HLA-DQB1*, *HLA-DQA1*	CHC susceptibility	(Miki et al., 2013)

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Table 1 (*continued*)

Pathogen/disease	Year	Population	Associated loci	Trait description	References
		Asian ancestry *Discovery:* Japan *Replication:* Japan			
	2014	European ancestry *Discovery:* U.S., France, UK, Italy *Replication:* U.S., France, Italy	*HLA-DQA1*, *HLA-DRB1*, *NOTCH4*	Susceptibility to mixed cryoglobulinemia related to CHC	(Zignego et al., 2014)
	2017	Asian ancestry *Discovery:* Japan *Replication:* Japan	*TLL1*	HCC development after HCV eradication	(Matsuura et al., 2017)
HCV and HIV co-infection	2016	European ancestry France	*OXTR*, *MAP1LC3BP1*	Liver fibrosis progression	(Ulveling et al., 2016)
Varicella Zooster virus (VZV)	2015	European, African, Hispanic ancestry U.S.	*HCP5*, *HLA-B*, *DHFR*	Herpes zoster susceptibility	(Crosslin et al., 2015)
Human Immunodeficiency Virus (HIV)	2007	European ancestry *Discovery:* Denmark, Italy, Spain, Switzerland, Australia *Replication:* Denmark, Italy, Spain, Switzerland, Australia	*HCP5*, *HLA-CHIV-1* viral load at set point	HIV-1 viral load at set point	(Fellay et al., 2007)
	2009	European ancestry *Discovery:* France *Replication:* Denmark, Italy, Spain, Switzerland, Australia	*HCP5*	Progression to AIDS	(Limou et al., 2009)
	2009	European ancestry U.S.	*HCP5*, *HLA-B*, *HLA-C*	HIV-1 viral load at set point	(Fellay et al., 2009)
	2010	European ancestry U.S.	*RYR3*	Susceptibility to atherosclerosis	(Shrestha et al., 2010)
	2010	European, African (African American or Afro-Caribbean), and Hispanic ancestry Canada, U.S., Australia	*HLA-C*, *MICA*, *HLA-B*, *HCP5*, *PSORS1C3*	HIV-1 viral load control	(International HIV Controllers Study et al., 2010)
	2011	European ancestry U.S.	*PARD3B*	Progression to AIDS	(Troyer et al., 2011)
	2015	European, African, Hispanic ancestry (NR)	*ACKR1* for Neutrophil count in HIV- infection; *UGT1A*, *UGT1A1*, *UGT1A3*, *UGT1A4*, *UGT1A5*, *UGT1A6*, *UGT1A7*, *UGT1A8*, *UGT1A9*, *UGT1A10*, *MROH2A* for Total bilirubin levels in HIV- infection	Multiple phenotypes measured by standard clinical laboratory practice	(Moore et al., 2015)
	2015	European ancestry U.S., Australia, France, Netherlands	*MICA*, *CCRL2*, *HLA-B*, *HLA-C*	HIV-1 viral load at set point	(McLaren et al., 2015)
Human Papillomavirus (HPV)	2011	European and Hispanic ancestry *Discovery:* Czech Republic, Hungary, Poland, Romania,Russian Federation, Slovakia *Replication:* Argentina, Brazil, Cuba	*HLA-DQB1*	HPV seroconversion	(Chen et al., 2011)
	2013	Asian ancestry *Discovery:* China *Replication:* China	*EXOC1*, *HLA-DPB2*, *GSDMB*, rs9277952 (locus:6p21.32)	HPV-related cervical carcer	(Shi et al., 2013)
	2013	European ancestry *Discovery:* Sweden *Replication:* Sweden	*MICA*, *HLA-DRB1*, *HLA-DQA1*, *HLA*	Susceptibility to cervical cancer.	(Chen et al., 2013)
	2016	European ancestry *Discovery:* Sweden *Replication:* Sweden	rs73730372 (locus:6p21.32)	Susceptibility to cervical cancer.	(Chen et al., 2016)
Influenza A virus (H1N1)	2015	European ancestry Spain	See Supplementary Table S1	Susceptibility to influenza A (H1N1) infection and disease severity	(Garcia-Etxebarria et al., 2015)
Bacteria					
Helicobacter pylori	2013	European ancestry Germany and Netherlands	*TLR-1*, *HSPA6/FCGR2A/B*	*H. pylori* seroprevalence defined using anti–*H. pylori* serum IgG antibody titers	(Mayerle et al., 2013)
Mycobacterium tuberculosis	2010	African ancestry *Discovery:* Ghana, The Gambia *Replication:* Ghana and Malawi	rs4331426 (locus 18q11.2)	Tuberculosis susceptibility	(Thye et al., 2010)
	2012	African, Asian and European ancestry *Discovery:* Ghana	*WT1*	Tuberculosis susceptibility	(Thye et al., 2012)

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Table 1 (*continued*)

Pathogen/disease	Year	Population	Associated loci	Trait description	References
		Replication: The Gambia, Indonesia and Russia			
	2014	African ancestry and other The Gambia, Ghana, Malawi, South Africa	*SMOC1*, *WT1*	Tuberculosis susceptibility	(Chimusa et al., 2014)
	2015	European and African ancestry *Discovery:* Russia *Replication:* Russia, The Gambia and Ghana	*ASAP1*	Tuberculosis susceptibility	(Curtis et al., 2015)
	2016[a]	African ancestry Uganda and Tanzania	*IL-12*	Tuberculosis resistance in HIV-positive individuals	(Sobota et al., 2016)
Subgengival bacterial biofilm (e.g.: *Porphyromonas gingivalis*)	2010	European ancestry *Discovery:* Germany *Replication:* Netherlands	*GLT6D1*	Periodontitis susceptibility	(Schaefer et al., 2010)
	2016	European ancestry *Discovery:* U.S. *Replication:* U.S. and Germany	*CLEC19A*, *TRA*, *GGTA2P*, *TM9SF2*, *IFI16*, *RBMS3*, *C1QTNF7*, *TSNARE*, *HPVC1*, *SLC15A4*, *PKP2*, *SNRPN*	Periodontal disease-related phenotypes	(Offenbacher et al., 2016)
	2017	Hispanic ancestry, European and African (African-American and Afro-Caribbean) ancestry *Discovery:* Hispanics/Latinos America *Replication:* U.S	rs149133391 (locus 1q42.2)	Periodontitis susceptibility	(Sanders et al., 2017)
Mouth carbohydrate-fermenting bacteria (e.g.: *Streptococcus mutans*)	2013	European ancestry (NR)	*AJAP1*, *LYZL2*	Dental caries-related phenotypes	(Shaffer et al., 2013)
	2014	European ancestry U.S.	*KPNA4* for Pit-and-Fissure caries	Dental caries susceptibility	(Zeng et al., 2014)
	2016	Hispanic/Latino ancestry U.S.	*NAMPT*, *BMP7*	Dental caries susceptibility	(Morrison et al., 2016)
Mycobacterium leprae	2009	Asian ancestry *Discovery:* China *Replication:* China	*RIPK2*, *TNFSF15*, *LACC1*, *NOD2*, *HLA-DR*, *CCDC122*	Leprosy susceptiility and progression	(Zhang et al., 2009)
	2011	Asian ancestry *Discovery:* China *Replication:* China	*IL23R*, *RAB32*, *CYLD*	Leprosy susceptiility	(Zhang et al., 2011)
	2015	Asian ancestry *Discovery:* China *Replication:* China	*IL23R*, *IL1RL1*, *IL12B*, *HLA-DRB1*, *RAB32*, *TNFSF15*, *NOD2*, *BATF3*, *CDH18*, *DEC1*, *EGR2*, *CCDC88B*, *CIITA*, *SIGLEC5*, *RIPK2*, *LACC1*, rs16948876 (locus 16q12.1)	Leprosy susceptiility	(H. Liu et al., 2015)
	2016	Asian ancestry *Discovery:* China *Replication:* China	*SYN2*, *BBS9*, *CTSB*, *MED30*	Leprosy susceptiility	(Wang et al., 2016)
Neisseria meningitidis	2010	European ancestry *Discovery:* UK *Replication:* Austria, Netherlands, Spain	*CFH*, *CFHR3*	Susceptibility to meningococcal disease	(Davila et al., 2010)
	2016	European ancestry *Discovery:* Spain *Replication:* Spain, UK	*CFH*	Susceptibility to meningococcal disease	(Martinon-Torres et al., 2016)
Propionibacterium acnes	2014	Asian ancestry *Discovery:* China *Replication:* China	*DDB2*, gene cluster including *SELL*, *SELP* and *SELE*	Severe acne susceptibility	(He et al., 2014)
	2014	European ancestry *Discovery:* UK *Replication:* UK	*FST*, *TGFB2*, *OVOL1*	Severe acne susceptibility	(Navarini et al., 2014)
Salmonella typhi	2014	Asian ancestry *Discovery:* Vietnam *Replication:* Vietnam and Nepalese	*HLA-DRB1*	Enteric fever susceptibility	(Dunstan et al., 2014)
Staphylococcus aureus	2015	Hispanic ancestry Mexico	*KAT2B* for intermittent carriage	*S. aureus* nasal carriage	(Brown et al., 2015)
	2016	European ancestry U.S.	*HLA-DRB1* for all *S. aureus* infections	Susceptibility to *S. aureus* and to skin and soft tissue *S. aureus* infections (SSTIs)	(DeLorenze et al., 2016)
Streptococcus pneumoniae	2016	African ancestry *Discovery:* Kenia *Replication:* Kenia	AC00600.5 and AC011288.2 (two overlapping intergenic non-coding RNA genes)	Pneumococcal bacteremia	(Kenyan Bacteraemia Study Group et al., 2016)
Parasites					
Leishmania donovani/ Leishmania infantum chagasi	2013	Asian and Hispanic ancestry *Discovery:* India, Brazil *Replication:* India	*HLA-DRB1-HLA-DQA1*	Visceral leishmaniasis susceptibility	(LeishGEN Consortium et al., 2013)
Plasmodium falciparum	2009		*HBB*	Severe malaria susceptibility	(Jallow et al., 2009)

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Table 1 (*continued*)

Pathogen/disease	Year	Population	Associated loci	Trait description	References
		African ancestry *Discovery:* The Gambia *Replication:* The Gambia			
	2012	African ancestry *Discovery:* The Gambia *Replication:* The Gambia and Ghana	*HBB*, *ABO*, *ATP2B4*, *MARVELD3*	Severe malaria susceptibility	(Timmann et al., 2012)
	2013	African ancestry The Gambia, Kenya, Malawi	*HBB*, *ABO*	Severe malaria susceptibility	(Band et al., 2013)
	2015	African ancestry *Discovery:* Kenya, Malawi, The Gambia *Replication:* Malawi, United Republic of Tanzania, Cameroon, Burkina Faso, The Gambia, Ghana, Mali	*HBB*, *ABO*, *ATP2B4*, *FREM3/GYPE* region	Severe malaria susceptibility	(Malaria Genomic Epidemiology Network et al., 2015)
Prion					
Prion (Creutzfeldt-Jakob disease)	2009	European and Oceanian ancestry *Discovery:* UK *Replication:* UK and Papua New Guinea	*PRNP*	Susceptibility to variant CJD	(Mead et al., 2009)
	2011	European ancestry *Discovery:* UK *Replication:* France, UK	*PRNP*, *MTMR7*, *NPAS2*	Susceptibility to variant CJD	(Sanchez-Juan et al., 2012)
	2015	European ancestry *Discovery:* Germany, Netherlands, UK *Replication:* Australia, Austria, France, Germany, Netherlands, Italy, Spain	*PRNP*, *GRM8*	Susceptibility to sporadic CJD	(Sanchez-Juan et al., 2015)
GWAS for response to treatment for infectious diseases					
Viruses					
Hepatitis C virus (HCV)	2009	European, African (African American or Afro-Caribbean) and Hispanic ancestry (NR)	*IFNL3/IFNL4* (European Ancestry)	Response to antiviral treatment with pegylated interferon-alpha combined with ribavirin (pegIFNα/ribavirin)	(Ge et al., 2009)
	2009	Asian ancestry *Discovery:* Japan *Replication:* Japan	*IFNL3/IFNL4*	Response to antiviral treatment with (pegIFNα/ribavirin)	(Tanaka et al., 2009)
	2009	European ancestry *Discovery:* Australia *Replication:* Germany, Italy, UK, Australia	*IFNL3*, *IFNL3/IFNL4*	Response to antiviral treatment with (pegIFNα/ribavirin)	(Suppiah et al., 2009)
	2010	European ancestry Germany, Switzerland	*IFNL2*, *IFNL3/IFNL4*, *IFNL1*	Response to antiviral treatment with (pegIFNα/ribavirin)	(Rauch et al., 2010)
	2010	European, African American and Hispanic ancestry U.S.	*ITPA*	Susceptibility to treatment-related anaemia	(Fellay et al., 2010)
	2010	Asian ancestry *Discovery:* Japan *Replication:* Japan	*ITPA*	Susceptibility to treatment-related anaemia	(Ochi et al., 2010)
	2011	Asian ancestry Taiwan, Japan	*IFNL3/IFNL4*	HCV treatment response	(Ochi et al., 2011)
	2011	Asian ancestry *Discovery:* Japan *Replication*: NR	*DDRGK1*, *ITPA* for Hb level and platelets count	Susceptibility to pegIFNα-induced thrombocytopenia and to RBV-induced anaemia	(Tanaka et al., 2011)
	2012	European and African (African-American and Afro-Caribbean) and Hispanic ancestry U.S.	*ITPA*	Susceptibility to thrombocytopenia, neutropenia, and leukopenia related to pegIFNα treatment	(Thompson et al., 2012)
	2012	Hispanic, European, and African (African American or Afro-Caribbean) (NR)	*IFNL3/IFNL4*	Lipid levels during and after HCV infection treatment and the interactions with sustained viral response (SVR)	(Clark et al., 2012)
Human Immunodeficiency Virus (HIV)	2011	Asian ancestry *Discovery:* Thailand *Replication:* Thailand	*CCHCR1*	Susceptibility to Nevirapine-induced rash	(Chantarangsu et al., 2011)
	2014	European, Hispanic, African (African American or Afro-Caribbean) ancestry U.S.	*RSPO4* (hispanic - Grade ≥ 2); *IL2RA*, *CXCL12*, rs9501753 (locus:6p25.3), *PTPRB* (European ancestry – Grade ≥ 3); *TANK*, *HDAC9,* rs801350	Susceptibility to peripheral neuropathy related to d4T/ddI-containing treatment	(Leger et al., 2014)

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Table 1 (*continued*)

Pathogen/disease	Year	Population	Associated loci	Trait description	References
			(locus:2q32.3), rs801378 (locus:2q32.3) (Hispanic - Grade ≥ 3)		
	2015[a]	European, African, and Hispanic ancestry (NR)	*SLC17A1*	Plasma Tenofovir and creatinine clearance after TDF/ emtricitabine containing regimens	(Wanga et al., 2015)
GWAS for response to vaccine					
Viruses					
Measles, Mumps and Rubella vaccine	2014	European ancestry U.S.	*ACO1*, *PTPRD*	Immune responses to rubella vaccination	(Kennedy et al., 2014)
	2014	European ancestry *Discovery:* Denmark *Replication:* Denmark	*IFI44L*, rs1318653 (locus:1q32.2), *CD46*, *ANO3*, *SCN1A*, rs11105468 (locus:12q21.33), *SCN2A* for febrile seizures; *IFI44L*, *SCN1A*, *ANO3*, *CD46*, *CD34* for febrile seizures MMR vaccine-related; *ANO3*, *SCN1A* for febrile seizures MMR vaccine-unrelated	Susceptibility to general and measles, mumps and rubella (MMR) vaccine-related febrile seizures	(Feenstra et al., 2014)
Hepatitis B vaccine	2011	Asian ancestry *Discovery:* Indonesia *Replication:* Indonesia	*HLA-DR*, *HLA*, *HLA-DPB1*	Immune response to HBV vaccine	(Png et al., 2011)
	2014	Asian ancestry *Discovery:* China *Replication:* China	*HLA-DRA*, *BTNL2*, *HLA-DRB1*, *C6orf10*	Immune response to HBV vaccine	(Pan et al., 2014)
Smallpox vaccine	2012	Hispanic, European and African (African-American and Afro-Caribbean) ancestry U.S.	*MKX*, rs10503951 (locus: 8p12), *GPR158*, *ZHX2*, *SPIRE1* (African ancestry); *PCDH15*, *PRKCQ* (Hispanic ancestry)	Immune response to smallpox vaccine	(Ovsyannikova et al., 2012)
	2012	European and African (African-American and Afro-Caribbean) ancestry U.S.	See Supplementary Table S1	Cytokine responses to smallpox vaccine	(Kennedy et al., 2012)

[a] Articles not in the GWAS catalog (as of April 24th, 2017).

infectious diseases or other conditions/traits. Although the sample size that is necessary to achieve an adequate statistical power depends on the genetic architecture of the analyzed trait, GWASs typically require large samples of individuals. This is because thousands (millions) of variants are simultaneously analyzed, making it difficult to disentangle true associations from false positives. Ideally, GWASs should enroll subject of shared and homogeneous ethnical ancestry, to avoid issues of population stratification, which can in turn produce spurious associations if not properly corrected. Moreover, phenotype heterogeneity (Bennett et al., 2011), environmental confounders (Pearson and Manolio, 2008), as well as misclassification of cases and controls (Pearson and Manolio, 2008) have been shown to affect GWAS reliability and power. Some of these issues may be particularly relevant in the field of infectious diseases.

3.1. Sample size, population structure, and environmental confounders

Large populations samples are often difficult to recruit in developing countries, due to limited resources, inadequate health facilities, and inefficient screening or diagnostic procedures. In these countries, however, the burden imposed by infectious diseases is highest (Jones et al., 2008; Mabey et al., 2004). Also, some populations in developing areas have complex demographic histories. This is the case of African populations, that are genetically highly diverse and display a limited extension of linkage disequilibrium (LD) compared to non-Africans (International HapMap Consortium et al., 2007). For instance, one of the first GWASs for infectious diseases genotyped individuals in West Africa to identify susceptibility variants for severe malaria (Jallow et al., 2009). The authors found considerable population stratification, which was corrected for using principal components analysis (PCA); signals of association at known malaria resistance loci (e.g. *HBB*) were difficult to retrieve due to weak LD between causal variants (e.g., HbS locus) and tag SNPs (Jallow et al., 2009). Populations from South and Central America also display relevant population structure due to recent admixture (Bryc et al., 2010). In a GWAS for visceral Leishmaniasis that included families from Brazil, ancestry differences and close relationships were efficiently corrected for using a linear mixed model (LeishGEN Consortium et al., 2013). These models are an alternative to those based on PCA and rely on the incorporation of genetic relatedness between individuals directly in the statistical model (see (Eu-Ahsunthornwattana et al., 2014; Hayes, 2013; Yang et al., 2014) for reviews and comparison among different linear mixed model methods).

Another issue often related to population structure is that of environmental confounders (Vilhjalmsson and Nordborg, 2013). A well-known example in the field of non-communicable diseases relates to type 2 diabetes (T2D) susceptibility. Several studies for T2D indicated that the proportion of Native American genetic ancestry is associated with lower socioeconomic status in admixed Latino populations from North and South America (Chakraborty et al., 1986; Florez et al., 2009; Martinez-Marignac et al., 2007; Parra et al., 2004). This effect is partially responsible for the generally higher incidence of T2D in Latinos. This exemplifies how the combined effect of genetic admixture and environmental factors has the potential to affect genetic associations. Indeed, poor socioeconomic conditions represent a risk factor for several infectious diseases (Baker et al., 2012; Braveman, 2011; Franco-Paredes et al., 2007; May, 2007; Semenza, 2010). Thus, possible environmental confounders must be accounted for to avoid spurious associations or loss of statistical power. However, even in the presence of admixture and environmental confounders, associations can be retrieved with confidence. In a GWAS for tuberculosis (TB), Chimusa and coworkers analyzed admixed South African Coloured case-control cohorts (Chimusa et al., 2014). After accounting for population stratification and hidden relatedness, they replicated a previously reported association at the *WT1* gene (Thye et al., 2012) and performed trans-ethnic fine mapping of the association signals (Table 1). The authors also found a positive correlation between San (an African ethnic group)

ancestry proportion and TB status. Although complete information was available for a minority of individuals, no correlation was detected between socioeconomic status and ancestry components, leading the authors to suggest that the association between San ancestry and TB is not merely explained by differences in socioeconomic conditions (Chimusa et al., 2014).

3.2. Phenotype heterogeneity and case/control misclassification

Perhaps, the two most important points that characterize GWAS for infectious diseases compared to studies of non-communicable conditions are phenotypic heterogeneity and case-control misclassification. An important source of heterogeneity in GWASs for infectious diseases derives from genetic variation in the pathogen. One of the best known examples of how the genotype of the infectious agent can interact with the host genome refers to hepatitis C virus. Among the most significant findings of GWASs for infectious diseases was the identification in 2009–2010 of variants at the *IFNL3/IFNL4* loci (previously known as *IL28B*) that associate with spontaneous clearance of HCV infection and with response to interferon-α/ribavirin therapy (Ge et al., 2009; Rauch et al., 2010; Suppiah et al., 2009; Tanaka et al., 2009) (Table 1). This finding set the basis for a personalized treatment of HCV infection (Matsuura et al., 2014). However, the effect of the *IFNL3/IFNL4* variants on response to therapy is much stronger for patients infected with HCV genotypes 1 and 4 than for those infected with genotypes 2, 3, and 6 (Rauch et al., 2010; Akkarathamrongsin et al., 2014). Interestingly, interferon-α/ribavirin therapy is less effective for patients infected with genotypes 1 and 4 compared to the other genotypes (European Association for the Study of the Liver, 2011). Thus, the prognostic value of the *IFNL3/IFNL4* variants is particularly relevant for patients infected with HCV genotypes that are poorly responsive to this treatment (Rauch et al., 2010). These observations well exemplify how important the interaction of the host and pathogen genomes can be. Very recently, a genome-to-genome GWAS for HCV infection was performed, shedding more light into the interaction between human *IFNL4/IFNL3* variants and HCV genetic diversity (Ansari et al., 2017) (see Conclusions and perspectives section).

Another notable example of how pathogen heterogeneity can interact with the host genotype refers to TB susceptibility. The human *Mycobacterium tuberculosis* complex (MTBC) consists of several major phylogenetic lineages whose names reflect their association with geographic areas (Brites and Gagneux, 2015). Candidate gene approaches have shown that host genetic variants can modulate susceptibility to TB caused by specific MTBC strains (Herb et al., 2008; Caws et al., 2008; Intemann et al., 2009; van Crevel et al., 2009; Salie et al., 2014). For instance, a variant in *TLR2* was specifically associated with an increased risk of TB caused by the Beijing strain in a Vietnamese population, whereas two *SLC11A1* polymorphisms were found to be significantly more common in patients having tuberculosis caused by *M. tuberculosis* Beijing genotype strains than in patients carrying other genotypes (Caws et al., 2008; van Crevel et al., 2009). In populations from Ghana, an *IRGM* polymorphism was found to protect against disease caused by the Euro-American lineage (Intemann et al., 2009), and polymorphisms in *ALOX5* were more strongly associated with TB caused by *M. africanum* West African 2 strain (Herb et al., 2008). Furthermore, associations of specific HLA class I alleles and disease caused by the Beijing, LAM, LCC and Quebec strains, as well as by the Euro-American or East Asian lineages, were found in a South African population (Salie et al., 2014).

Therefore, the genetic heterogeneity of MTBC may limit the reproducibility of GWASs, as different cohorts may indeed include patients with distinct TB epidemiologies and with TB caused by different *M. tuberculosis* strains.

Finally, misclassification of cases or controls is an issue for several association studies. In the case of infections, a major problem is the difficulty to assess exposure in the control population. For instance, it is sometimes impossible to determine whether individuals recruited as uninfected controls (e.g., based on serology) are seronegative because they were exposed but did not acquire the infection or because they were never or rarely exposed to the pathogen. Cases are also sometimes problematic to define. For instance, seropositivity can result from different routes of exposure, in turn associated with distinct probabilities of infection, and possibly modulated by diverse genetic factors. Moreover, the probability of infection may depend on several factors, including the genetic characteristics of the pathogen, the infectiousness of the transmitting individual, the general health status at the moment of exposure (this is clearly important for nosocomial infections, for instance).

Some of these issues are evident in a GWAS for susceptibility to HIV-1 infection. McLaren and coworkers combined information from multiple studies to obtain case-control cohorts of > 6300 HIV-1 positive cases and 7200 general population HIV-1 negative controls (McLaren et al., 2013). Cases derived from different studies and were infected via diverse routes (i.e., parenteral and sexual). No information was available for controls on HIV-1 exposure (e.g., at risk behavior or possible parenteral exposure). The study failed to detect association with HIV infection susceptibility other than the known *CCR5Δ32* variant. An association signal at the *HLA-B/HLA-C* genes was not confirmed after correcting for frailty (survival) bias (McLaren et al., 2013). These results led to the conclusion that genetic variants that modulate HIV-1 acquisition are either rare or have small effects. However, as the authors note, the study design has a high potential for misclassification of both cases and controls (McLaren et al., 2013). Indeed, cases may include subjects with low HIV-1 susceptibility who were infected due to very high exposure (e.g. via multiple blood transfusions), whereas controls may comprise subjects who never exposed themselves to the virus. Because studies on high-risk populations indicated that the proportion of subjects who are naturally resistant to HIV-1 is around 20% (Plummer et al., 1999; Fowke et al., 1996), it can be hypothesized that as many as 80% of controls would seroconvert if exposed. McLaren and coworkers estimated that the sample size of their GWAS provided 80% power for variants with 0.1 allele frequency and genotype relative risk (GRR) of 1.3. Their calculations also show that if ~30%, ~60%, or ~80% of cases were misclassified as controls, GRRs of 2, 3, or 4 would be respectively necessary to achieve the same power (McLaren et al., 2013). In fact, the authors did detect association for the *CCR5Δ32* variant, indicating that polymorphisms with strong effect could be identified.

Another situation that may potentially lead to classification biases is reinfection. For instance, HCV reinfection is relatively common in high-risk groups (e.g., drug users) (Grebely et al., 2009; Grebely et al., 2012; Midgard et al., 2016). If individuals are classified as persistently infected (chronic hepatitis C, CHC) based on viral loads measurements with relatively long intervals between tests, cases of clearance and reinfection can potentially be classified as persistent infections (Grebely et al., 2009; Grebely et al., 2012).

4. GWAS for viral infections

4.1. HIV-1

In 2007, Fellay and coworkers performed the first GWAS for an infectious disease by investigating viral set-point in HIV-1 infection (Fellay et al., 2007). This pilot study paved the way for several other GWASs. Indeed, the two signals detected within the *HLA* class I gene region were since confirmed by several studies (Fellay et al., 2009; Limou et al., 2009; International HIV Controllers Study et al., 2010) (Table 1, Fig. 2). Additional GWASs focused on HIV-1 viral load, progression to AIDS, and susceptibility to infection (Table 1). Their results have been extensively reviewed elsewhere (van Manen et al., 2012).

In recent years, GWASs for HIV-1 infection have also focused on understanding the host determinants of response to standard and

experimental therapies, as well as on detecting variants responsible for susceptibility to treatment-related adverse effects (Table 1 and Supplementary Table S1) (Chantarangsu et al., 2011; Leger et al., 2014; Wanga et al., 2015) (Table 1 and Supplementary Table S1).

4.2. HBV and HCV

Susceptibility to Hepatitis B and Hepatitits C viruses (HBV and HCV) was also extensively investigated in GWASs. Worldwide, chronic HBV or HCV infections represent the major causes of progressive liver disease, including liver cirrhosis (LC) and hepatocellular carcinoma (HCC) (Shirvani-Dastgerdi et al., 2016). HBV predominantly affects Southeast Asia and the East Pacific, where it reaches the highest prevalence in the world (Custer et al., 2004). It is thus not surprising that most GWASs performed to date genotyped individuals of Asian ancestry (Table 1).

Genetic variations in HLA class II loci (*HLA-DP* and *HLA-DQ*) were significantly associated with susceptibility to chronic HBV infection and with HBV-related HCC (Mbarek et al., 2011; Kamatani et al., 2009; Nishida et al., 2012; Jiang et al., 2013; Jiang et al., 2015; Li et al., 2012; Kim et al., 2013; Hu et al., 2013; Chang et al., 2014; Tan et al., 2017) (Table 1, Fig. 2). Interestingly, host genetic variants in HLA class II genes were also found in association with hepatitis B vaccine response (Png et al., 2011; Pan et al., 2014) (Table 1).

In 2015, Jiang et al. (2015) performed the largest GWAS on a Chinese population including about 18,400 among cases (chronically-infected) and controls (seronegative). The study confirmed most of the previously reported associations in *HLA* class II genes and detected a new variant, rs1883832 in *CD40*, strongly associated with HBV chronic infection (Table 1, Fig. 2). rs1883832 influences *CD40* expression by affecting its translational efficiency (Jacobson et al., 2005). This association was confirmed, although not at genome-wide significant level, by a recent GWAS that analyzed chronically HBV-infected and spontaneously recovered subjects (Li et al., 2016). In this study, the authors also identified an intergenic variant at 8p21.3 which represents an expression quantitative trait locus (eQTL) for the *INTS10* (integrator complex subunit 10) gene (Table 1). Interestingly, the authors demonstrated that INTS10 suppresses HBV replication in liver cells via IRF3, and confirmed decreased INTS10 protein levels in plasma samples of chronically HBV-infected patients compared to subjects who spontaneously cleared infection (Li et al., 2016).

Although these studies have opened up new horizons of research, analyses in populations of different ancestries are strictly required.

As mentioned above, a landmark discovery of GWASs for HCV infection was the identification of the *IFNL3/IFNL4* association. In addition to this locus, variants in HLA class II loci were also found to affect viral clearance and disease progression in chronic HCV infection (Table 1, Fig. 2). In addition, polymorphisms in apoptosis-related genes such as *RNF7*, *TULP1*, and *MERTK* were associated with liver fibrosis, whereas variants in *DEPDC5* and *MICA* were described as modulators of HCV-related hepatocellular carcinoma risk (Table 1, Fig. 2).

4.3. Other widespread viral infections

The GWA strategy was also exploited to investigate other infections caused by viral pathogens with worldwide diffusion. These include Human Papillomavirus (HPV), Varicella Zooster virus (VZV), and Influenza A virus (IAV). Overall, these works unveiled a limited number of associations, sometimes as a consequence of small sample sizes and, consequently, modest statistical power.

In the case of HPV, most GWASs for susceptibility to infection and progression to cervical carcinoma confirmed associations to *HLA* class II genes (Table 1, Fig. 2). It should be noted, however, that some of these studies did not directly test HPV infection status, nor HPV type, making it difficult to determine which trait these associations refer to. An interesting observation is that polymorphisms in the *EXCO1* and *GSDMB* genes were associated with progression to cervical carcinoma (Shi et al., 2013) (Table 1). *EXOC1* encodes a subunit of the exocyst complex involved in host innate immune response against DNA antigens (Ishikawa et al., 2009), whereas *GSDMB* codes for the cancer-associated gasdermin-like protein, which is highly expressed in cervical cancer cells (Sun et al., 2008). These data suggest that both immunological and carcinogenic factors contribute to the risk of cervical cancer development.

With respect to VZV, a GWAS was performed to investigate risk factors for herpes zoster (Crosslin et al., 2015). Although the study had limited power and potential for control misclassification (e.g., individuals who never suffered from primary infection with VZV are not at risk of virus reactivation), a significant association was detected in the MHC region where the non-coding *HCP5* (HLA Complex P5) gene maps (Table 1). Intriguingly, variants in this region were also associated with delayed progression to AIDS (Table 1, Fig. 2). *HCP5* derives from an endogenous retroviral element with sequence homology to the HIV-1 *pol* gene (Kulski and Dawkins, 1999) and is primarily expressed in immune system cells (Liu et al., 2008). The function of this noncoding gene and its role (if any) in restricting viral infection remain to be determined. In fact, a functional study showed that HCP5 does not restrict HIV-1 infection in vitro (Yoon et al., 2010), and refinement of the association signals within the *HLA* region indicated that the *HCP5* variant associated with HIV-1 control is indeed a marker for the HLA-B*5701 allele (Fellay et al., 2009; Trachtenberg et al., 2009). Likewise, *HCP5* variants that reached genome-wide significance in the VZV GWAS are in strong linkage disequilibrium with polymorphisms in the *HLA-B* gene region (Crosslin et al., 2015). It is thus possible that HCP5 has no effect on viral infection per se, but its variants tag specific *HLA* class I alleles/haplotypes.

As for IAV, a single study analyzed susceptibility to H1N1 virus infection (Garcia-Etxebarria et al., 2015). The authors found no genome-wide significant associations when severe influenza cases were compared to mild cases. Conversely, several SNPs reached the significance threshold when severe and mild cases were compared to the general population (Table 1 and Supplementary Table S1). However, these associations were obtained on very small samples of patients and controls, and no replication cohort was analyzed.

Finally, we draw attention to a recent GWAS that searched for genetic variants associated with diarrhoeal episodes in young children (1–2 years old) (Bustamante et al., 2016). All subjects were recruited in developed countries, where the majority of diarrhoeal episodes are caused by viral infections (Wiegering et al., 2011). Despite the potential issues of phenotype heterogeneity, a significant association was found for variants in *FUT2*, a gene encoding an alpha (1,2)-fucosyltransferase which participates in the production of histo-blood group antigens (Table 1). In particular, the activity of FUT2 determines the expression of the ABO histo-blood group antigens on the gastrointestinal mucosa and in bodily secretions. Genetic diversity at the *FUT2* gene is maintained in human populations by balancing selection (Koda et al., 2001; Fumagalli et al., 2009) and common *FUT2* null alleles are present in many populations (Kelly et al., 1995; Koda et al., 1996; Liu et al., 1998). In homozygotes, these alleles determine the “non-secretor” phenotype. In the GWAS for diarrhoeal episodes, non-secretors were found to be at lower risk compared to secretors, a result in line with candidate-gene studies that associated the non-secretor status with protection from Rotavirus and Norovirus infections (which represent the leading causes of diarrhoeal disease in developed regions) (Wiegering et al., 2011; Lindesmith et al., 2003; Carlsson et al., 2009; Imbert-Marcille et al., 2014; Thorven et al., 2005). In line with the balancing selection scenario, however, candidate-gene studies associated the non-secretor status with higher risk for infection by different pathogens, including *Neisseria meningitidis*, *Streptococcus pneumoniae*, and *Candida* spp. (Blackwell et al., 1986a; Blackwell et al., 1986b; Chaim et al., 1997). More recently, non-secretors were also found to be at higher risk to develop Crohn's disease (Franke et al., 2010; McGovern et al., 2010). The molecular mechanism underlying the different

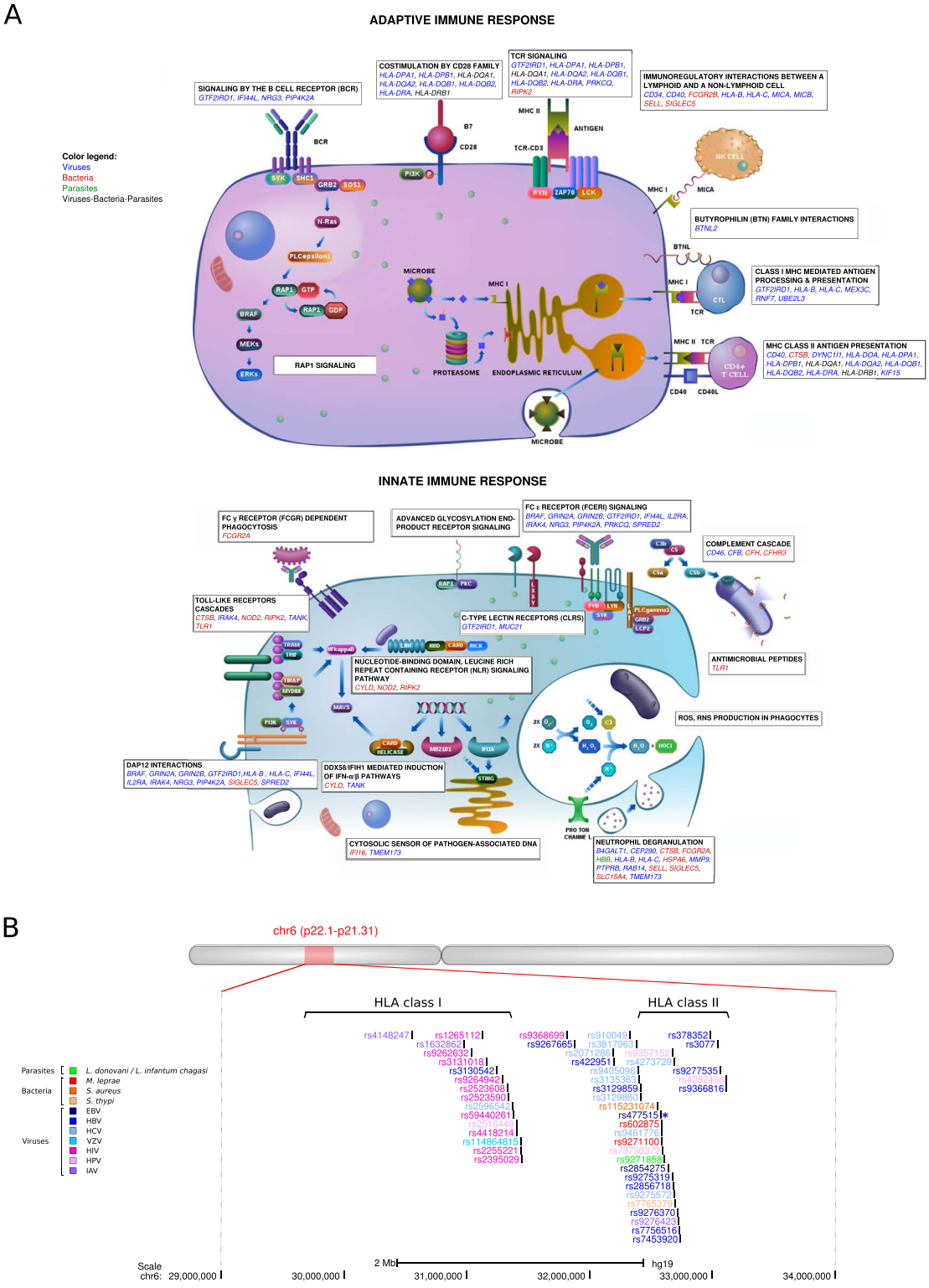

Fig. 2. A. Schematic representation of adaptive and innate immunity pathways derived by the Reactome database (http://www.reactome.org/), version (v61) (Fabregat et al., 2016; Milacic et al., 2012) (StableIDs: R-HSA-1280218 and R-HSA-168249).
Black boxes show sub-pathway names and contributing genes (as derived from Reactome): only genes that carry genetic variants associated in GWASs are reported (see Table 1). Color codes are shown in the legend. B. Schematic view of *HLA* class I and II loci. SNPs reported are associated to different traits related to pathogen (see Table 1). Asterisk denote association to multiple pathogens. Color codes and genomic coordinates (hg19) are reported.

predisposition to infection (and to Crohn's disease) of secretors and non-secretors most likely stems from the fact that both pathogenic and commensal microorganisms exploit oligosaccharides on the gastro-intestinal mucosa for cytoadherence.

5. GWASs for bacterial infections

Studies on the genetic susceptibility to bacterial infections have investigated a wide variety of conditions, either resulting from specific

infections (e.g., tuberculosis, pneumococcal bacteremia) or deriving from more heterogenous situations (e.g., periodontitis).

5.1. Specific infections

GWASs for infections caused by *Neisseria meningitidis* (Davila et al., 2010; Martinon-Torres et al., 2016), *Helicobacter pylori* (Mayerle et al., 2013), and *Mycobacterium leprae* (Zhang et al., 2009), strongly pointed to a role for risk variants in genes of the innate immune system. For *H. pylori*, variants in *TLR1*, known to be essential for innate immunity against bacterial infection, were identified as strongly associated with seroprevalence (Table 1, Fig. 2). For *N. meningitidis*, two GWASs for meningitis and septicaemia identified variants in the *CFH* gene region (Davila et al., 2010; Martinon-Torres et al., 2016) (Table 1, Fig. 2). C*FH* encodes complement factor H, a regulator of the complement system, which is bound by *N. meningitidis* to escape complement mediated killing (Schneider et al., 2009).

In the case of leprosy, a single GWAS identified candidate susceptibility genes encoding proteins involved in innate immune response (*NOD2*, *TNFSF15*, and *RIPK2*) (Table 1, Fig. 2). Furthermore, in a GWAS for leprosy in the Chinese population, H. Liu et al. (2015) found an overlap between their hits and those for autoimmunity/inflammatory diseases. For example, association with *CCDC88B*, identified in the leprosy GWAS (Table 1), was also reported for primary biliary cirrhosis, sarcoidosis, and inflammatory bowel disease. Likewise, SNPs in *TNFSF15*, *LRRK2*, *IL18RAP/IL1RL1*, and *LACC1/CCDC122* represent susceptibility loci for both leprosy and Crohn's disease (Jostins et al., 2012; J.Z. Liu et al., 2015). This observation points to a shared immunological basis for infectious and inflammatory conditions (H. Liu et al., 2015). However, the study also showed that, whereas some shared loci (*RIPK2* and *LACC1/CCDC122*) had concordant effects on the risk for leprosy and for inflammatory/autoimmune diseases, some others (e.g., *IL18RAP/IL1RL1*) showed opposite or discordant risk effects. These findings suggest a complex scenario and a delicate balance between response to infection and autoimmunity/chronic inflammation (Sironi and Clerici, 2010).

As expected, genes of the adaptive immune system also turned out to harbor polymorphisms associated with susceptibility to infections. Variants in the MHC region were identified as risk factors for leprosy (Zhang et al., 2009; H. Liu et al., 2015), *Staphylococcus aureus* infection (DeLorenze et al., 2016), enteric fever caused by *Salmonella typhi* (Dunstan et al., 2014), and TB (Sveinbjornsson et al., 2016) (Table 1, Fig. 2). For this latter infection, several GWASs have been performed (Table 1 and Supplementary Table 1). The *WT1* association mentioned above was detected in two independent studies (Chimusa et al., 2014; Thye et al., 2012) and recently confirmed, although with a *p* value that did not reach genome-wide significance, in a family-based Moroccan discovery sample (Grant et al., 2016). The functional role played by *WT1*, a zinc-finger transcription factor, in TB susceptibility remains to be elucidated. An interesting possibility is that WT1 regulates cytokine expression or activation of the vitamin D receptor (Maurer et al., 2001). Instead, the role played by *ASAP1*, a gene associated to TB in a Russian discovery cohort and replicated in African populations (Table 1), is somehow clearer, as its protein product regulates dendritic cell migration (Curtis et al., 2015). However, the signals in these genes showed very small effects (*WT1*) or failed to replicate (*ASAP1*) in a recent large TB study in the Icelandic population (Sveinbjornsson et al., 2016). This GWAS is a nice example of the power of imputation to enormously extend the number of analyzed variants. In fact, the authors used whole-genome sequencing of 2636 Icelanders to impute 28.3 million SNPs and insertions/deletions for > 100,000 chip-typed individuals. These included subjects with pulmonary TB or infected with *M. tuberculosis*. This large-scale study detected association signals at MHC class II loci, which were validated in Russian and Croatian samples (Sveinbjornsson et al., 2016). As discussed above, the low reproducibility of associations across studies and populations may in part reflect local differences in circulating *M. tuberculosis* strains (Sveinbjornsson et al., 2016). Finally, we mention that variants nearby the *IL12B* gene, which encodes a subunit of interleukin 12, were recently associated to TB in African populations (from Tanzania and Uganda) (Sobota et al., 2016). In this GWAS, the authors used an interesting approach by including in the study only HIV-1 positive individuals. The underlying rationale was that HIV-positive individuals who do not develop TB despite living in endemic areas should be genetically resistant and ideally suited to detect variants with strong effect. Indeed, the identified variant has a strong protective effect and may modulate *IL12B* expression (Sobota et al., 2016). Although this signal has not been replicated yet, it is worth mentioning that loss-of-function mutations in *IL12B* cause mendelian susceptibility to mycobacterial disease, a rare condition characterized by the development of clinical symptoms following infection with weakly virulent mycobacteria (Picard et al., 2002).

A nice example of the ability of GWASs to identify unexpected associations was provided by a recent study on bacteremia caused by *Streptococcus pneumoniae* (Kenyan Bacteraemia Study Group et al., 2016). By investigating a population of Kenyan children, Rautanen and coworkers identified an association peak located in the introns of two separate intergenic long non-coding RNAs (lncRNAs) annotated as *AC011288.2* and *AC006000.5* (Table 1). Interestingly, the risk allele is relatively rare and restricted to populations of African ancestry, underscoring the relevance of population-specific variants in disease susceptibility. Assessing AC011288.2 RNA expression in leukocyte cell subsets, Rautanen and coworkers observed expression in neutrophils only. These cells are known to play a major role in pneumococcal clearance (Gingles et al., 2001; Brinkmann et al., 2004) and their count is an independent predictor of pneumococcal bacteremia in febrile children (Kuppermann et al., 1998).

Thousands of lncRNA genes have been identified in the human genome (Atianand and Fitzgerald, 2014) and growing evidence suggests that these molecules are involved in gene regulation in different cell-types and tissues, including the immune system (Atianand and Fitzgerald, 2014). In 2013, using inter-crosses of mouse strains, Gomez and coworkers provided the first direct demonstration that a lncRNA (termed NeST) can modulate the outcome of infection (Gomez et al., 2013). In particular, NeST was shown to be responsible for the persistence of Theiler's virus in the central nervous system, as well as for the clearance of *Salmonella* infection (Gomez et al., 2013). These data suggest that additional lncRNA await identification as important players in immune response and infectious disease susceptibility.

5.2. Caries, periodontitis, and acne

GWASs have also been applied to identify genetic determinants for very common human condition characterized by a strong interaction between environmental factors and the infecting/commensal bacteria. These include caries, which is caused by a wide array of carbohydrate-fermenting bacteria, (Larsen and Fiehn, 2017), periodontitis, where an anaerobic bacterial biofilm participates in disease onset and progression (Larsen and Fiehn, 2017), as well as acne, which is characterized by overgrowth of *Propionibacterium acnes*.

For dental caries a variety of loci were identified via GWASs. Studies in adults have yielded significant and “suggestive” associations within or near genes with roles in tooth development and host defense. Among these we mention *LYZL2*, encoding a bacteriolytic agent (Shaffer et al., 2013), *NAMPT*, which is involved in periodontal healing (Morrison et al., 2016), and *BMP7*, a tooth development gene (Morrison et al., 2016) (Table 1). To date, none of the dental caries loci identified in GWASs in adults have been followed up in fine-mapping or replication studies. Importantly, given the complexity of caries etiology and the spectrum of contributing environmental factors, some authors speculated that the effects of some genetic variants may vary across different populations (Morrison et al., 2016).

Although several GWASs were conducted for periodontitis, only few of them successfully identified implicated loci (Table 1 and Supplementary Table S1). Among them, the first GWAS for periodontitis (Schaefer et al., 2010) studied the aggressive type of disease and identified an association with a marker in the *GLT6D1* gene (encoding a glycosyltransferase) (Table 1). Functional experiments suggested that reduced GATA3 binding affinity to the *GLT6D1* locus could be a component of the pathophysiology of periodontitis.

Subsequently, Offenbacher et al. (2016) used a promising approach that combined clinical phenotypes, biological intermediates of microbial burden, and measures of local inflammation to derive periodontal complex traits (PCTs). PCTs were carried forward to GWAS to identify PCT-associated loci among European American adult participants (Table 1). The authors found several significant signals in loci that included genes involved in immune response and epithelial barrier function. However, candidate loci did not associate with current clinically determined periodontal disease categories upon replication.

Finally, GWASs were also used to find associations between genetic variants and severe acne susceptibility. The top signals identified in a Chinese population included a SNP within the promoter region of *DDB2* (a novel androgen receptor-interacting protein), as well as variants in *SELL/SELP/SELE* gene cluster (Table 1). These selectins have important roles in regulating cutaneous inflammation (He et al., 2014) (Fig. 2). Instead, a GWAS conducted in a UK population identified genes linked to the TGFβ cell signaling pathway and to skin homeostasis, namely *OVOL1*, *FST* and *TGFB2* (Navarini et al., 2014) (Table 1).

6. GWASs for parasitic and prion diseases

Parasitic infections, either caused by protozoa or by helminths, affect millions of people worldwide. For many parasitic diseases a heritable component has been demonstrated (Verra et al., 2009; Williams-Blangero et al., 2011; Dold and Holland, 2011; Choi et al., 2003). However very few GWAS were conducted; their results are summarized in Table 1 and were reviewed elsewhere (Mangano and Modiano, 2014). We add herein that a recent GWAS explored the genetic susceptibility to malaria (Malaria Genomic Epidemiology Network et al., 2015). Beyond confirming loci previously associated with severe malaria (*HBB*, *ABO*, *ATP2B4*) (Jallow et al., 2009; Timmann et al., 2012; Band et al., 2013), this study identified additional variants on chromosome 4, between *FREM3* and a cluster of three glycophorin genes (*GYPE*, *GYPB*, and *GYPA*) (Table 1). Glycophorins are sialoglycoproteins abundantly expressed on the erythrocyte membrane, where they play a functional role in invasion by *Plasmodium falciparum*. In a recent follow-up study, the authors identified an array of large copy number variants (CNVs) affecting the *GYPA* and *GYPB* genes (Leffler et al., 2017). One of the identified CNVs (*DUP4*) is associated with resistance to severe malaria and explains the GWAS association signal (Malaria Genomic Epidemiology Network et al., 2015).

The most common form of human prion disease in humans is Creutzfeldt-Jacob disease (CJD), which is classified as sporadic, acquired (iatrogenic or variant) or familial (Iwasaki, 2017). Variants in *PRPN*, encoding the prion protein (PrP), are the best known genetic factor for susceptibility to CJD (Owen et al., 1990; Mead et al., 2009) (Table 1). Nevertheless, associations to other genomic loci (MTMR7 and NPAS2 for variant CJD (Sanchez-Juan et al., 2012), GRM8 for sporadic CJD (Sanchez-Juan et al., 2015)) were recently reported (Table 1). *MTMR7* is specifically expressed in the central nervous system (CNS) and is involved in the phosphatidylinositol pathway, whereas *NPAS2* encodes a transcription factor implicated in neuronal function. Interestingly, the CJD susceptibility variant in *NPAS2* is in strong linkage disequilibrium with an SNP that regulates *PLCD3 in trans* (Sanchez-Juan et al., 2012). Because *PLCD3* encodes a catabolic enzyme of the phosphatidylinositol pathway, these data implicate this pathway in the susceptibility to variant CJD. As for *GRM8*, it encodes a member of the metabotropic glutamate receptor family. Other members of this family are involved in cellular signal transduction triggered by PrP (Um et al., 2013). Thus, these data highlight the ability of GWASs to pinpoint molecular disease pathways.

7. GWAS in non-human mammals

In comparison to human GWASs, association studies in domestic and laboratory animals offer advantages and disadvantages. Model animals, for instance, can be infected with a known dose of a genetically homogeneous pathogen, removing part of the variability associated to exposure routes and load in humans, as well as to the genetic heterogeneity of the infecting pathogen. Due to their peculiar demographic histories, both model and domestic animals often display extensive linkage disequilibrium and genetic homogeneity, at least within breeds or strains (Alhaddad et al., 2013; Badke et al., 2012; Boyko et al., 2010; Flint and Eskin, 2012; Lindblad-Toh et al., 2005). This implies that GWASs can be carried out using much fewer markers and samples than required in human studies. The other side of the coin is that the often complex breeding strategies pose challenges related to population structure, cryptic relatedness, and extensive selective sweeps resulting from artificial selection. These factors need to be accurately corrected for, to avoid spurious associations and loss of statistical power. Popular methods to account for these effects include the use of PCA to explicitly model ancestry contributions (Price et al., 2006) and the application of mixed model association methods (see (Hayes, 2013; Yang et al., 2014; Flint and Eskin, 2012) for review).

7.1. Mouse studies

In the field of mouse genetics, an important contribution to the mapping of complex traits came from the Collaborative Cross (CC), a collaborative effort aimed at providing the scientific community with a large panel of recombinant inbred mouse strains derived from genetically diverse founders (Churchill et al., 2004; Maurizio and Ferris, 2017). As founders are both classic inbred strains and wild-derived strains, the resulting mouse panel has higher genetic diversity and less population structure than other mouse-based resources. Within the CC framework, an ancestry-based approach was shown to be superior to marker-based methods for mapping QTLs (Aylor et al., 2011). The utility of this approach in the field of infectious diseases was initially demonstrated by a genome-wide scan of incipient CC lines for susceptibility to *Aspergillus fumigatus*, a pathogen that recapitulates in mice the signs of human aspergillosis (Durrant et al., 2011). The authors found that CC lines were heterogenous in terms of susceptibility to *A. fumigatus* infection, measured as survival days after infection, and the broad-sense heritability of this phenotype was 0.78. The genome-wide scan identified several QTLs, including one on chromosome 8 that contained the *Irf2* gene and another one on chromosome 10 covering cytokine (*Il20ra*, *Il22ra*) and interferon (*Ifngr1*) receptors (Durrant et al., 2011). Incipient CC lines were then used to investigate the genetic susceptibility to IAV infection by recording several IAV-induced phenotypes, including virus replication, airway inflammation, weight loss, and pulmonary edema. Interestingly, a highly significant QTL on chromosome 16 (*Hrl1*, *H*ost *r*esponse to *I*nfluenza), was identified (Ferris et al., 2013). *Hrl1* explained a considerable proportion of variation in several phenotypes and encompassed a genomic region where the *Mx1* gene maps. Because *Mx1* is a well-known IAV resistance gene (Staeheli et al., 1988), these findings provide a nice validation of the CC approach. Additional QTLs were mapped in the study and suggested that variants in *Il16* and/or *Nox4* (*Hrl2*) modulate IAV-induced weight loss (Ferris et al., 2013).

More recently, incipient CC lines were used to identify variants in *Trim55* associated with vascular cuffing after infection with a mouse adapted SARS-CoV strain (Gralinski et al., 2015) and QTLs for survival to *Klebsiella pneumoniae* infection (Vered et al., 2014). Importantly, CC mice have been used to create improved models of EBOV (*Ebola virus*)

and WNV (*West Nile virus*) infection (Graham et al., 2016; Graham et al., 2015; Rasmussen et al., 2014) and mouse populations showing diverse susceptibility to *M. tuberculosis* and *Pseudomonas aeruginosa* (Lore et al., 2015; Smith et al., 2016). These models await genome-wide scans to unveil the genetic determinants of infection susceptibility and severity.

7.2. Associations in dogs

Dogs have also proven useful models for the mapping of variants associated with infectious disease phenotypes. Dog breeds represent genetic isolates deriving from a few founder individuals and subject to strong artificial selection. Thus, breeds differ in several phenotypes. One of these is granulomatous colitis, which is caused by mucosally invasive *Escherichia coli* (Simpson et al., 2006) and is described in boxers and bulldogs only (Craven et al., 2011; Manchester et al., 2013). Within a larger project that assessed several traits and diseases, Hayward and coworkers performed a within-breed GWAS for granulomatous colitis and identified a strong association signal within a genomic region where several members of the *SLAM* (signaling lymphocyte activation molecule) gene family map (Hayward et al., 2016). Interestingly, variants in the corresponding human genomic region have been associated with the susceptibility to Crohn's disease and ulcerative colitis (Franke et al., 2010; J.Z. Liu et al., 2015; Barrett et al., 2008). These data indicate that, both in dogs and in humans, genes within this region contribute to the maintenance of intestinal immune homeostasis in the presence of commensal or pathogenic bacteria.

7.3. GWASs in cattle and swine

In cows, GWASs have been widely applied to the field of infectious disease susceptibility. This is clearly motivated by the fact that infections cause a major economic burden in the cattle industry worldwide. In this context, GWASs and other genomic approaches are regarded as powerful strategies to develop breeding programs aimed at the generation of less susceptible livestock (Raszek et al., 2016).

One of the most investigated traits was Johne's disease, a chronic gastrointestinal tract disease caused by *Mycobacterium avium* subspecies *paratuberculosis*. Several GWASs have been performed, mostly on naturally infected Holsteins and Jerseys (common breeds of dairy cattle): associated variants with small effect were identified in several analyses, but reproducibility among studies was extremely low, resulting in no confidently associated marker (Alpay et al., 2014; Kirkpatrick et al., 2011; Minozzi et al., 2010; Neibergs et al., 2010; Pant et al., 2010; Settles et al., 2009; van Hulzen et al., 2012; Zare et al., 2014). Although the reasons for low across-study consistency are likely manifold and include different criteria to classify phenotypes and different statistical procedures, these results suggest that loci with a major effect on Johne's disease do not exist, at least in these breeds. Likewise, GWASs for susceptibility to bovine tuberculosis (caused by *Mycobacterium bovis*) yielded inconsistent results (Bermingham et al., 2014; Finlay et al., 2012; Kassahun et al., 2015; Richardson et al., 2016). Efforts to identify susceptibility alleles for other infectious diseases detected small-effect loci with poor replicability (reviewed in (Raszek et al., 2016)). To date, the greatest success was obtained for mastitis, which is commonly caused by bacterial infections; regions spanning the *DCK*, *SLC4A4*, and *EDN3* genes were detected in at least two studies (Kanazawa et al., 1989; Sahana et al., 2013; Sodeland et al., 2011; Wu et al., 2015). The functional role of these genes in mastitis and response to invading bacteria remains to be evaluated.

As is the case for cattle, infections represent major economic problems for the swine industry, with one viral pathogen, porcine reproductive and respiratory syndrome virus (PRRSV) accounting for substantial burden (Dekkers et al., 2017). Several GWASs for PRRSV susceptibility converged to identify a major locus on chromosome 4 (reviewed in (Dekkers et al., 2017)). Fine mapping of the QTL region and a further functional genomics work identified a variant in the *GBP5* gene as likely causal (Dekkers et al., 2017). *GPB5* encodes an interferon-inducible guanosine triphosphatase which plays central roles in cell-intrinsic immunity. In humans, GBP5 acts as a restriction factor for HIV (Krapp et al., 2016). For the purpose of swine breeding, this result is relevant as a variation at *GBP5* can be used for marker-assisted selection (Dekkers et al., 2017).

8. Conclusions and perspectives

As detailed above, GWASs for infectious diseases have provided important biological insight and, in some cases, the results have opened the way to personalized therapy (Booth et al., 2012). Huge gaps however remain, with a number of infections still not addressed by GWAS or similar approaches. For instance, hundreds of millions of people are infected by helminths (Hotez et al., 2008), but no GWAS has investigated the genetic susceptibility to these parasites even though linkage studies provided evidence for several QTLs (reviewed in (Mangano and Modiano, 2014)). Diarrhoea and meningitis also account for a heavy health burden, especially among children in developing countries (World Health Organization, http://apps.who.int/gho/data/node.home). Nonetheless, only two studies provided genome-wide scans for genetic associations to these conditions (Bustamante et al., 2016; Davila et al., 2010).

The general trend in the field of complex traits is to shift from GWAS to next-generation sequencing approaches (exome or genome sequencing). These latter provide several advantages over GWASs, which mainly derive from the possibility to identify rare or private risk variants. However, next-generation approaches require sample sizes even larger than GWASs (Auer et al., 2016; Zuk et al., 2014) and the amount of phenotypic variance that is explained by rare penetrant variants may largely differ among traits. We consider that important knowledge on infectious disease susceptibility (and related traits) can be still gained by GWASs, especially for those conditions that have never been investigated using this approach.

A promising strategy for future GWASs will be to leverage information from the host's and pathogen's genomes. An interesting step forward in this direction came from a study that generated human genome-wide genotyping data of antiretroviral naive patients and almost complete HIV-1 genome sequences to systematically search for associations between host and virus variants (genome-to-genome scan) (Bartha et al., 2013). The authors found strong associations between SNPs that tag *HLA* class I alleles and viral mutations in CTL (cytotoxic T lymphocyte) epitopes. These results clearly highlight the selective pressure imposed by the host immune system on the viral genome. No signals were detected outside the *HLA* class I loci and, on the viral genome, most selected sites were located in Gag and Nef. However, the majority of host-associated HIV-1 mutations were found to have no or little effect on viral load, suggesting that the virus can compensate for selective pressure with little fitness cost (Bartha et al., 2013). More recently, Ansari et al. (2017) performed a genome-to-genome scans in patients chronically infected with HCV. As in the HIV-1 study, the authors found that the adaptive immune system exerts a selective pressure on the viral genome and drives the evolution of several positions across the HCV genome. Importantly, Ansari and coworkers also showed that the host genotype for a functional *IFNL4* variant modulates viral load only when the individuals are infected by a virus that carries a specific amino acid residue (serine) at position 2414 in the NS5A protein. This result clearly indicates that the host and viral genomes interact to determine the control of infection (Ansari et al., 2017). The majority of patients recruited in the study were infected with genotype 3 and HCV is genetically heterogeneous, suggesting that other and possibly different interactions exist in patients infected by distinct HCV genotypes.

The functional polymorphism in *IFNL4* is a dinucleotide variant (ss469415590, TT/ΔG) and the effect of the “favorable” TT allele is recessive (Prokunina-Olsson et al., 2013). This finding highlights the possible relevance of non-additive models in genetic associations. In

particular, overodominant models may be particularly worth exploring in the field of infectious diseases. Remarkable examples of heterozygote advantage include those described for *HBB* and *G6PD* in relation to malaria. Heterozygosity at *HLA* genes has also been shown to protect against different infections (reviewed in (Quintana-Murci, 2016)), and the same is true for a common variant in *TIRAP*, with heterozygotes protected from malaria, invasive pneumococcal disease, bacteremia, and TB (Khor et al., 2007). Heterozygosity for a common polymorphism in *PRNP* also confers relative resistance to prion diseases (Mead et al., 2003). Overdominance causes multiple alleles to be maintained at a locus via balancing selection (reviewed in (Quintana-Murci, 2016)). A well-known example of this phenomenon is described above for the *FUT2* gene. The maintenance of multiple ABO histo-blood groups, which most likely resulted from the selective pressure exerted by different pathogens, is also due to balancing selection (reviewed in (Quintana-Murci, 2016)). Several works have indicated that targets of balancing selection in primate genomes have often evolved in response to pathogen-driven selective pressures (Leffler et al., 2013; Ferrer-Admetlla et al., 2008; Azevedo et al., 2015; Fumagalli and Sironi, 2014), making overdominance an appealing model to test for resistance against infection. It should however be noted that the action of balancing selection does not necessarily imply that heterozygotes are protected against a specific diseases. Epitomal in this respect is the case of *FUT2* described above, as well as that of *ABO*: individuals with O histo-blood group are protected against severe malaria and cerebral malaria, but at higher risk of developing highly symptomatic cholera infection (Malaria Genomic Epidemiology Network and Malaria Genomic Epidemiology Network, 2014; Cooling, 2015). Interestingly, large-scale studies that focused on specific variants involved in resistance to malaria (Malaria Genomic Epidemiology Network and Malaria Genomic Epidemiology Network, 2014; Clarke et al., 2017) indicated that *G6PD* deficiency also results in different susceptibility phenotypes. Thus, the level of *G6PD* activity is associated with decreased risk of cerebral malaria, but with increased risk of severe malarial anaemia (Malaria Genomic Epidemiology Network and Malaria Genomic Epidemiology Network, 2014; Clarke et al., 2017). Moreover, by using a Bayesian statistical framework that allows for heterogeneity of effects across populations and phenotypes, the authors showed that homozygotes for the derived allele of a variant in the 5′ upstream region of *CD40LG* have significantly reduced risk of severe malaria in The Gambia, but significantly increased risk in Kenya (Malaria Genomic Epidemiology Network and Malaria Genomic Epidemiology Network, 2014). Finally, a significant epistatic interaction was noted between the *HbC* variant and an SNP in *ATP2B4*, this latter encoding a major erythrocyte calcium channel (Malaria Genomic Epidemiology Network and Malaria Genomic Epidemiology Network, 2014). Overall, these results indicate that models of genetic resistance/susceptibility are often complex and that statistical methods that incorporate heterogeneity across populations and phenotypes may improve the power and reliability of GWASs.

For infectious diseases, a particular role may be played by interactions within *HLA* genes or among *HLA* variants and polymorphisms located outside the major histocompatibility complex. One example of this latter scenario relates to polymorphic variants in *HLA-C* and in the *MIR148A* gene (for microRNA-148a, mir-148a). Kulkarni et al. (2011) identified a polymorphism in the 3'UTR of *HLA-C* which affects a miR-148a binding site and associates with HLA-C expression levels, as well as with HIV-1 control. More recently, the same authors showed that an insertion/deletion polymorphism flanking *MIR148A* modulates the expression of this microRNA and the level of HIV-1 control only in individuals carrying *HLA-C* alleles with an intact miR-148a binding site. The *MIR148A* variant has no effect on HIV-1 control among subjects who carry *HLA-C* alleles that do not bind miR-148A (Kulkarni et al., 2013). Situations similar to the one described by Kulkarni and coworkers may be common and may be particularly important for *HLA* class I and *KIR* loci, as they biologically interact as binding partners. For instance, epistatic interactions among specific *KIR* and *HLA* loci have been shown to modulate the progression to AIDS (Hancock et al., 2008; Gaudieri et al., 2005; Martin et al., 2007), as well as the spontaneous (Thons et al., 2017; Khakoo et al., 2004) and therapy-induced clearance of HCV infection (Ahlenstiel et al., 2008). Likewise, interactions within the MHC may be common and relevant in modulating infection-related phenotypes. Indeed, it was recently shown that non-additive and interaction effects within *HLA* loci are widespread and modulate the risk of different autoimmune diseases (Lenz et al., 2015).

Taking these possibilities into account would certainly benefit the discovery of novel genetic effects modulating infection susceptibility or progression.

Finally, we note that, as recently highlighted, association studies have been dramatically skewed in terms of population inclusion: a 2016 survey of GWASs in the Catalog indicated that 81% of analyzed samples were of European ancestry and 14% of Asian ancestry (Popejoy and Fullerton, 2016). All other populations remained severely underrepresented. This trend is somehow attenuated in the studies we reviewed herein, as populations of Asian origin were included in > 33% of studies (most of them on HBV, HCV, and mycobacterial infections), whereas 14% and 17% of GWASs analyzed at least one cohort of African or Hispanic/Latino ancestry, respectively. However, only two studies, both of them on prion diseases, included Pacific Islanders (from Papua New Guinea) and no GWAS recruited Australian aborigines or other native peoples. These percentages clearly highlight the need to extend GWASs analysis for infectious diseases to under-represented populations. This is required to ensure that the benefits of research are equally distributed, especially in light of the recent evidence of limited portability of GWAS results across populations (Martin et al., 2017).

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References

Ahlenstiel, G., Martin, M.P., Gao, X., Carrington, M., Rehermann, B., 2008. Distinct KIR/HLA compound genotypes affect the kinetics of human antiviral natural killer cell responses. J. Clin. Invest. 118, 1017–1026.

Akkarathamrongsin, S., Thong, V.D., Payungporn, S., Poovorawan, K., Prapunwattana, P., Poovorawan, Y., Tangkijvanich, P., 2014. IFNL3 (IL28B) and IFNL4 polymorphisms are associated with treatment response in Thai patients infected with HCV genotype 1, but not with genotypes 3 and 6. J. Med. Virol. 86, 1482–1490.

Alhaddad, H., Khan, R., Grahn, R.A., Gandolfi, B., Mullikin, J.C., Cole, S.A., Gruffydd-Jones, T.J., Haggstrom, J., Lohi, H., Longeri, M., Lyons, L.A., 2013. Extent of linkage disequilibrium in the domestic cat, *Felis silvestris* catus, and its breeds. PLoS One 8, e53537.

Alpay, F., Zare, Y., Kamalludin, M.H., Huang, X., Shi, X., Shook, G.E., Collins, M.T., Kirkpatrick, B.W., 2014. Genome-wide association study of susceptibility to infection by *Mycobacterium avium* subspecies paratuberculosis in Holstein cattle. PLoS One 9, e111704.

Ansari, M.A., Pedergnana, V., L C Ip, C., Magri, A., Von Delft, A., Bonsall, D., Chaturvedi, N., Bartha, I., Smith, D., Nicholson, G., McVean, G., Trebes, A., Piazza, P., Fellay, J., Cooke, G., Foster, G.R., STOP-HCV Consortium, Hudson, E., McLauchlan, J., Simmonds, P., Bowden, R., Klenerman, P., Barnes, E., Spencer, C.C.A., 2017. Genome-to-genome analysis highlights the effect of the human innate and adaptive immune systems on the hepatitis C virus. Nat. Genet.

Atianand, M.K., Fitzgerald, K.A., 2014. Long non-coding RNAs and control of gene expression in the immune system. Trends Mol. Med. 20, 623–631.

Auer, P.L., Reiner, A.P., Wang, G., Kang, H.M., Abecasis, G.R., Altshuler, D., Bamshad, M.J., Nickerson, D.A., Tracy, R.P., Rich, S.S., NHLBI GO Exome Sequencing Project, Leal, S.M., 2016. Guidelines for large-scale sequence-based complex trait association studies: lessons learned from the NHLBI exome sequencing project. Am. J. Hum. Genet. 99, 791–801.

Aylor, D.L., Valdar, W., Foulds-Mathes, W., Buus, R.J., Verdugo, R.A., Baric, R.S., Ferris, M.T., Frelinger, J.A., Heise, M., Frieman, M.B., Gralinski, L.E., Bell, T.A., Didion, J.D., Hua, K., Nehrenberg, D.L., Powell, C.L., Steigerwalt, J., Xie, Y., Kelada, S.N., Collins, F.S., Yang, I.V., Schwartz, D.A., Branstetter, L.A., Chesler, E.J., Miller, D.R., Spence, J., Liu, E.Y., McMillan, L., Sarkar, A., Wang, J., Wang, W., Zhang, Q., Broman, K.W., Korstanje, R., Durrant, C., Mott, R., Iraqi, F.A., Pomp, D., Threadgill, D., de Villena, F.P., Churchill, G.A., 2011. Genetic analysis of complex traits in the emerging Collaborative Cross. Genome Res. 21, 1213–1222.

Azevedo, L., Serrano, C., Amorim, A., Cooper, D.N., 2015. Trans-species polymorphism in humans and the great apes is generally maintained by balancing selection that modulates the host immune response. Hum. Genomics 9 (21-015-0043-1).

Badke, Y.M., Bates, R.O., Ernst, C.W., Schwab, C., Steibel, J.P., 2012. Estimation of linkage disequilibrium in four US pig breeds. BMC Genomics 13 (24-2164-13-24).

Baker, M.G., Barnard, L.T., Kvalsvig, A., Verrall, A., Zhang, J., Keall, M., Wilson, N., Wall, T., Howden-Chapman, P., 2012. Increasing incidence of serious infectious diseases and inequalities in New Zealand: a national epidemiological study. Lancet 379, 1112–1119.

Band, G., Le, Q.S., Jostins, L., Pirinen, M., Kivinen, K., Jallow, M., Sisay-Joof, F., Bojang, K., Pinder, M., Sirugo, G., Conway, D.J., Nyirongo, V., Kachala, D., Molyneux, M., Taylor, T., Ndila, C., Peshu, N., Marsh, K., Williams, T.N., Alcock, D., Andrews, R., Edkins, S., Gray, E., Hubbart, C., Jeffreys, A., Rowlands, K., Schuldt, K., Clark, T.G., Small, K.S., Teo, Y.Y., Kwiatkowski, D.P., Rockett, K.A., Barrett, J.C., Spencer, C.C., Malaria Genomic Epidemiology Network, Malaria Genomic Epidemiological Network, 2013. Imputation-based meta-analysis of severe malaria in three African populations. PLoS Genet. 9, e1003509.

Barrett, J.C., Hansoul, S., Nicolae, D.L., Cho, J.H., Duerr, R.H., Rioux, J.D., Brant, S.R., Silverberg, M.S., Taylor, K.D., Barmada, M.M., Bitton, A., Dassopoulos, T., Datta, L.W., Green, T., Griffiths, A.M., Kistner, E.O., Murtha, M.T., Regueiro, M.D., Rotter, J.I., Schumm, L.P., Steinhart, A.H., Targan, S.R., Xavier, R.J., NIDDK IBD Genetics Consortium, Libioulle, C., Sandor, C., Lathrop, M., Belaiche, J., Dewit, O., Gut, I., Heath, S., Laukens, D., Mni, M., Rutgeerts, P., Van Gossum, A., Zelenika, D., Franchimont, D., Hugot, J.P., de Vos, M., Vermeire, S., Louis, E., Belgian-French IBD Consortium, Wellcome Trust Case Control Consortium, Cardon, L.R., Anderson, C.A., Drummond, H., Nimmo, E., Ahmad, T., Prescott, N.J., Onnie, C.M., Fisher, S.A., Marchini, J., Ghori, J., Bumpstead, S., Gwilliam, R., Tremelling, M., Deloukas, P., Mansfield, J., Jewell, D., Satsangi, J., Mathew, C.G., Parkes, M., Georges, M., Daly, M.J., 2008. Genome-wide association defines more than 30 distinct susceptibility loci for Crohn's disease. Nat. Genet. 40, 955–962.

Bartha, I., Carlson, J.M., Brumme, C.J., McLaren, P.J., Brumme, Z.L., John, M., Haas, D.W., Martinez-Picado, J., Dalmau, J., Lopez-Galindez, C., Casado, C., Rauch, A., Gunthard, H.F., Bernasconi, E., Vernazza, P., Klimkait, T., Yerly, S., O'Brien, S.J., Listgarten, J., Pfeifer, N., Lippert, C., Fusi, N., Kutalik, Z., Allen, T.M., Muller, V., Harrigan, P.R., Heckerman, D., Telenti, A., Fellay, J., 2013. A genome-to-genome analysis of associations between human genetic variation, HIV-1 sequence diversity, and viral control. elife 2, e01123.

Bennett, S.N., Caporaso, N., Fitzpatrick, A.L., Agrawal, A., Barnes, K., Boyd, H.A., Cornelis, M.C., Hansel, N.N., Heiss, G., Heit, J.A., Kang, J.H., Kittner, S.J., Kraft, P., Lowe, W., Marazita, M.L., Monroe, K.R., Pasquale, L.R., Ramos, E.M., van Dam, R.M., Udren, J., Williams, K., GENEVA Consortium, 2011. Phenotype harmonization and cross-study collaboration in GWAS consortia: the GENEVA experience. Genet. Epidemiol. 35, 159–173.

Bermingham, M.L., Bishop, S.C., Woolliams, J.A., Pong-Wong, R., Allen, A.R., McBride, S.H., Ryder, J.J., Wright, D.M., Skuce, R.A., McDowell, S.W., Glass, E.J., 2014. Genome-wide association study identifies novel loci associated with resistance to bovine tuberculosis. Heredity (Edinb) 112, 543–551.

Blackwell, C.C., Jonsdottir, K., Hanson, M., Todd, W.T., Chaudhuri, A.K., Mathew, B., Brettle, R.P., Weir, D.M., 1986a. Non-secretion of ABO antigens predisposing to infection by *Neisseria meningitidis* and *Streptococcus pneumoniae*. Lancet 2, 284–285.

Blackwell, C.C., Jonsdottir, K., Hanson, M.F., Weir, D.M., 1986b. Non-secretion of ABO blood group antigens predisposing to infection by *Haemophilus influenzae*. Lancet 2, 687.

Booth, D.R., Ahlenstiel, G., George, J., 2012. Pharmacogenomics of hepatitis C infections: personalizing therapy. Genome Med. 4, 99.

Boyko, A.R., Quignon, P., Li, L., Schoenebeck, J.J., Degenhardt, J.D., Lohmueller, K.E., Zhao, K., Brisbin, A., Parker, H.G., vonHoldt, B.M., Cargill, M., Auton, A., Reynolds, A., Elkahloun, A.G., Castelhano, M., Mosher, D.S., Sutter, N.B., Johnson, G.S., Novembre, J., Hubisz, M.J., Siepel, A., Wayne, R.K., Bustamante, C.D., Ostrander, E.A., 2010. A simple genetic architecture underlies morphological variation in dogs. PLoS Biol. 8, e1000451.

Braveman, P., 2011. Accumulating knowledge on the social determinants of health and infectious disease. Public Health Rep. 126 (Suppl. 3), 28–30.

Brinkmann, V., Reichard, U., Goosmann, C., Fauler, B., Uhlemann, Y., Weiss, D.S., Weinrauch, Y., Zychlinsky, A., 2004. Neutrophil extracellular traps kill bacteria. Science 303, 1532–1535.

Brites, D., Gagneux, S., 2015. Co-evolution of *Mycobacterium tuberculosis* and Homo sapiens. Immunol. Rev. 264, 6–24.

Brown, E.L., Below, J.E., Fischer, R.S., Essigmann, H.T., Hu, H., Huff, C., Robinson, D.A., Petty, L.E., Aguilar, D., Bell, G.I., Hanis, C.L., 2015. Genome-wide association study of staphylococcus aureus carriage in a community-based sample of Mexican-Americans in Starr County, Texas. PLoS One 10, e0142130.

Bryc, K., Velez, C., Karafet, T., Moreno-Estrada, A., Reynolds, A., Auton, A., Hammer, M., Bustamante, C.D., Ostrer, H., 2010. Colloquium paper: genome-wide patterns of population structure and admixture among Hispanic/Latino populations. Proc. Natl. Acad. Sci. U. S. A. 107 (Suppl. 2), 8954–8961.

Bustamante, M., Standl, M., Bassat, Q., Vilor-Tejedor, N., Medina-Gomez, C., Bonilla, C., Ahluwalia, T.S., Bacelis, J., Bradfield, J.P., Tiesler, C.M., Rivadeneira, F., Ring, S., Vissing, N.H., Fink, N.R., Jugessur, A., Mentch, F.D., Ballester, F., Kriebel, J., Kiefte-de Jong, J.C., Wolsk, H.M., Llop, S., Thiering, E., Beth, S.A., Timpson, N.J., Andersen, J., Schulz, H., Jaddoe, V.W., Evans, D.M., Waage, J., Hakonarson, H., Grant, S.F., Jacobsson, B., Bonnelykke, K., Bisgaard, H., Davey Smith, G., Moll, H.A., Heinrich, J., Estivill, X., Sunyer, J., 2016. A genome-wide association meta-analysis of diarrhoeal disease in young children identifies FUT2 locus and provides plausible biological pathways. Hum. Mol. Genet. 25, 4127–4142.

Carlsson, B., Kindberg, E., Buesa, J., Rydell, G.E., Lidon, M.F., Montava, R., Abu Mallouh, R., Grahn, A., Rodriguez-Diaz, J., Bellido, J., Arnedo, A., Larson, G., Svensson, L., 2009. The G428A nonsense mutation in FUT2 provides strong but not absolute protection against symptomatic GII.4 Norovirus infection. PLoS One 4, e5593.

Caws, M., Thwaites, G., Dunstan, S., Hawn, T.R., Lan, N.T., Thuong, N.T., Stepniewska, K., Huyen, M.N., Bang, N.D., Loc, T.H., Gagneux, S., van Soolingen, D., Kremer, K., van der Sande, M., Small, P., Anh, P.T., Chinh, N.T., Quy, H.T., Duyen, N.T., Tho, D.Q., Hieu, N.T., Torok, E., Hien, T.T., Dung, N.H., Nhu, N.T., Duy, P.M., van Vinh Chau, N., Farrar, J., 2008. The influence of host and bacterial genotype on the development of disseminated disease with *Mycobacterium tuberculosis*. PLoS Pathog. 4, e1000034.

Chaim, W., Foxman, B., Sobel, J.D., 1997. Association of recurrent vaginal candidiasis and secretory ABO and Lewis phenotype. J Infect Dis 176, 828–830.

Chakraborty, R., Ferrell, R.E., Stern, M.P., Haffner, S.M., Hazuda, H.P., Rosenthal, M., 1986. Relationship of prevalence of non-insulin-dependent diabetes mellitus to Amerindian admixture in the Mexican Americans of San Antonio, Texas. Genet. Epidemiol. 3, 435–454.

Chang, S.W., Fann, C.S., Su, W.H., Wang, Y.C., Weng, C.C., Yu, C.J., Hsu, C.L., Hsieh, A.R., Chien, R.N., Chu, C.M., Tai, D.I., 2014. A genome-wide association study on chronic HBV infection and its clinical progression in male Han-Taiwanese. PLoS One 9, e99724.

Chantarangsu, S., Mushiroda, T., Mahasirimongkol, S., Kiertiburanakul, S., Sungkanuparph, S., Manosuthi, W., Tantisiriwat, W., Charoenyingwattana, A., Sura, T., Takahashi, A., Kubo, M., Kamatani, N., Chantratita, W., Nakamura, Y., 2011. Genome-wide association study identifies variations in 6p21.3 associated with nevirapine-induced rash. Clin. Infect. Dis. 53, 341–348.

Chen, D., McKay, J.D., Clifford, G., Gaborieau, V., Chabrier, A., Waterboer, T., Zaridze, D., Lissowska, J., Rudnai, P., Fabianova, E., Bencko, V., Janout, V., Foretova, L., Mates, I.N., Szeszenia-Dabrowska, N., Curado, M.P., Koifman, S., Menezes, A., Wunsch-Filho, V., Eluf-Neto, J., Fernandez Garrote, L., Matos, E., Zelenika, D., Boland, A., Boffetta, P., Pawlita, M., Lathrop, M., Brennan, P., 2011. Genome-wide association study of HPV seropositivity. Hum. Mol. Genet. 20, 4714–4723.

Chen, D., Juko-Pecirep, I., Hammer, J., Ivansson, E., Enroth, S., Gustavsson, I., Feuk, L., Magnusson, P.K., McKay, J.D., Wilander, E., Gyllensten, U., 2013. Genome-wide association study of susceptibility loci for cervical cancer. J. Natl. Cancer Inst. 105, 624–633.

Chen, D., Enroth, S., Liu, H., Sun, Y., Wang, H., Yu, M., Deng, L., Xu, S., Gyllensten, U., 2016. Pooled analysis of genome-wide association studies of cervical intraepithelial neoplasia 3 (CIN3) identifies a new susceptibility locus. Oncotarget 7, 42216–42224.

Chimusa, E.R., Zaitlen, N., Daya, M., Moller, M., van Helden, P.D., Mulder, N.J., Price, A.L., Hoal, E.G., 2014. Genome-wide association study of ancestry-specific TB risk in the South African Coloured population. Hum. Mol. Genet. 23, 796–809.

Choi, E.H., Nutman, T.B., Chanock, S.J., 2003. Genetic variation in immune function and susceptibility to human filariasis. Expert. Rev. Mol. Diagn. 3, 367–374.

Churchill, G.A., Airey, D.C., Allayee, H., Angel, J.M., Attie, A.D., Beatty, J., Beavis, W.D., Belknap, J.K., Bennett, B., Berrettini, W., Bleich, A., Bogue, M., Broman, K.W., Buck, K.J., Buckler, E., Burmeister, M., Chesler, E.J., Cheverud, J.M., Clapcote, S., Cook, M.N., Cox, R.D., Crabbe, J.C., Crusio, W.E., Darvasi, A., Deschepper, C.F., Doerge, R.W., Farber, C.R., Forejt, J., Gaile, D., Garlow, S.J., Geiger, H., Gershenfeld, H., Gordon, T., Gu, J., Gu, W., de Haan, G., Hayes, N.L., Heller, C., Himmelbauer, H., Hitzemann, R., Hunter, K., Hsu, H.C., Iraqi, F.A., Ivandic, B., Jacob, H.J., Jansen, R.C., Jepsen, K.J., Johnson, D.K., Johnson, T.E., Kempermann, G., Kendziorski, C., Kotb, M., Kooy, R.F., Llamas, B., Lammert, F., Lassalle, J.M., Lowenstein, P.R., Lu, L., Lusis, A., Manly, K.F., Marcucio, R., Matthews, D., Medrano, J.F., Miller, D.R., Mittleman, G., Mock, B.A., Mogil, J.S., Montagutelli, X., Morahan, G., Morris, D.G., Mott, R., Nadeau, J.H., Nagase, H., Nowakowski, R.S., O'Hara, B.F., Osadchuk, A.V., Page, G.P., Paigen, B., Paigen, K., Palmer, A.A., Pan, H.J., Peltonen-Palotie, L., Peirce, J., Pomp, D., Pravenec, M., Prows, D.R., Qi, Z., Reeves, R.H., Roder, J., Rosen, G.D., Schadt, E.E., Schalkwyk, L.C., Seltzer, Z., Shimomura, K., Shou, S., Sillanpaa, M.J., Siracusa, L.D., Snoeck, H.W., Spearow, J.L., Svenson, K., Tarantino, L.M., Threadgill, D., Toth, L.A., Valdar, W., de Villena, F.P., Warden, C., Whatley, S., Williams, R.W., Wiltshire, T., Yi, N., Zhang, D., Zhang, M., Zou, F., Complex Trait Consortium, 2004. The collaborative cross, a community resource for the genetic analysis of complex traits. Nat. Genet. 36, 1133–1137.

Clark, P.J., Thompson, A.J., Zhu, M., Vock, D.M., Zhu, Q., Ge, D., Patel, K., Harrison, S.A., Urban, T.J., Naggie, S., Fellay, J., Tillmann, H.L., Shianna, K., Noviello, S., Pedicone, L.D., Esteban, R., Kwo, P., Sulkowski, M.S., Afdhal, N., Albrecht, J.K., Goldstein, D.B., McHutchison, J.G., Muir, A.J., IDEAL investigators, 2012. Interleukin 28B polymorphisms are the only common genetic variants associated with low-density lipoprotein cholesterol (LDL-C) in genotype-1 chronic hepatitis C and determine the association between LDL-C and treatment response. J. Viral Hepat. 19, 332–340.

Clarke, G.M., Rockett, K., Kivinen, K., Hubbart, C., Jeffreys, A.E., Rowlands, K., Jallow, M., Conway, D.J., Bojang, K.A., Pinder, M., Usen, S., Sisay-Joof, F., Sirugo, G., Toure, O., Thera, M.A., Konate, S., Sissoko, S., Niangaly, A., Poudiougou, B., Mangano, V.D., Bougouma, E.C., Sirima, S.B., Modiano, D., Amenga-Etego, L.N., Ghansah, A., Koram, K.A., Wilson, M.D., Enimil, A., Evans, J., Amodu, O.K., Olaniyan, S., Apinjoh, T., Mugri, R., Ndi, A., Ndila, C.M., Uyoga, S., Macharia, A., Peshu, N., Williams, T.N., Manjurano, A., Sepulveda, N., Clark, T.G., Riley, E., Drakeley, C., Reyburn, H., Nyirongo, V., Kachala, D., Molyneux, M., Dunstan, S.J., Phu, N.H., Quyen, N.N., Thai, C.Q., Hien, T.T., Manning, L., Laman, M., Siba, P., Karunajeewa, H., Allen, S., Allen, A., Davis, T.M., Michon, P., Mueller, I., Molloy, S.F., Campino, S., Kerasidou, A., Cornelius, V.J., Hart, L., Shah, S.S., Band, G., Spencer, C.C., Agbenyega, T., Achidi, E., Doumbo, O.K., Farrar, J., Marsh, K., Taylor, T., Kwiatkowski, D.P., MalariaGEN Consortium, 2017. Characterisation of the opposing effects of G6PD deficiency on cerebral malaria and severe malarial anaemia. elife 6. http://dx.doi.org/10.7554/eLife.15085.

Cooling, L., 2015. Blood groups in infection and host susceptibility. Clin. Microbiol. Rev. 28, 801–870.

Cortes, A., Brown, M.A., 2011. Promise and pitfalls of the Immunochip. Arthritis Res. Ther. 13, 101.

Craven, M., Mansfield, C.S., Simpson, K.W., 2011. Granulomatous colitis of boxer dogs. Vet. Clin. North Am. Small Anim. Pract. 41, 433–445.

van Crevel, R., Parwati, I., Sahiratmadja, E., Marzuki, S., Ottenhoff, T.H., Netea, M.G., van der Ven, A., Nelwan, R.H., van der Meer, J.W., Alisjahbana, B., van de Vosse, E., 2009. Infection with *Mycobacterium tuberculosis* Beijing genotype strains is associated with polymorphisms in SLC11A1/NRAMP1 in Indonesian patients with tuberculosis. J Infect Dis 200, 1671–1674.

Crosslin, D.R., Carrell, D.S., Burt, A., Kim, D.S., Underwood, J.G., Hanna, D.S., Comstock, B.A., Baldwin, E., de Andrade, M., Kullo, I.J., Tromp, G., Kuivaniemi, H., Borthwick, K.M., McCarty, C.A., Peissig, P.L., Doheny, K.F., Pugh, E., Kho, A., Pacheco, J., Hayes, M.G., Ritchie, M.D., Verma, S.S., Armstrong, G., Stallings, S., Denny, J.C., Carroll, R.J., Crawford, D.C., Crane, P.K., Mukherjee, S., Bottinger, E., Li, R., Keating, B., Mirel, D.B., Carlson, C.S., Harley, J.B., Larson, E.B., Jarvik, G.P., 2015. Genetic variation in the HLA region is associated with susceptibility to herpes zoster. Genes Immun. 16, 1–7.

Curtis, J., Luo, Y., Zenner, H.L., Cuchet-Lourenco, D., Wu, C., Lo, K., Maes, M., Alisaac, A.,

Stebbings, E., Liu, J.Z., Kopanitsa, L., Ignatyeva, O., Balabanova, Y., Nikolayevskyy, V., Baessmann, I., Thye, T., Meyer, C.G., Nurnberg, P., Horstmann, R.D., Drobniewski, F., Plagnol, V., Barrett, J.C., Nejentsev, S., 2015. Susceptibility to tuberculosis is associated with variants in the ASAP1 gene encoding a regulator of dendritic cell migration. Nat. Genet. 47, 523–527.
Custer, B., Sullivan, S.D., Hazlet, T.K., Iloeje, U., Veenstra, D.L., Kowdley, K.V., 2004. Global epidemiology of hepatitis B virus. J. Clin. Gastroenterol. 38, S158–68.
Davila, S., Wright, V.J., Khor, C.C., Sim, K.S., Binder, A., Breunis, W.B., Inwald, D., Nadel, S., Betts, H., Carrol, E.D., de Groot, R., Hermans, P.W., Hazelzet, J., Emonts, M., Lim, C.C., Kuijpers, T.W., Martinon-Torres, F., Salas, A., Zenz, W., Levin, M., Hibberd, M.L., International Meningococcal Genetics Consortium, 2010. Genome-wide association study identifies variants in the CFH region associated with host susceptibility to meningococcal disease. Nat. Genet. 42, 772–776.
Dekkers, J., Rowland, R.R., Lunney, J.K., Plastow, G., 2017. Host genetics of response to porcine reproductive and respiratory syndrome in nursery pigs. Vet. Microbiol.
DeLorenze, G.N., Nelson, C.L., Scott, W.K., Allen, A.S., Ray, G.T., Tsai, A.L., Quesenberry Jr., C.P., Fowler Jr., V.G., 2016. Polymorphisms in HLA class II genes are associated with susceptibility to *Staphylococcus aureus* infection in a White Population. J Infect Dis 213, 816–823.
Dewan, A., Liu, M., Hartman, S., Zhang, S.S., Liu, D.T., Zhao, C., Tam, P.O., Chan, W.M., Lam, D.S., Snyder, M., Barnstable, C., Pang, C.P., Hoh, J., 2006. HTRA1 promoter polymorphism in wet age-related macular degeneration. Science 314, 989–992.
Dold, C., Holland, C.V., 2011. Investigating the underlying mechanism of resistance to Ascaris infection. Microbes Infect. 13, 624–631.
Duggal, P., Thio, C.L., Wojcik, G.L., Goedert, J.J., Mangia, A., Latanich, R., Kim, A.Y., Lauer, G.M., Chung, R.T., Peters, M.G., Kirk, G.D., Mehta, S.H., Cox, A.L., Khakoo, S.I., Alric, L., Cramp, M.E., Donfield, S.M., Edlin, B.R., Tobler, L.H., Busch, M.P., Alexander, G., Rosen, H.R., Gao, X., Abdel-Hamid, M., Apps, R., Carrington, M., Thomas, D.L., 2013. Genome-wide association study of spontaneous resolution of hepatitis C virus infection: data from multiple cohorts. Ann. Intern. Med. 158, 235–245.
Dunstan, S.J., Hue, N.T., Han, B., Li, Z., Tram, T.T., Sim, K.S., Parry, C.M., Chinh, N.T., Vinh, H., Lan, N.P., Thieu, N.T., Vinh, P.V., Koirala, S., Dongol, S., Arjyal, A., Karkey, A., Shilpakar, O., Dolecek, C., Foo, J.N., Phuong le, T., Lanh, M.N., Do, T., Aung, T., Hon, D.N., Teo, Y.Y., Hibberd, M.L., Anders, K.L., Okada, Y., Raychaudhuri, S., Simmons, C.P., Baker, S., de Bakker, P.I., Basnyat, B., Hien, T.T., Farrar, J.J., Khor, C.C., 2014. Variation at HLA-DRB1 is associated with resistance to enteric fever. Nat. Genet. 46, 1333–1336.
Durrant, C., Tayem, H., Yalcin, B., Cleak, J., Goodstadt, L., de Villena, F.P., Mott, R., Iraqi, F.A., 2011. Collaborative Cross mice and their power to map host susceptibility to *Aspergillus fumigatus* infection. Genome Res. 21, 1239–1248.
Eu-Ahsunthornwattana, J., Miller, E.N., Fakiola, M., Wellcome Trust Case Control Consortium 2, Jeronimo, S.M., Blackwell, J.M., Cordell, H.J., 2014. Comparison of methods to account for relatedness in genome-wide association studies with family-based data. PLoS Genet. 10, e1004445.
European Association for the Study of the Liver, 2011. EASL Clinical Practice Guidelines: management of hepatitis C virus infection. J. Hepatol. 55, 245–264.
Fabregat, A., Sidiropoulos, K., Garapati, P., Gillespie, M., Hausmann, K., Haw, R., Jassal, B., Jupe, S., Korninger, F., McKay, S., Matthews, L., May, B., Milacic, M., Rothfels, K., Shamovsky, V., Webber, M., Weiser, J., Williams, M., Wu, G., Stein, L., Hermjakob, H., D'Eustachio, P., 2016. The Reactome pathway knowledgebase. Nucleic Acids Res. 44, D481–7.
Feenstra, B., Pasternak, B., Geller, F., Carstensen, L., Wang, T., Huang, F., Eitson, J.L., Hollegaard, M.V., Svanstrom, H., Vestergaard, M., Hougaard, D.M., Schoggins, J.W., Jan, L.Y., Melbye, M., Hviid, A., 2014. Common variants associated with general and MMR vaccine-related febrile seizures. Nat. Genet. 46, 1274–1282.
Fellay, J., Shianna, K.V., Ge, D., Colombo, S., Ledergerber, B., Weale, M., Zhang, K., Gumbs, C., Castagna, A., Cossarizza, A., Cozzi-Lepri, A., De Luca, A., Easterbrook, P., Francioli, P., Mallal, S., Martinez-Picado, J., Miro, J.M., Obel, N., Smith, J.P., Wyniger, J., Descombes, P., Antonarakis, S.E., Letvin, N.L., McMichael, A.J., Haynes, B.F., Telenti, A., Goldstein, D.B., 2007. A whole-genome association study of major determinants for host control of HIV-1. Science 317, 944–947.
Fellay, J., Ge, D., Shianna, K.V., Colombo, S., Ledergerber, B., Cirulli, E.T., Urban, T.J., Zhang, K., Gumbs, C.E., Smith, J.P., Castagna, A., Cozzi-Lepri, A., De Luca, A., Easterbrook, P., Gunthard, H.F., Mallal, S., Mussini, C., Dalmau, J., Martinez-Picado, J., Miro, J.M., Obel, N., Wolinsky, S.M., Martinson, J.J., Detels, R., Margolick, J.B., Jacobson, L.P., Descombes, P., Antonarakis, S.E., Beckmann, J.S., O'Brien, S.J., Letvin, N.L., McMichael, A.J., Haynes, B.F., Carrington, M., Feng, S., Telenti, A., Goldstein, D.B., NIAID Center for HIV/AIDS Vaccine Immunology (CHAVI), 2009. Common genetic variation and the control of HIV-1 in humans. PLoS Genet. 5, e1000791.
Fellay, J., Thompson, A.J., Ge, D., Gumbs, C.E., Urban, T.J., Shianna, K.V., Little, L.D., Qiu, P., Bertelsen, A.H., Watson, M., Warner, A., Muir, A.J., Brass, C., Albrecht, J., Sulkowski, M., McHutchison, J.G., Goldstein, D.B., 2010. ITPA gene variants protect against anaemia in patients treated for chronic hepatitis C. Nature 464, 405–408.
Ferrer-Admetlla, A., Bosch, E., Sikora, M., Marques-Bonet, T., Ramirez-Soriano, A., Muntasell, A., Navarro, A., Lazarus, R., Calafell, F., Bertranpetit, J., Casals, F., 2008. Balancing selection is the main force shaping the evolution of innate immunity genes. J. Immunol. 181, 1315–1322.
Ferris, M.T., Aylor, D.L., Bottomly, D., Whitmore, A.C., Aicher, L.D., Bell, T.A., Bradel-Tretheway, B., Bryan, J.T., Buus, R.J., Gralinski, L.E., Haagmans, B.L., McMillan, L., Miller, D.R., Rosenzweig, E., Valdar, W., Wang, J., Churchill, G.A., Threadgill, D.W., McWeeney, S.K., Katze, M.G., Pardo-Manuel de Villena, F., Baric, R.S., Heise, M.T., 2013. Modeling host genetic regulation of influenza pathogenesis in the collaborative cross. PLoS Pathog. 9, e1003196.
Finlay, E.K., Berry, D.P., Wickham, B., Gormley, E.P., Bradley, D.G., 2012. A genome wide association scan of bovine tuberculosis susceptibility in Holstein-Friesian dairy cattle. PLoS One 7, e30545.
Flint, J., Eskin, E., 2012. Genome-wide association studies in mice. Nat. Rev. Genet. 13, 807–817.
Florez, J.C., Price, A.L., Campbell, D., Riba, L., Parra, M.V., Yu, F., Duque, C., Saxena, R., Gallego, N., Tello-Ruiz, M., Franco, L., Rodriguez-Torres, M., Villegas, A., Bedoya, G., Aguilar-Salinas, C.A., Tusie-Luna, M.T., Ruiz-Linares, A., Reich, D., 2009. Strong association of socioeconomic status with genetic ancestry in Latinos: implications for admixture studies of type 2 diabetes. Diabetologia 52, 1528–1536.
Fowke, K.R., Nagelkerke, N.J., Kimani, J., Simonsen, J.N., Anzala, A.O., Bwayo, J.J., MacDonald, K.S., Ngugi, E.N., Plummer, F.A., 1996. Resistance to HIV-1 infection among persistently seronegative prostitutes in Nairobi, Kenya. Lancet 348, 1347–1351.
Franco-Paredes, C., Jones, D., Rodriguez-Morales, A.J., Santos-Preciado, J.I., 2007. Commentary: improving the health of neglected populations in Latin America. BMC Public Health 7, 11.
Franke, A., McGovern, D.P., Barrett, J.C., Wang, K., Radford-Smith, G.L., Ahmad, T., Lees, C.W., Balschun, T., Lee, J., Roberts, R., Anderson, C.A., Bis, J.C., Bumpstead, S., Ellinghaus, D., Festen, E.M., Georges, M., Green, T., Haritunians, T., Jostins, L., Latiano, A., Mathew, C.G., Montgomery, G.W., Prescott, N.J., Raychaudhuri, S., Rotter, J.I., Schumm, P., Sharma, Y., Simms, L.A., Taylor, K.D., Whiteman, D., Wijmenga, C., Baldassano, R.N., Barclay, M., Bayless, T.M., Brand, S., Buning, C., Cohen, A., Colombel, J.F., Cottone, M., Stronati, L., Denson, T., De Vos, M., D'Inca, R., Dubinsky, M., Edwards, C., Florin, T., Franchimont, D., Gearry, R., Glas, J., Van Gossum, A., Guthery, S.L., Halfvarson, J., Verspaget, H.W., Hugot, J.P., Karban, A., Laukens, D., Lawrance, I., Lemann, M., Levine, A., Libioulle, C., Louis, E., Mowat, C., Newman, W., Panes, J., Phillips, A., Proctor, D.D., Regueiro, M., Russell, R., Rutgeerts, P., Sanderson, J., Sans, M., Seibold, F., Steinhart, A.H., Stokkers, P.C., Torkvist, L., Kullak-Ublick, G., Wilson, D., Walters, T., Targan, S.R., Brant, S.R., Rioux, J.D., D'Amato, M., Weersma, R.K., Kugathasan, S., Griffiths, A.M., Mansfield, J.C., Vermeire, S., Duerr, R.H., Silverberg, M.S., Satsangi, J., Schreiber, S., Cho, J.H., Annese, V., Hakonarson, H., Daly, M.J., Parkes, M., 2010. Genome-wide meta-analysis increases to 71 the number of confirmed Crohn's disease susceptibility loci. Nat. Genet. 42, 1118–1125.
Fumagalli, M., Sironi, M., 2014. Human genome variability, natural selection and infectious diseases. Curr. Opin. Immunol. 30, 9–16.
Fumagalli, M., Cagliani, R., Pozzoli, U., Riva, S., Comi, G.P., Menozzi, G., Bresolin, N., Sironi, M., 2009. Widespread balancing selection and pathogen-driven selection at blood group antigen genes. Genome Res. 19, 199–212.
Garcia-Etxebarria, K., Bracho, M.A., Galan, J.C., Pumarola, T., Castilla, J., Ortiz de Lejarazu, R., Rodriguez-Dominguez, M., Quintela, I., Bonet, N., Garcia-Garcera, M., Dominguez, A., Gonzalez-Candelas, F., Calafell, F., CIBERESP Cases and Controls in Pandemic Influenza Working Group, 2015. No major host genetic risk factor contributed to A(H1N1)2009 influenza severity. PLoS One 10, e0135983.
Gaudieri, S., DeSantis, D., McKinnon, E., Moore, C., Nolan, D., Witt, C.S., Mallal, S.A., Christiansen, F.T., 2005. Killer immunoglobulin-like receptors and HLA act both independently and synergistically to modify HIV disease progression. Genes Immun. 6, 683–690.
Ge, D., Fellay, J., Thompson, A.J., Simon, J.S., Shianna, K.V., Urban, T.J., Heinzen, E.L., Qiu, P., Bertelsen, A.H., Muir, A.J., Sulkowski, M., McHutchison, J.G., Goldstein, D.B., 2009. Genetic variation in IL28B predicts hepatitis C treatment-induced viral clearance. Nature 461, 399–401.
Gingles, N.A., Alexander, J.E., Kadioglu, A., Andrew, P.W., Kerr, A., Mitchell, T.J., Hopes, E., Denny, P., Brown, S., Jones, H.B., Little, S., Booth, G.C., McPheat, W.L., 2001. Role of genetic resistance in invasive pneumococcal infection: identification and study of susceptibility and resistance in inbred mouse strains. Infect. Immun. 69, 426–434.
Gomez, J.A., Wapinski, O.L., Yang, Y.W., Bureau, J.F., Gopinath, S., Monack, D.M., Chang, H.Y., Brahic, M., Kirkegaard, K., 2013. The NeST long ncRNA controls microbial susceptibility and epigenetic activation of the interferon-gamma locus. Cell 152, 743–754.
Graham, J.B., Thomas, S., Swarts, J., McMillan, A.A., Ferris, M.T., Suthar, M.S., Treuting, P.M., Ireton, R., Gale Jr., M., Lund, J.M., 2015. Genetic diversity in the collaborative cross model recapitulates human West Nile virus disease outcomes. MBio 6, e00493–15.
Graham, J.B., Swarts, J.L., Wilkins, C., Thomas, S., Green, R., Sekine, A., Voss, K.M., Ireton, R.C., Mooney, M., Choonoo, G., Miller, D.R., Treuting, P.M., Pardo Manuel de Villena, F., Ferris, M.T., McWeeney, S., Gale Jr., M., Lund, J.M., 2016. A mouse model of chronic West Nile virus disease. PLoS Pathog. 12, e1005996.
Gralinski, L.E., Ferris, M.T., Aylor, D.L., Whitmore, A.C., Green, R., Frieman, M.B., Deming, D., Menachery, V.D., Miller, D.R., Buus, R.J., Bell, T.A., Churchill, G.A., Threadgill, D.W., Katze, M.G., McMillan, L., Valdar, W., Heise, M.T., Pardo-Manuel de Villena, F., Baric, R.S., 2015. Genome wide identification of SARS-CoV susceptibility loci using the collaborative cross. PLoS Genet. 11, e1005504.
Grant, A.V., Sabri, A., Abid, A., Abderrahmani Rhorfi, I., Benkirane, M., Souhi, H., Naji Amrani, H., Alaoui-Tahiri, K., Gharbaoui, Y., Lazrak, F., Sentissi, I., Manessouri, M., Belkheiri, S., Zaid, S., Bouraqadi, A., El Amraoui, N., Hakam, M., Belkadi, A., Orlova, M., Boland, A., Deswarte, C., Amar, L., Bustamante, J., Boisson-Dupuis, S., Casanova, J.L., Schurr, E., El Baghdadi, J., Abel, L., 2016. A genome-wide association study of pulmonary tuberculosis in Morocco. Hum. Genet. 135, 299–307.
Grebely, J., Thomas, D.L., Dore, G.J., 2009. HCV reinfection studies and the door to vaccine development. J. Hepatol. 51, 628–631.
Grebely, J., Prins, M., Hellard, M., Cox, A.L., Osburn, W.O., Lauer, G., Page, K., Lloyd, A.R., Dore, G.J., International Collaboration of Incident HIV and Hepatitis C in Injecting Cohorts (InC3), 2012. Hepatitis C virus clearance, reinfection, and persistence, with insights from studies of injecting drug users: towards a vaccine. Lancet Infect. Dis. 12, 408–414.
Hancock, A.M., Witonsky, D.B., Gordon, A.S., Eshel, G., Pritchard, J.K., Coop, G., Di Rienzo, A., 2008. Adaptations to climate in candidate genes for common metabolic disorders. PLoS Genet. 4, e32.
Hayes, B., 2013. Overview of statistical methods for genome-wide association studies (GWAS). Methods Mol. Biol. 1019, 149–169.
Hayward, J.J., Castelhano, M.G., Oliveira, K.C., Corey, E., Balkman, C., Baxter, T.L., Casal, M.L., Center, S.A., Fang, M., Garrison, S.J., Kalla, S.E., Korniliev, P., Kotlikoff, M.I., Moise, N.S., Shannon, L.M., Simpson, K.W., Sutter, N.B., Todhunter, R.J., Boyko, A.R., 2016. Complex disease and phenotype mapping in the domestic dog. Nat.

Commun. 7, 10460.
He, L., Wu, W.J., Yang, J.K., Cheng, H., Zuo, X.B., Lai, W., Gao, T.W., Ma, C.L., Luo, N., Huang, J.Q., Lu, F.Y., Liu, Y.Q., Huang, Y.J., Lu, Q.J., Zhang, H.L., Wang, L., Wang, W.Z., Wang, M.M., Xiao, S.X., Sun, Q., Li, C.Y., Bai, Y.P., Li, H., Zhou, Z.C., Zhou, F.S., Chen, G., Liang, B., Qi, J., Yang, X.Y., Yang, T., Zheng, X., Sun, L.D., Zhang, X.J., Zhang, Y.P., 2014. Two new susceptibility loci 1q24.2 and 11p11.2 confer risk to severe acne. Nat. Commun. 5, 2870.
Herb, F., Thye, T., Niemann, S., Browne, E.N., Chinbuah, M.A., Gyapong, J., Osei, I., Owusu-Dabo, E., Werz, O., Rusch-Gerdes, S., Horstmann, R.D., Meyer, C.G., 2008. ALOX5 variants associated with susceptibility to human pulmonary tuberculosis. Hum. Mol. Genet. 17, 1052–1060.
Hotez, P.J., Brindley, P.J., Bethony, J.M., King, C.H., Pearce, E.J., Jacobson, J., 2008. Helminth infections: the great neglected tropical diseases. J. Clin. Invest. 118, 1311–1321.
Hu, Z., Liu, Y., Zhai, X., Dai, J., Jin, G., Wang, L., Zhu, L., Yang, Y., Liu, J., Chu, M., Wen, J., Xie, K., Du, G., Wang, Q., Zhou, Y., Cao, M., Liu, L., He, Y., Wang, Y., Zhou, G., Jia, W., Lu, J., Li, S., Liu, J., Yang, H., Shi, Y., Zhou, W., Shen, H., 2013. New loci associated with chronic hepatitis B virus infection in Han Chinese. Nat. Genet. 45, 1499–1503.
van Hulzen, K.J., Schopen, G.C., van Arendonk, J.A., Nielen, M., Koets, A.P., Schrooten, C., Heuven, H.C., 2012. Genome-wide association study to identify chromosomal regions associated with antibody response to *Mycobacterium avium* subspecies paratuberculosis in milk of Dutch Holstein-Friesians. J. Dairy Sci. 95, 2740–2748.
Imbert-Marcille, B.M., Barbe, L., Dupe, M., Le Moullac-Vaidye, B., Besse, B., Peltier, C., Ruvoen-Clouet, N., Le Pendu, J., 2014. A FUT2 gene common polymorphism determines resistance to rotavirus A of the P[8] genotype. J Infect Dis 209, 1227–1230.
Intemann, C.D., Thye, T., Niemann, S., Browne, E.N., Amanua Chinbuah, M., Enimil, A., Gyapong, J., Osei, I., Owusu-Dabo, E., Helm, S., Rusch-Gerdes, S., Horstmann, R.D., Meyer, C.G., 2009. Autophagy gene variant IRGM-261T contributes to protection from tuberculosis caused by *Mycobacterium tuberculosis* but not by *M. africanum* strains. PLoS Pathog. 5, e1000577.
International HapMap Consortium, Frazer, K.A., Ballinger, D.G., Cox, D.R., Hinds, D.A., Stuve, L.L., Gibbs, R.A., Belmont, J.W., Boudreau, A., Hardenbol, P., Leal, S.M., Pasternak, S., Wheeler, D.A., Willis, T.D., Yu, F., Yang, H., Zeng, C., Gao, Y., Hu, H., Hu, W., Li, C., Lin, W., Liu, S., Pan, H., Tang, X., Wang, J., Wang, W., Yu, J., Zhang, B., Zhang, Q., Zhao, H., Zhao, H., Zhou, J., Gabriel, S.B., Barry, R., Blumenstiel, B., Camargo, A., Defelice, M., Faggart, M., Goyette, M., Gupta, S., Moore, J., Nguyen, H., Onofrio, R.C., Parkin, M., Roy, J., Stahl, E., Winchester, E., Ziaugra, L., Altshuler, D., Shen, Y., Yao, Z., Huang, W., Chu, X., He, Y., Jin, L., Liu, Y., Shen, Y., Sun, W., Wang, H., Wang, Y., Wang, Y., Xiong, X., Xu, L., Waye, M.M., Tsui, S.K., Xue, H., Wong, J.T., Galver, L.M., Fan, J.B., Gunderson, K., Murray, S.S., Oliphant, A.R., Chee, M.S., Montpetit, A., Chagnon, F., Ferretti, V., Leboeuf, M., Olivier, J.F., Phillips, M.S., Roumy, S., Sallee, C., Verner, A., Hudson, T.J., Kwok, P.Y., Cai, D., Koboldt, D.C., Miller, R.D., Pawlikowska, L., Taillon-Miller, P., Xiao, M., Tsui, L.C., Mak, W., Song, Y.Q., Tam, P.K., Nakamura, Y., Kawaguchi, T., Kitamoto, T., Morizono, T., Nagashima, A., Ohnishi, Y., Sekine, A., Tanaka, T., Tsunoda, T., Deloukas, P., Bird, C.P., Delgado, M., Dermitzakis, E.T., Gwilliam, R., Hunt, S., Morrison, J., Powell, D., Stranger, B.E., Whittaker, P., Bentley, D.R., Daly, M.J., de Bakker, P.I., Barrett, J., Chretien, Y.R., Maller, J., McCarroll, S., Patterson, N., Pe'er, I., Price, A., Purcell, S., Richter, D.J., Sabeti, P., Saxena, R., Schaffner, S.F., Sham, P.C., Varilly, P., Altshuler, D., Stein, L.D., Krishnan, L., Smith, A.V., Tello-Ruiz, M.K., Thorisson, G.A., Chakravarti, A., Chen, P.E., Cutler, D.J., Kashuk, C.S., Lin, S., Abecasis, G.R., Guan, W., Li, Y., Munro, H.M., Qin, Z.S., Thomas, D.J., McVean, G., Auton, A., Bottolo, L., Cardin, N., Eyheramendy, S., Freeman, C., Marchini, J., Myers, S., Spencer, C., Stephens, M., Donnelly, P., Cardon, L.R., Clarke, G., Evans, D.M., Morris, A.P., Weir, B.S., Tsunoda, T., Mullikin, J.C., Sherry, S.T., Feolo, M., Skol, A., Zhang, H., Zeng, C., Zhao, H., Matsuda, I., Fukushima, Y., Macer, D.R., Suda, E., Rotimi, C.N., Adebamowo, C.A., Ajayi, I., Aniagwu, T., Marshall, P.A., Nkwodimmah, C., Royal, C.D., Leppert, M.F., Dixon, M., Peiffer, A., Qiu, R., Kent, A., Kato, K., Niikawa, N., Adewole, I.F., Knoppers, B.M., Foster, M.W., Clayton, E.W., Watkin, J., Gibbs, R.A., Belmont, J.W., Muzny, D., Nazareth, L., Sodergren, E., Weinstock, G.M., Wheeler, D.A., Yakub, I., Gabriel, S.B., Onofrio, R.C., Richter, D.J., Ziaugra, L., Birren, B.W., Daly, M.J., Altshuler, D., Wilson, R.K., Fulton, L.L., Rogers, J., Burton, J., Carter, N.P., Clee, C.M., Griffiths, M., Jones, M.C., McLay, K., Plumb, R.W., Ross, M.T., Sims, S.K., Willey, D.L., Chen, Z., Han, H., Kang, L., Godbout, M., Wallenburg, J.C., L'Archeveque, P., Bellemare, G., Saeki, K., Wang, H., An, D., Fu, H., Li, Q., Wang, Z., Wang, R., Holden, A.L., Brooks, L.D., McEwen, J.E., Guyer, M.S., Wang, V.O., Peterson, J.L., Shi, M., Spiegel, J., Sung, L.M., Zacharia, L.F., Collins, F.S., Kennedy, K., Jamieson, R., Stewart, J., 2007. A second generation human haplotype map of over 3.1 million SNPs. Nature 449, 851–861.
International HIV Controllers Study, Pereyra, F., Jia, X., McLaren, P.J., Telenti, A., de Bakker, P.I., Walker, B.D., Ripke, S., Brumme, C.J., Pulit, S.L., Carrington, M., Kadie, C.M., Carlson, J.M., Heckerman, D., Graham, R.R., Plenge, R.M., Deeks, S.G., Gianniny, L., Crawford, G., Sullivan, J., Gonzalez, E., Davies, L., Camargo, A., Moore, J.M., Beattie, N., Gupta, S., Crenshaw, A., Burtt, N.P., Guiducci, C., Gupta, N., Gao, X., Qi, Y., Yuki, Y., Piechocka-Trocha, A., Cutrell, E., Rosenberg, R., Moss, K.L., Lemay, P., O'Leary, J., Schaefer, T., Verma, P., Toth, I., Block, B., Baker, B., Rothchild, A., Lian, J., Proudfoot, J., Alvino, D.M., Vine, S., Addo, M.M., Allen, T.M., Altfeld, M., Henn, M.R., Le Gall, S., Streeck, H., Haas, D.W., Kuritzkes, D.R., Robbins, G.K., Shafer, R.W., Gulick, R.M., Shikuma, C.M., Haubrich, R., Riddler, S., Sax, P.E., Daar, E.S., Ribaudo, H.J., Agan, B., Agarwal, S., Ahern, R.L., Allen, B.L., Altidor, S., Altschuler, E.L., Ambardar, S., Anastos, K., Anderson, B., Anderson, V., Andrady, U., Antoniskis, D., Bangsberg, D., Barbaro, D., Barrie, W., Bartczak, J., Barton, S., Basden, P., Basgoz, N., Bazner, S., Bellos, N.C., Benson, A.M., Berger, J., Bernard, N.F., Bernard, A.M., Birch, C., Bodner, S.J., Bolan, R.K., Boudreaux, E.T., Bradley, M., Braun, J.F., Brndjar, J.E., Brown, S.J., Brown, K., Brown, S.T., Burack, J., Bush, L.M., Cafaro, V., Campbell, O., Campbell, J., Carlson, R.H., Carmichael, J.K., Casey, K.K., Cavacuiti, C., Celestin, G., Chambers, S.T., Chez, N., Chirch, L.M., Cimoch, P.J., Cohen, D., Cohn, L.E., Conway, B., Cooper, D.A., Cornelson, B., Cox, D.T., Cristofano, M.V., Cuchural Jr., G., Czartoski, J.L., Dahman, J.M., Daly, J.S., Davis, B.T., Davis, K., Davod, S.M., DeJesus, E., Dietz, C.A., Dunham, E., Dunn, M.E., Ellerin, T.B., Eron, J.J., Fangman, J.J., Farel, C.E., Ferlazzo, H., Fidler, S., Fleenor-Ford, A., Frankel, R., Freedberg, K.A., French, N.K., Fuchs, J.D., Fuller, J.D., Gaberman, J., Gallant, J.E., Gandhi, R.T., Garcia, E., Garmon, D., Gathe Jr., J.C., Gaultier, C.R., Gebre, W., Gilman, F.D., Gilson, I., Goepfert, P.A., Gottlieb, M.S., Goulston, C., Groger, R.K., Gurley, T.D., Haber, S., Hardwicke, R., Hardy, W.D., Harrigan, P.R., Hawkins, T.N., Heath, S., Hecht, F.M., Henry, W.K., Hladek, M., Hoffman, R.P., Horton, J.M., Hsu, R.K., Huhn, G.D., Hunt, P., Hupert, M.J., Illeman, M.L., Jaeger, H., Jellinger, R.M., John, M., Johnson, J.A., Johnson, K.L., Johnson, H., Johnson, K., Joly, J., Jordan, W.C., Kauffman, C.A., Khanlou, H., Killian, R.K., Kim, A.Y., Kim, D.D., Kinder, C.A., Kirchner, J.T., Kogelman, L., Kojic, E.M., Korthuis, P.T., Kurisu, W., Kwon, D.S., LaMar, M., Lampiris, H., Lanzafame, M., Lederman, M.M., Lee, D.M., Lee, J.M., Lee, M.J., Lee, E.T., Lemoine, J., Levy, J.A., Llibre, J.M., Liguori, M.A., Little, S.J., Liu, A.Y., Lopez, A.J., Loutfy, M.R., Loy, D., Mohammed, D.Y., Man, A., Mansour, M.K., Marconi, V.C., Markowitz, M., Marques, R., Martin, J.N., Martin Jr., H.L., Mayer, K.H., McElrath, M.J., McGhee, T.A., McGovern, B.H., McGowan, K., McIntyre, D., Mcleod, G.X., Menezes, P., Mesa, G., Metroka, C.E., Meyer-Olson, D., Miller, A.O., Montgomery, K., Mounzer, K.C., Nagami, E.H., Nagin, I., Nahass, R.G., Nelson, M.O., Nielsen, C., Norene, D.L., O'Connor, D.H., Ojikutu, B.O., Okulicz, J., Oladehin, O.O., Oldfield 3rd, E.C., Olender, S.A., Ostrowski, M., Owen Jr., W.F., Pae, E., Parsonnet, J., Pavlatos, A.M., Perlmutter, A.M., Pierce, M.N., Pincus, J.M., Pisani, L., Price, L.J., Proia, L., Prokesch, R.C., Pujet, H.C., Ramgopal, M., Rathod, A., Rausch, M., Ravishankar, J., Rhame, F.S., Richards, C.S., Richman, D.D., Rodes, B., Rodriguez, M., Rose 3rd, R.C., Rosenberg, E.S., Rosenthal, D., Ross, P.E., Rubin, D.S., Rumbaugh, E., Saenz, L., Salvaggio, M.R., Sanchez, W.C., Sanjana, V.M., Santiago, S., Schmidt, W., Schuitemaker, H., Sestak, P.M., Shalit, P., Shay, W., Shirvani, V.N., Silebi, V.I., Sizemore Jr., J.M., Skolnik, P.R., Sokol-Anderson, M., Sosman, J.M., Stabile, P., Stapleton, J.T., Starrett, S., Stein, F., Stellbrink, H.J., Sterman, F.L., Stone, V.E., Stone, D.R., Tambussi, G., Taplitz, R.A., Tedaldi, E.M., Telenti, A., Theisen, W., Torres, R., Tosiello, L., Tremblay, C., Tribble, M.A., Trinh, P.D., Tsao, A., Ueda, P., Vaccaro, A., Valadas, E., Vanig, T.J., Vecino, I., Vega, V.M., Veikley, W., Wade, B.H., Walworth, C., Wanidworanun, C., Ward, D.J., Warner, D.A., Weber, R.D., Webster, D., Weis, S., Wheeler, D.A., White, D.J., Wilkins, E., Winston, A., Wlodaver, C.G., van't Wout, A., Wright, D.P., Yang, O.O., Yurdin, D.L., Zabukovic, B.W., Zachary, K.C., Zeeman, B., Zhao, M., 2010. The major genetic determinants of HIV-1 control affect HLA class I peptide presentation. Science 330, 1551–1557.
Ishikawa, H., Ma, Z., Barber, G.N., 2009. STING regulates intracellular DNA-mediated, type I interferon-dependent innate immunity. Nature 461, 788–792.
Iwasaki, Y., 2017. Creutzfeldt-Jakob disease. Neuropathology 37, 174–188.
Jacobson, E.M., Concepcion, E., Oashi, T., Tomer, Y., 2005. A Graves' disease-associated Kozak sequence single-nucleotide polymorphism enhances the efficiency of CD40 gene translation: a case for translational pathophysiology. Endocrinology 146, 2684–2691.
Jallow, M., Teo, Y.Y., Small, K.S., Rockett, K.A., Deloukas, P., Clark, T.G., Kivinen, K., Bojang, K.A., Conway, D.J., Pinder, M., Sirugo, G., Sisay-Joof, F., Usen, S., Auburn, S., Bumpstead, S.J., Campino, S., Coffey, A., Dunham, A., Fry, A.E., Green, A., Gwilliam, R., Hunt, S.E., Inouye, M., Jeffreys, A.E., Mendy, A., Palotie, A., Potter, S., Ragoussis, J., Rogers, J., Rowlands, K., Somaskantharajah, E., Whittaker, P., Widden, C., Donnelly, P., Howie, B., Marchini, J., Morris, A., Sanjoaquin, M., Achidi, E.A., Agbenyega, T., Allen, A., Amodu, O., Corran, P., Djimde, A., Dolo, A., Doumbo, O.K., Drakeley, C., Dunstan, S., Evans, J., Farrar, J., Fernando, D., Hien, T.T., Horstmann, R.D., Ibrahim, M., Karunaweera, N., Kokwaro, G., Koram, K.A., Lemnge, M., Makani, J., Marsh, K., Michon, P., Modiano, D., Molyneux, M.E., Mueller, I., Parker, M., Peshu, N., Plowe, C.V., Puijalon, O., Reeder, J., Reyburn, H., Riley, E.M., Sakuntabhai, A., Singhasivanon, P., Sirima, S., Tall, A., Taylor, T.E., Thera, M., Troye-Blomberg, M., Williams, T.N., Wilson, M., Kwiatkowski, D.P., Wellcome Trust Case Control Consortium, Malaria Genomic Epidemiology Network, 2009. Genome-wide and fine-resolution association analysis of malaria in West Africa. Nat. Genet.
Jiang, D.K., Sun, J., Cao, G., Liu, Y., Lin, D., Gao, Y.Z., Ren, W.H., Long, X.D., Zhang, H., Ma, X.P., Wang, Z., Jiang, W., Chen, T.Y., Gao, Y., Sun, L.D., Long, J.R., Huang, H.X., Wang, D., Yu, H., Zhang, P., Tang, L.S., Peng, B., Cai, H., Liu, T.T., Zhou, P., Liu, F., Lin, X., Tao, S., Wan, B., Sai-Yin, H.X., Qin, L.X., Yin, J., Liu, L., Wu, C., Pei, Y., Zhou, Y.F., Zhai, Y., Lu, P.X., Tan, A., Zuo, X.B., Fan, J., Chang, J., Gu, X., Wang, N.J., Li, Y., Liu, Y.K., Zhai, K., Zhang, H., Hu, Z., Liu, J., Yi, Q., Xiang, Y., Shi, R., Ding, Q., Zheng, W., Shu, X.O., Mo, Z., Shugart, Y.Y., Zhang, X.J., Zhou, G., Shen, H., Zheng, S.L., Xu, J., Yu, L., 2013. Genetic variants in STAT4 and HLA-DQ genes confer risk of hepatitis B virus-related hepatocellular carcinoma. Nat. Genet. 45, 72–75.
Jiang, D.K., Ma, X.P., Yu, H., Cao, G., Ding, D.L., Chen, H., Huang, H.X., Gao, Y.Z., Wu, X.P., Long, X.D., Zhang, H., Zhang, Y., Gao, Y., Chen, T.Y., Ren, W.H., Zhang, P., Shi, Z., Jiang, W., Wan, B., Saiyin, H., Yin, J., Zhou, Y.F., Zhai, Y., Lu, P.X., Zhang, H., Gu, X., Tan, A., Wang, J.B., Zuo, X.B., Sun, L.D., Liu, J.O., Yi, Q., Mo, Z., Zhou, G., Liu, Y., Sun, J., Shugart, Y.Y., Zheng, S.L., Zhang, X.J., Xu, J., Yu, L., 2015. Genetic variants in five novel loci including CFB and CD40 predispose to chronic hepatitis B. Hepatology 62, 118–128.
Jones, K.E., Patel, N.G., Levy, M.A., Storeygard, A., Balk, D., Gittleman, J.L., Daszak, P., 2008. Global trends in emerging infectious diseases. Nature 451, 990–993.
Jostins, L., Ripke, S., Weersma, R.K., Duerr, R.H., McGovern, D.P., Hui, K.Y., Lee, J.C., Schumm, L.P., Sharma, Y., Anderson, C.A., Essers, J., Mitrovic, M., Ning, K., Cleynen, I., Theatre, E., Spain, S.L., Raychaudhuri, S., Goyette, P., Wei, Z., Abraham, C., Achkar, J.P., Ahmad, T., Amininejad, L., Ananthakrishnan, A.N., Andersen, V., Andrews, J.M., Baidoo, L., Balschun, T., Bampton, P.A., Bitton, A., Boucher, G., Brand, S., Buning, C., Cohain, A., Cichon, S., D'Amato, M., De Jong, D., Devaney, K.L., Dubinsky, M., Edwards, C., Ellinghaus, D., Ferguson, L.R., Franchimont, D., Fransen, K., Gearry, R., Georges, M., Gieger, C., Glas, J., Haritunians, T., Hart, A., Hawkey, C., Hedl, M., Hu, X., Karlsen, T.H., Kupcinskas, L., Kugathasan, S., Latiano, A., Laukens, D., Lawrance, I.C., Lees, C.W., Louis, E., Mahy, G., Mansfield, J., Morgan, A.R., Mowat, C., Newman, W., Palmieri, O., Ponsioen, C.Y., Potocnik, U., Prescott, N.J., Regueiro, M., Rotter, J.I., Russell, R.K., Sanderson, J.D., Sans, M., Satsangi, J., Schreiber, S., Simms, L.A., Sventoraityte, J., Targan, S.R., Taylor, K.D., Tremelling, M., Verspaget, H.W., De Vos, M., Wijmenga, C., Wilson, D.C., Winkelmann, J., Xavier, R.J., Zeissig, S., Zhang, B., Zhang, C.K., Zhao, H., International IBD Genetics Consortium (IIBDGC), Silverberg, M.S., Annese, V., Hakonarson, H., Brant, S.R.,

Radford-Smith, G., Mathew, C.G., Rioux, J.D., Schadt, E.E., Daly, M.J., Franke, A., Parkes, M., Vermeire, S., Barrett, J.C., Cho, J.H., 2012. Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. Nature 491, 119–124.

Kamatani, Y., Wattanapokayakit, S., Ochi, H., Kawaguchi, T., Takahashi, A., Hosono, N., Kubo, M., Tsunoda, T., Kamatani, N., Kumada, H., Puseenam, A., Sura, T., Daigo, Y., Chayama, K., Chantratita, W., Nakamura, Y., Matsuda, K., 2009. A genome-wide association study identifies variants in the HLA-DP locus associated with chronic hepatitis B in Asians. Nat. Genet. 41, 591–595.

Kanazawa, E., Sekikawa, M., Kamiakito, Y., Ozaki, T., 1989. Quantitative investigation on irregular cusps in lower permanent molars. Nichidai Koko Kagaku 15, 450–456.

Kassahun, Y., Mattiangeli, V., Ameni, G., Hailu, E., Aseffa, A., Young, D.B., Hewinson, R.G., Vordermeier, H.M., Bradley, D.G., 2015. Admixture mapping of tuberculosis and pigmentation-related traits in an African-European hybrid cattle population. Front. Genet. 6, 210.

Kelly, R.J., Rouquier, S., Giorgi, D., Lennon, G.G., Lowe, J.B., 1995. Sequence and expression of a candidate for the human Secretor blood group alpha(1,2)fucosyltransferase gene (FUT2). Homozygosity for an enzyme-inactivating nonsense mutation commonly correlates with the non-secretor phenotype. J. Biol. Chem. 270, 4640–4649.

Kennedy, R.B., Ovsyannikova, I.G., Pankratz, V.S., Haralambieva, I.H., Vierkant, R.A., Poland, G.A., 2012. Genome-wide analysis of polymorphisms associated with cytokine responses in smallpox vaccine recipients. Hum. Genet. 131, 1403–1421.

Kennedy, R.B., Ovsyannikova, I.G., Haralambieva, I.H., Lambert, N.D., Pankratz, V.S., Poland, G.A., 2014. Genome-wide SNP associations with rubella-specific cytokine responses in measles-mumps-rubella vaccine recipients. Immunogenetics 66, 493–499.

Kenyan Bacteraemia Study Group, Wellcome Trust Case Control Consortium 2 (WTCCC2), Rautanen, A., Pirinen, M., Mills, T.C., Rockett, K.A., Strange, A., Ndungu, A.W., Naranbhai, V., Gilchrist, J.J., Bellenguez, C., Freeman, C., Band, G., Bumpstead, S.J., Edkins, S., Giannoulatou, E., Gray, E., Dronov, S., Hunt, S.E., Langford, C., Pearson, R.D., Su, Z., Vukcevic, D., Macharia, A.W., Uyoga, S., Ndila, C., Mturi, N., Njuguna, P., Mohammed, S., Berkley, J.A., Mwangi, I., Mwarumba, S., Kitsao, B.S., Lowe, B.S., Morpeth, S.C., Khandwalla, I., Kilifi Bacteraemia Surveillance Group, Blackwell, J.M., Bramon, E., Brown, M.A., Casas, J.P., Corvin, A., Duncanson, A., Jankowski, J., Markus, H.S., Mathew, C.G., Palmer, C.N., Plomin, R., Sawcer, S.J., Trembath, R.C., Viswanathan, A.C., Wood, N.W., Deloukas, P., Peltonen, L., Williams, T.N., Scott, J.A., Chapman, S.J., Donnelly, P., Hill, A.V., Spencer, C.C., 2016. Polymorphism in a lincRNA associates with a doubled risk of pneumococcal bacteremia in Kenyan children. Am. J. Hum. Genet. 98, 1092–1100.

Khakoo, S.I., Thio, C.L., Martin, M.P., Brooks, C.R., Gao, X., Astemborski, J., Cheng, J., Goedert, J.J., Vlahov, D., Hilgartner, M., Cox, S., Little, A.M., Alexander, G.J., Cramp, M.E., O'Brien, S.J., Rosenberg, W.M., Thomas, D.L., Carrington, M., 2004. HLA and NK cell inhibitory receptor genes in resolving hepatitis C virus infection. Science 305, 872–874.

Khor, C.C., Chapman, S.J., Vannberg, F.O., Dunne, A., Murphy, C., Ling, E.Y., Frodsham, A.J., Walley, A.J., Kyrieleis, O., Khan, A., Aucan, C., Segal, S., Moore, C.E., Knox, K., Campbell, S.J., Lienhardt, C., Scott, A., Aaby, P., Sow, O.Y., Grignani, R.T., Sillah, J., Sirugo, G., Peshu, N., Williams, T.N., Maitland, K., Davies, R.J., Kwiatkowski, D.P., Day, N.P., Yala, D., Crook, D.W., Marsh, K., Berkley, J.A., O'Neill, L.A., Hill, A.V., 2007. A Mal functional variant is associated with protection against invasive pneumococcal disease, bacteremia, malaria and tuberculosis. Nat. Genet. 39, 523–528.

Khor, C.C., Chau, T.N., Pang, J., Davila, S., Long, H.T., Ong, R.T., Dunstan, S.J., Wills, B., Farrar, J., Van Tram, T., Gan, T.T., Binh, N.T., Tri le, T., Lien le, B., Tuan, N.M., Tham, N.T., Lanh, M.N., Nguyet, N.M., Hieu, N.T., Van N Vinh Chau, N., Thuy, T.T., Tan, D.E., Sakuntabhai, A., Teo, Y.Y., Hibberd, M.L., Simmons, C.P., 2011. Genome-wide association study identifies susceptibility loci for dengue shock syndrome at MICB and PLCE1. Nat. Genet. 43, 1139–1141.

Kim, Y.J., Kim, H.Y., Lee, J.H., Yu, S.J., Yoon, J.H., Lee, H.S., Kim, C.Y., Cheong, J.Y., Cho, S.W., Park, N.H., Park, B.L., Namgoong, S., Kim, L.H., Cheong, H.S., Shin, H.D., 2013. A genome-wide association study identified new variants associated with the risk of chronic hepatitis B. Hum. Mol. Genet. 22, 4233–4238.

Kirkpatrick, B.W., Shi, X., Shook, G.E., Collins, M.T., 2011. Whole-Genome association analysis of susceptibility to paratuberculosis in Holstein cattle. Anim. Genet. 42, 149–160.

Klein, R.J., Zeiss, C., Chew, E.Y., Tsai, J.Y., Sackler, R.S., Haynes, C., Henning, A.K., SanGiovanni, J.P., Mane, S.M., Mayne, S.T., Bracken, M.B., Ferris, F.L., Ott, J., Barnstable, C., Hoh, J., 2005. Complement factor H polymorphism in age-related macular degeneration. Science 308, 385–389.

Koda, Y., Soejima, M., Liu, Y., Kimura, H., 1996. Molecular basis for secretor type alpha (1,2)-fucosyltransferase gene deficiency in a Japanese population: a fusion gene generated by unequal crossover responsible for the enzyme deficiency. Am. J. Hum. Genet. 59, 343–350.

Koda, Y., Tachida, H., Pang, H., Liu, Y., Soejima, M., Ghaderi, A.A., Takenaka, O., Kimura, H., 2001. Contrasting patterns of polymorphisms at the ABO-secretor gene (FUT2) and plasma alpha(1,3)fucosyltransferase gene (FUT6) in human populations. Genetics 158, 747–756.

Krapp, C., Hotter, D., Gawanbacht, A., McLaren, P.J., Kluge, S.F., Sturzel, C.M., Mack, K., Reith, E., Engelhart, S., Ciuffi, A., Hornung, V., Sauter, D., Telenti, A., Kirchhoff, F., 2016. Guanylate binding protein (GBP) 5 is an interferon-inducible inhibitor of HIV-1 infectivity. Cell Host Microbe 19, 504–514.

Kulkarni, S., Savan, R., Qi, Y., Gao, X., Yuki, Y., Bass, S.E., Martin, M.P., Hunt, P., Deeks, S.G., Telenti, A., Pereyra, F., Goldstein, D., Wolinsky, S., Walker, B., Young, H.A., Carrington, M., 2011. Differential microRNA regulation of HLA-C expression and its association with HIV control. Nature 472, 495–498.

Kulkarni, S., Qi, Y., O'hUigin, C., Pereyra, F., Ramsuran, V., McLaren, P., Fellay, J., Nelson, G., Chen, H., Liao, W., Bass, S., Apps, R., Gao, X., Yuki, Y., Lied, A., Ganesan, A., Hunt, P.W., Deeks, S.G., Wolinsky, S., Walker, B.D., Carrington, M., 2013. Genetic interplay between HLA-C and MIR148A in HIV control and Crohn disease. Proc. Natl. Acad. Sci. U. S. A. 110, 20705–20710.

Kulski, J.K., Dawkins, R.L., 1999. The P5 multicopy gene family in the MHC is related in sequence to human endogenous retroviruses HERV-L and HERV-16. Immunogenetics 49, 404–412.

Kumar, V., Kato, N., Urabe, Y., Takahashi, A., Muroyama, R., Hosono, N., Otsuka, M., Tateishi, R., Omata, M., Nakagawa, H., Koike, K., Kamatani, N., Kubo, M., Nakamura, Y., Matsuda, K., 2011. Genome-wide association study identifies a susceptibility locus for HCV-induced hepatocellular carcinoma. Nat. Genet. 43, 455–458.

Kumar, V., Cheng, S.C., Johnson, M.D., Smeekens, S.P., Wojtowicz, A., Giamarellos-Bourboulis, E., Karjalainen, J., Franke, L., Withoff, S., Plantinga, T.S., van de Veerdonk, F.L., van der Meer, J.W.M., Joosten, L.A.B., Bochud, P.Y., Marchetti, O., Perfect, J.R., Xavier, R., Kullberg, B.J., Wijmenga, C., Netea, M.G., 2014. Immunochip SNP array identifies novel genetic variants conferring susceptibility to candidaemia. Nat. Commun. 5, 4675.

Kuppermann, N., Fleisher, G.R., Jaffe, D.M., 1998. Predictors of occult pneumococcal bacteremia in young febrile children. Ann. Emerg. Med. 31, 679–687.

Larsen, T., Fiehn, N.E., 2017. Dental biofilm infections - an update. APMIS 125, 376–384.

Leffler, E.M., Gao, Z., Pfeifer, S., Segurel, L., Auton, A., Venn, O., Bowden, R., Bontrop, R., Wall, J.D., Sella, G., Donnelly, P., McVean, G., Przeworski, M., 2013. Multiple instances of ancient balancing selection shared between humans and chimpanzees. Science 339, 1578–1582.

Leffler, E.M., Band, G., Busby, G.B.J., Kivinen, K., Le, Q.S., Clarke, G.M., Bojang, K.A., Conway, D.J., Jallow, M., Sisay-Joof, F., Bougouma, E.C., Mangano, V.D., Modiano, D., Sirima, S.B., Achidi, E., Apinjoh, T.O., Marsh, K., Ndila, C.M., Peshu, N., Williams, T.N., Drakeley, C., Manjurano, A., Reyburn, H., Riley, E., Kachala, D., Molyneux, M., Nyirongo, V., Taylor, T., Thornton, N., Tilley, L., Grimsley, S., Drury, E., Stalker, J., Cornelius, V., Hubbart, C., Jeffreys, A.E., Rowlands, K., Rockett, K.A., Spencer, C.C.A., Kwiatkowski, D.P., Malaria Genomic Epidemiology Network, 2017. Resistance to malaria through structural variation of red blood cell invasion receptors. Science 356. http://dx.doi.org/10.1126/science.aam6393. (Epub 2017 May 18).

Leger, P.D., Johnson, D.H., Robbins, G.K., Shafer, R.W., Clifford, D.B., Li, J., McLaren, P.J., Haas, D.W., 2014. Genome-wide association study of peripheral neuropathy with D-drug-containing regimens in AIDS Clinical Trials Group protocol 384. J. Neuro-Oncol. 20, 304–308.

LeishGEN Consortium, Wellcome Trust Case Control Consortium 2, Fakiola, M., Strange, A., Cordell, H.J., Miller, E.N., Pirinen, M., Su, Z., Mishra, A., Mehrotra, S., Monteiro, G.R., Band, G., Bellenguez, C., Dronov, S., Edkins, S., Freeman, C., Giannoulatou, E., Gray, E., Hunt, S.E., Lacerda, H.G., Langford, C., Pearson, R., Pontes, N.N., Rai, M., Singh, S.P., Smith, L., Sousa, O., Vukcevic, D., Bramon, E., Brown, M.A., Casas, J.P., Corvin, A., Duncanson, A., Jankowski, J., Markus, H.S., Mathew, C.G., Palmer, C.N., Plomin, R., Rautanen, A., Sawcer, S.J., Trembath, R.C., Viswanathan, A.C., Wood, N.W., Wilson, M.E., Deloukas, P., Peltonen, L., Christiansen, F., Witt, C., Jeronimo, S.M., Sundar, S., Spencer, C.C., Blackwell, J.M., Donnelly, P., 2013. Common variants in the HLA-DRB1-HLA-DQA1 HLA class II region are associated with susceptibility to visceral leishmaniasis. Nat. Genet. 45, 208–213.

Lenz, T.L., Deutsch, A.J., Han, B., Hu, X., Okada, Y., Eyre, S., Knapp, M., Zhernakova, A., Huizinga, T.W., Abecasis, G., Becker, J., Boeckxstaens, G.E., Chen, W.M., Franke, A., Gladman, D.D., Gockel, I., Gutierrez-Achury, J., Martin, J., Nair, R.P., Nothen, M.M., Onengut-Gumuscu, S., Rahman, P., Rantapaa-Dahlqvist, S., Stuart, P.E., Tsoi, L.C., van Heel, D.A., Worthington, J., Wouters, M.M., Klareskog, L., Elder, J.T., Gregersen, P.K., Schumacher, J., Rich, S.S., Wijmenga, C., Sunyaev, S.R., de Bakker, P.I., Raychaudhuri, S., 2015. Widespread non-additive and interaction effects within HLA loci modulate the risk of autoimmune diseases. Nat. Genet. 47, 1085–1090.

Li, S., Qian, J., Yang, Y., Zhao, W., Dai, J., Bei, J.X., Foo, J.N., McLaren, P.J., Li, Z., Yang, J., Shen, F., Liu, L., Yang, J., Li, S., Pan, S., Wang, Y., Li, W., Zhai, X., Zhou, B., Shi, L., Chen, X., Chu, M., Yan, Y., Wang, J., Cheng, S., Shen, J., Jia, W., Liu, J., Yang, J., Wen, Z., Li, A., Zhang, Y., Zhang, G., Luo, X., Qin, H., Chen, M., Wang, H., Jin, L., Lin, D., Shen, H., He, L., de Bakker, P.I., Wang, H., Zeng, Y.X., Wu, M., Hu, Z., Shi, Y., Liu, J., Zhou, W., 2012. GWAS identifies novel susceptibility loci on 6p21.32 and 21q21.3 for hepatocellular carcinoma in chronic hepatitis B virus carriers. PLoS Genet. 8, e1002791.

Li, Y., Si, L., Zhai, Y., Hu, Y., Hu, Z., Bei, J.X., Xie, B., Ren, Q., Cao, P., Yang, F., Song, Q., Bao, Z., Zhang, H., Han, Y., Wang, Z., Chen, X., Xia, X., Yan, H., Wang, R., Zhang, Y., Gao, C., Meng, J., Tu, X., Liang, X., Cui, Y., Liu, Y., Wu, X., Li, Z., Wang, H., Li, Z., Hu, B., He, M., Gao, Z., Xu, X., Ji, H., Yu, C., Sun, Y., Xing, B., Yang, X., Zhang, H., Tan, A., Wu, C., Jia, W., Li, S., Zeng, Y.X., Shen, H., He, F., Mo, Z., Zhang, H., Zhou, G., 2016. Genome-wide association study identifies 8p21.3 associated with persistent hepatitis B virus infection among Chinese. Nat. Commun. 7, 11664.

Limou, S., Le Clerc, S., Coulonges, C., Carpentier, W., Dina, C., Delaneau, O., Labib, T., Taing, L., Sladek, R., Deveau, C., Ratsimandresey, R., Montes, M., Spadoni, J.L., Lelievre, J.D., Levy, Y., Therwath, A., Schachter, F., Matsuda, F., Gut, I., Froguel, P., Delfraissy, J.F., Hercberg, S., Zagury, J.F., ANRS Genomic Group, 2009. Genomewide association study of an AIDS-nonprogression cohort emphasizes the role played by HLA genes (ANRS Genomewide Association Study 02). J Infect Dis 199, 419–426.

Lindblad-Toh, K., Wade, C.M., Mikkelsen, T.S., Karlsson, E.K., Jaffe, D.B., Kamal, M., Clamp, M., Chang, J.L., Kulbokas 3rd, E.J., Zody, M.C., Mauceli, E., Xie, X., Breen, M., Wayne, R.K., Ostrander, E.A., Ponting, C.P., Galibert, F., Smith, D.R., DeJong, P.J., Kirkness, E., Alvarez, P., Biagi, T., Brockman, W., Butler, J., Chin, C.W., Cook, A., Cuff, J., Daly, M.J., DeCaprio, D., Gnerre, S., Grabherr, M., Kellis, M., Kleber, M., Bardeleben, C., Goodstadt, L., Heger, A., Hitte, C., Kim, L., Koepfli, K.P., Parker, H.G., Pollinger, J.P., Searle, S.M., Sutter, N.B., Thomas, R., Webber, C., Baldwin, J., Abebe, A., Abouelleil, A., Aftuck, L., Ait-Zahra, M., Aldredge, T., Allen, N., An, P., Anderson, S., Antoine, C., Arachchi, H., Aslam, A., Ayotte, L., Bachantsang, P., Barry, A., Bayul, T., Benamara, M., Berlin, A., Bessette, D., Blitshteyn, B., Bloom, T., Blye, J., Boguslavskiy, L., Bonnet, C., Boukhgalter, B., Brown, A., Cahill, P., Calixte, N., Camarata, J., Cheshatsang, Y., Chu, J., Citroen, M., Collymore, A., Cooke, P., Dawoe, T., Daza, R., Decktor, K., DeGray, S., Dhargay, N., Dooley, K., Dooley, K., Dorje, P., Dorjee, K., Dorris, L., Duffey, N., Dupes, A., Egbiremolen, O., Elong, R., Falk, J., Farina, A., Faro, S., Ferguson, D., Ferreira, P., Fisher, S., FitzGerald, M., Foley, K., Foley, C., Franke, A., Friedrich, D., Gage, D., Garber, M., Gearin, G., Giannoukos, G., Goode, T., Goyette, A., Graham, J., Grandbois, E., Gyaltsen, K., Hafez, N., Hagopian, D., Hagos, B., Hall, J., Healy, C., Hegarty, R., Honan, T., Horn, A., Houde, N., Hughes,

L., Hunnicutt, L., Husby, M., Jester, B., Jones, C., Kamat, A., Kanga, B., Kells, C., Khazanovich, D., Kieu, A.C., Kisner, P., Kumar, M., Lance, K., Landers, T., Lara, M., Lee, W., Leger, J.P., Lennon, N., Leuper, L., LeVine, S., Liu, J., Liu, X., Lokyitsang, Y., Lokyitsang, T., Lui, A., Macdonald, J., Major, J., Marabella, R., Maru, K., Matthews, C., McDonough, S., Mehta, T., Meldrim, J., Melnikov, A., Meneus, L., Mihalev, A., Mihova, T., Miller, K., Mittelman, R., Mlenga, V., Mulrain, L., Munson, G., Navidi, A., Naylor, J., Nguyen, T., Nguyen, N., Nguyen, C., Nguyen, T., Nicol, R., Norbu, N., Norbu, C., Novod, N., Nyima, T., Olandt, P., O'Neill, B., O'Neill, K., Osman, S., Oyono, L., Patti, C., Perrin, D., Phunkhang, P., Pierre, F., Priest, M., Rachupka, A., Raghuraman, S., Rameau, R., Ray, V., Raymond, C., Rege, F., Rise, C., Rogers, J., Rogov, P., Sahalie, J., Settipalli, S., Sharpe, T., Shea, T., Sheehan, M., Sherpa, N., Shi, J., Shih, D., Sloan, J., Smith, C., Sparrow, T., Stalker, J., Stange-Thomann, N., Stavropoulos, S., Stone, C., Stone, S., Sykes, S., Tchuinga, P., Tenzing, P., Tesfaye, S., Thoulutsang, D., Thoulutsang, Y., Topham, K., Topping, I., Tsamla, T., Vassiliev, H., Venkataraman, V., Vo, A., Wangchuk, T., Wangdi, T., Weiand, M., Wilkinson, J., Wilson, A., Yadav, S., Yang, S., Yang, X., Young, G., Yu, Q., Zainoun, J., Zembek, L., Zimmer, A., Lander, E.S., 2005. Genome sequence, comparative analysis and haplotype structure of the domestic dog. Nature 438, 803–819.

Lindesmith, L., Moe, C., Marionneau, S., Ruvoen, N., Jiang, X., Lindblad, L., Stewart, P., LePendu, J., Baric, R., 2003. Human susceptibility and resistance to Norwalk virus infection. Nat. Med. 9, 548–553.

Liu, Y., Koda, Y., Soejima, M., Pang, H., Schlaphoff, T., du Toit, E.D., Kimura, H., 1998. Extensive polymorphism of the FUT2 gene in an African (Xhosa) population of South Africa. Hum. Genet. 103, 204–210.

Liu, Y., Helms, C., Liao, W., Zaba, L.C., Duan, S., Gardner, J., Wise, C., Miner, A., Malloy, M.J., Pullinger, C.R., Kane, J.P., Saccone, S., Worthington, J., Bruce, I., Kwok, P.Y., Menter, A., Krueger, J., Barton, A., Saccone, N.L., Bowcock, A.M., 2008. A genome-wide association study of psoriasis and psoriatic arthritis identifies new disease loci. PLoS Genet. 4, e1000041.

Liu, L., Li, J., Yao, J., Yu, J., Zhang, J., Ning, Q., Wen, Z., Yang, D., He, Y., Kong, X., Song, Q., Chen, M., Yang, H., Liu, Q., Li, S., Lin, J., 2011. A genome-wide association study with DNA pooling identifies the variant rs11866328 in the GRIN2A gene that affects disease progression of chronic HBV infection. Viral Immunol. 24, 397–402.

Liu, H., Irwanto, A., Fu, X., Yu, G., Yu, Y., Sun, Y., Wang, C., Wang, Z., Okada, Y., Low, H., Li, Y., Liany, H., Chen, M., Bao, F., Li, J., You, J., Zhang, Q., Liu, J., Chu, T., Andiappan, A.K., Wang, N., Niu, G., Liu, D., Yu, X., Zhang, L., Tian, H., Zhou, G., Rotzschke, O., Chen, S., Zhang, X., Liu, J., Zhang, F., 2015. Discovery of six new susceptibility loci and analysis of pleiotropic effects in leprosy. Nat. Genet. 47, 267–271.

Liu, J.Z., van Sommeren, S., Huang, H., Ng, S.C., Alberts, R., Takahashi, A., Ripke, S., Lee, J.C., Jostins, L., Shah, T., Abedian, S., Cheon, J.H., Cho, J., Daryani, N.E., Franke, L., Fuyuno, Y., Hart, A., Juyal, R.C., Juyal, G., Kim, W.H., Morris, A.P., Poustchi, H., Newman, W.G., Midha, V., Orchard, T.R., Vahedi, H., Sood, A., Sung, J.J., Malekzadeh, R., Westra, H.J., Yamazaki, K., Yang, S.K., International Multiple Sclerosis Genetics Consortium, International IBD Genetics Consortium, Barrett, J.C., Franke, A., Alizadeh, B.Z., Parkes, M., B, K.T., Daly, M.J., Kubo, M., Anderson, C.A., Weersma, R.K., 2015. Association analyses identify 38 susceptibility loci for inflammatory bowel disease and highlight shared genetic risk across populations. Nat. Genet. 47, 979–986.

Lore, N.I., Iraqi, F.A., Bragonzi, A., 2015. Host genetic diversity influences the severity of Pseudomonas aeruginosa pneumonia in the Collaborative Cross mice. BMC Genet. 16 (106-015-0260-6).

Mabey, D., Peeling, R.W., Ustianowski, A., Perkins, M.D., 2004. Diagnostics for the developing world. Nat. Rev. Microbiol. 2, 231–240.

MacArthur, J., Bowler, E., Cerezo, M., Gil, L., Hall, P., Hastings, E., Junkins, H., McMahon, A., Milano, A., Morales, J., Pendlington, Z.M., Welter, D., Burdett, T., Hindorff, L., Flicek, P., Cunningham, F., Parkinson, H., 2017. The new NHGRI-EBI Catalog of published genome-wide association studies (GWAS Catalog). Nucleic Acids Res. 45, D896–D901.

Malaria Genomic Epidemiology Network, Malaria Genomic Epidemiology Network, 2014. Reappraisal of known malaria resistance loci in a large multicenter study. Nat. Genet. 46, 1197–1204.

Malaria Genomic Epidemiology Network, Band, G., Rockett, K.A., Spencer, C.C., Kwiatkowski, D.P., 2015. A novel locus of resistance to severe malaria in a region of ancient balancing selection. Nature 526, 253–257.

Manchester, A.C., Hill, S., Sabatino, B., Armentano, R., Carroll, M., Kessler, B., Miller, M., Dogan, B., McDonough, S.P., Simpson, K.W., 2013. Association between granulomatous colitis in French Bulldogs and invasive *Escherichia coli* and response to fluoroquinolone antimicrobials. J. Vet. Intern. Med. 27, 56–61.

van Manen, D., van 't Wout, A.B., Schuitemaker, H., 2012. Genome-wide association studies on HIV susceptibility, pathogenesis and pharmacogenomics. Retrovirology 9 (70-4690-9-70).

Mangano, V.D., Modiano, D., 2014. Host genetics and parasitic infections. Clin. Microbiol. Infect. 20, 1265–1275.

Maniangou, B., Legrand, N., Alizadeh, M., Guyet, U., Willem, C., David, G., Charpentier, E., Walencik, A., Retiere, C., Gagne, K., 2017. Killer immunoglobulin-like receptor allele determination using next-generation sequencing technology. Front. Immunol. 8, 547.

Martin, M.P., Qi, Y., Gao, X., Yamada, E., Martin, J.N., Pereyra, F., Colombo, S., Brown, E.E., Shupert, W.L., Phair, J., Goedert, J.J., Buchbinder, S., Kirk, G.D., Telenti, A., Connors, M., O'Brien, S.J., Walker, B.D., Parham, P., Deeks, S.G., McVicar, D.W., Carrington, M., 2007. Innate partnership of HLA-B and KIR3DL1 subtypes against HIV-1. Nat. Genet. 39, 733–740.

Martin, A.R., Gignoux, C.R., Walters, R.K., Wojcik, G.L., Neale, B.M., Gravel, S., Daly, M.J., Bustamante, C.D., Kenny, E.E., 2017. Human demographic history impacts genetic risk prediction across diverse populations. Am. J. Hum. Genet. 100, 635–649.

Martinez-Marignac, V.L., Valladares, A., Cameron, E., Chan, A., Perera, A., Globus-Goldberg, R., Wacher, N., Kumate, J., McKeigue, P., O'Donnell, D., Shriver, M.D., Cruz, M., Parra, E.J., 2007. Admixture in Mexico City: implications for admixture mapping of type 2 diabetes genetic risk factors. Hum. Genet. 120, 807–819.

Martinon-Torres, F., Png, E., Khor, C.C., Davila, S., Wright, V.J., Sim, K.S., Vega, A., Fachal, L., Inwald, D., Nadel, S., Carrol, E.D., Martinon-Torres, N., Alonso, S.M., Carracedo, A., Morteruel, E., Lopez-Bayon, J., Torre, A.C., Monge, C.C., de Aguilar, P.A., Torne, E.E., Martinez-Padilla, M.D., Martinon-Sanchez, J.M., Levin, M., Hibberd, M.L., Salas, A., ESIGEM network, ESPID meningococcal consortium - UK, EUCLIDS consortium members - Imperial College London (www.euclids-project.eu), 2016. Natural resistance to Meningococcal Disease related to CFH loci: meta-analysis of genome-wide association studies. Sci Rep 6, 35842.

Matsuura, K., Watanabe, T., Tanaka, Y., 2014. Role of IL28B for chronic hepatitis C treatment toward personalized medicine. J. Gastroenterol. Hepatol. 29, 241–249.

Matsuura, K., Sawai, H., Ikeo, K., Ogawa, S., Iio, E., Isogawa, M., Shimada, N., Komori, A., Toyoda, H., Kumada, T., Namisaki, T., Yoshiji, H., Sakamoto, N., Nakagawa, M., Asahina, Y., Kurosaki, M., Izumi, N., Enomoto, N., Kusakabe, A., Kajiwara, E., Itoh, Y., Ide, T., Tamori, A., Matsubara, M., Kawada, N., Shirabe, K., Tomita, E., Honda, M., Kaneko, S., Nishina, S., Suetsugu, A., Hiasa, Y., Watanabe, H., Genda, T., Sakaida, I., Nishiguchi, S., Takaguchi, K., Tanaka, E., Sugihara, J., Shimada, M., Kondo, Y., Kawai, Y., Kojima, K., Nagasaki, M., Tokunaga, K., Tanaka, Y., Japanese Genome-Wide Association Study Group for Viral Hepatitis, 2017. Genome-wide association study identifies TLL1 variant associated with development of hepatocellular carcinoma after eradication of hepatitis C virus infection. Gastroenterology 152, 1383–1394.

Matzaraki, V., Kumar, V., Wijmenga, C., Zhernakova, A., 2017. The MHC locus and genetic susceptibility to autoimmune and infectious diseases. Genome Biol. 18, 76.

Maurer, U., Jehan, F., Englert, C., Hubinger, G., Weidmann, E., DeLuca, H.F., Bergmann, L., 2001. The Wilms' tumor gene product (WT1) modulates the response to 1,25-dihydroxyvitamin D3 by induction of the vitamin D receptor. J. Biol. Chem. 276, 3727–3732.

Maurizio, P.L., Ferris, M.T., 2017. The collaborative cross resource for systems genetics research of infectious diseases. Methods Mol. Biol. 1488, 579–596.

May, R.M., 2007. Parasites, people and policy: infectious diseases and the Millennium Development Goals. Trends Ecol. Evol. 22, 497–503.

Mayerle, J., den Hoed, C.M., Schurmann, C., Stolk, L., Homuth, G., Peters, M.J., Capelle, L.G., Zimmermann, K., Rivadeneira, F., Gruska, S., Volzke, H., de Vries, A.C., Volker, U., Teumer, A., van Meurs, J.B., Steinmetz, I., Nauck, M., Ernst, F., Weiss, F.U., Hofman, A., Zenker, M., Kroemer, H.K., Prokisch, H., Uitterlinden, A.G., Lerch, M.M., Kuipers, E.J., 2013. Identification of genetic loci associated with Helicobacter pylori serologic status. JAMA 309, 1912–1920.

Mbarek, H., Ochi, H., Urabe, Y., Kumar, V., Kubo, M., Hosono, N., Takahashi, A., Kamatani, Y., Miki, D., Abe, H., Tsunoda, T., Kamatani, N., Chayama, K., Nakamura, Y., Matsuda, K., 2011. A genome-wide association study of chronic hepatitis B identified novel risk locus in a Japanese population. Hum. Mol. Genet. 20, 3884–3892.

McGovern, D.P., Jones, M.R., Taylor, K.D., Marciante, K., Yan, X., Dubinsky, M., Ippoliti, A., Vasiliauskas, E., Berel, D., Derkowski, C., Dutridge, D., Fleshner, P., Shih, D.Q., Melmed, G., Mengesha, E., King, L., Pressman, S., Haritunians, T., Guo, X., Targan, S.R., Rotter, J.I., International IBD Genetics Consortium, 2010. Fucosyltransferase 2 (FUT2) non-secretor status is associated with Crohn's disease. Hum. Mol. Genet. 19, 3468–3476.

McLaren, P.J., Coulonges, C., Ripke, S., van den Berg, L., Buchbinder, S., Carrington, M., Cossarizza, A., Dalmau, J., Deeks, S.G., Delaneau, O., De Luca, A., Goedert, J.J., Haas, D., Herbeck, J.T., Kathiresan, S., Kirk, G.D., Lambotte, O., Luo, M., Mallal, S., van Manen, D., Martinez-Picado, J., Meyer, L., Miro, J.M., Mullins, J.I., Obel, N., O'Brien, S.J., Pereyra, F., Plummer, F.A., Poli, G., Qi, Y., Rucart, P., Sandhu, M.S., Shea, P.R., Schuitemaker, H., Theodorou, I., Vannberg, F., Veldink, J., Walker, B.D., Weintrob, A., Winkler, C.A., Wolinsky, S., Telenti, A., Goldstein, D.B., de Bakker, P.I., Zagury, J.F., Fellay, J., 2013. Association study of common genetic variants and HIV-1 acquisition in 6,300 infected cases and 7,200 controls. PLoS Pathog. 9, e1003515.

McLaren, P.J., Coulonges, C., Bartha, I., Lenz, T.L., Deutsch, A.J., Bashirova, A., Buchbinder, S., Carrington, M.N., Cossarizza, A., Dalmau, J., De Luca, A., Goedert, J.J., Gurdasani, D., Haas, D.W., Herbeck, J.T., Johnson, E.O., Kirk, G.D., Lambotte, O., Luo, M., Mallal, S., van Manen, D., Martinez-Picado, J., Meyer, L., Miro, J.M., Mullins, J.I., Obel, N., Poli, G., Sandhu, M.S., Schuitemaker, H., Shea, P.R., Theodorou, I., Walker, B.D., Weintrob, A.C., Winkler, C.A., Wolinsky, S.M., Raychaudhuri, S., Goldstein, D.B., Telenti, A., de Bakker, P.I., Zagury, J.F., Fellay, J., 2015. Polymorphisms of large effect explain the majority of the host genetic contribution to variation of HIV-1 virus load. Proc. Natl. Acad. Sci. U. S. A. 112, 14658–14663.

Mead, S., Stumpf, M.P., Whitfield, J., Beck, J.A., Poulter, M., Campbell, T., Uphill, J.B., Goldstein, D., Alpers, M., Fisher, E.M., Collinge, J., 2003. Balancing selection at the prion protein gene consistent with prehistoric kurulike epidemics. Science 300, 640–643.

Mead, S., Poulter, M., Uphill, J., Beck, J., Whitfield, J., Webb, T.E., Campbell, T., Adamson, G., Deriziotis, P., Tabrizi, S.J., Hummerich, H., Verzilli, C., Alpers, M.P., Whittaker, J.C., Collinge, J., 2009. Genetic risk factors for variant Creutzfeldt-Jakob disease: a genome-wide association study. Lancet Neurol. 8, 57–66.

Midgard, H., Weir, A., Palmateer, N., Lo Re 3rd, V., Pineda, J.A., Macias, J., Dalgard, O., 2016. HCV epidemiology in high-risk groups and the risk of reinfection. J. Hepatol. 65, S33–45.

Miki, D., Ochi, H., Hayes, C.N., Abe, H., Yoshima, T., Aikata, H., Ikeda, K., Kumada, H., Toyota, J., Morizono, T., Tsunoda, T., Kubo, M., Nakamura, Y., Kamatani, N., Chayama, K., 2011. Variation in the DEPDC5 locus is associated with progression to hepatocellular carcinoma in chronic hepatitis C virus carriers. Nat. Genet. 43, 797–800.

Miki, D., Ochi, H., Takahashi, A., Hayes, C.N., Urabe, Y., Abe, H., Kawaoka, T., Tsuge, M., Hiraga, N., Imamura, M., Kawakami, Y., Aikata, H., Takahashi, S., Akuta, N., Suzuki, F., Ikeda, K., Kumada, H., Karino, Y., Toyota, J., Tsunoda, T., Kubo, M., Kamatani, N., Nakamura, Y., Chayama, K., 2013. HLA-DQB1*03 confers susceptibility to chronic hepatitis C in Japanese: a genome-wide association study. PLoS One 8, e84226.

Milacic, M., Haw, R., Rothfels, K., Wu, G., Croft, D., Hermjakob, H., D'Eustachio, P., Stein, L., 2012. Annotating cancer variants and anti-cancer therapeutics in reactome. Cancers (Basel) 4, 1180–1211.

Minozzi, G., Buggiotti, L., Stella, A., Strozzi, F., Luini, M., Williams, J.L., 2010. Genetic

loci involved in antibody response to *Mycobacterium avium* ssp. paratuberculosis in cattle. PLoS One 5, e11117.
Moore, C.B., Verma, A., Pendergrass, S., Verma, S.S., Johnson, D.H., Daar, E.S., Gulick, R.M., Haubrich, R., Robbins, G.K., Ritchie, M.D., Haas, D.W., 2015. Phenome-wide association study relating pretreatment laboratory parameters with human genetic variants in AIDS clinical trials group protocols. Open Forum. Infect. Dis. 2, ofu113.
Morrison, J., Laurie, C.C., Marazita, M.L., Sanders, A.E., Offenbacher, S., Salazar, C.R., Conomos, M.P., Thornton, T., Jain, D., Laurie, C.A., Kerr, K.F., Papanicolaou, G., Taylor, K., Kaste, L.M., Beck, J.D., Shaffer, J.R., 2016. Genome-wide association study of dental caries in the Hispanic Communities Health Study/Study of Latinos (HCHS/SOL). Hum. Mol. Genet. 25, 807–816.
Navarini, A.A., Simpson, M.A., Weale, M., Knight, J., Carlavan, I., Reiniche, P., Burden, D.A., Layton, A., Bataille, V., Allen, M., Pleass, R., Pink, A., Creamer, D., English, J., Munn, S., Walton, S., Acne Genetic Study Group, Willis, C., Deret, S., Voegel, J.J., Spector, T., Smith, C.H., Trembath, R.C., Barker, J.N., 2014. Genome-wide association study identifies three novel susceptibility loci for severe Acne vulgaris. Nat. Commun. 5, 4020.
Neibergs, H.L., Settles, M.L., Whitlock, R.H., Taylor, J.F., 2010. GSEA-SNP identifies genes associated with Johne's disease in cattle. Mamm. Genome 21, 419–425.
Nishida, N., Sawai, H., Matsuura, K., Sugiyama, M., Ahn, S.H., Park, J.Y., Hige, S., Kang, J.H., Suzuki, K., Kurosaki, M., Asahina, Y., Mochida, S., Watanabe, M., Tanaka, E., Honda, M., Kaneko, S., Orito, E., Itoh, Y., Mita, E., Tamori, A., Murawaki, Y., Hiasa, Y., Sakaida, I., Korenaga, M., Hino, K., Ide, T., Kawashima, M., Mawatari, Y., Sageshima, M., Ogasawara, Y., Koike, A., Izumi, N., Han, K.H., Tanaka, Y., Tokunaga, K., Mizokami, M., 2012. Genome-wide association study confirming association of HLA-DP with protection against chronic hepatitis B and viral clearance in Japanese and Korean. PLoS One 7, e39175.
Norman, P.J., Hollenbach, J.A., Nemat-Gorgani, N., Marin, W.M., Norberg, S.J., Ashouri, E., Jayaraman, J., Wroblewski, E.E., Trowsdale, J., Rajalingam, R., Oksenberg, J.R., Chiaroni, J., Guethlein, L.A., Traherne, J.A., Ronaghi, M., Parham, P., 2016. Defining KIR and HLA class I genotypes at highest resolution via high-throughput sequencing. Am. J. Hum. Genet. 99, 375–391.
Ochi, H., Maekawa, T., Abe, H., Hayashida, Y., Nakano, R., Kubo, M., Tsunoda, T., Hayes, C.N., Kumada, H., Nakamura, Y., Chayama, K., 2010. ITPA polymorphism affects ribavirin-induced anemia and outcomes of therapy—a genome-wide study of Japanese HCV virus patients. Gastroenterology 139, 1190–1197.
Ochi, H., Maekawa, T., Abe, H., Hayashida, Y., Nakano, R., Imamura, M., Hiraga, N., Kawakami, Y., Aimitsu, S., Kao, J.H., Kubo, M., Tsunoda, T., Kumada, H., Nakamura, Y., Hayes, C.N., Chayama, K., 2011. IL-28B predicts response to chronic hepatitis C therapy—fine-mapping and replication study in Asian populations. J. Gen. Virol. 92, 1071–1081.
Offenbacher, S., Divaris, K., Barros, S.P., Moss, K.L., Marchesan, J.T., Morelli, T., Zhang, S., Kim, S., Sun, L., Beck, J.D., Laudes, M., Munz, M., Schaefer, A.S., North, K.E., 2016. Genome-wide association study of biologically informed periodontal complex traits offers novel insights into the genetic basis of periodontal disease. Hum. Mol. Genet. 25, 2113–2129.
Ovsyannikova, I.G., Kennedy, R.B., O'Byrne, M., Jacobson, R.M., Pankratz, V.S., Poland, G.A., 2012. Genome-wide association study of antibody response to smallpox vaccine. Vaccine 30, 4182–4189.
Owen, F., Poulter, M., Collinge, J., Crow, T.J., 1990. Codon 129 changes in the prion protein gene in Caucasians. Am. J. Hum. Genet. 46, 1215–1216.
Pan, L., Zhang, L., Zhang, W., Wu, X., Li, Y., Yan, B., Zhu, X., Liu, X., Yang, C., Xu, J., Zhou, G., Xu, A., Li, H., Liu, Y., 2014. A genome-wide association study identifies polymorphisms in the HLA-DR region associated with non-response to hepatitis B vaccination in Chinese Han populations. Hum. Mol. Genet. 23, 2210–2219.
Pant, S.D., Schenkel, F.S., Verschoor, C.P., You, Q., Kelton, D.F., Moore, S.S., Karrow, N.A., 2010. A principal component regression based genome wide analysis approach reveals the presence of a novel QTL on BTA7 for MAP resistance in holstein cattle. Genomics 95, 176–182.
Parra, E.J., Hoggart, C.J., Bonilla, C., Dios, S., Norris, J.M., Marshall, J.A., Hamman, R.F., Ferrell, R.E., McKeigue, P.M., Shriver, M.D., 2004. Relation of type 2 diabetes to individual admixture and candidate gene polymorphisms in the Hispanic American population of San Luis Valley, Colorado. J. Med. Genet. 41, e116.
Patin, E., Kutalik, Z., Guergnon, J., Bibert, S., Nalpas, B., Jouanguy, E., Munteanu, M., Bousquet, L., Argiro, L., Halfon, P., Boland, A., Mullhaupt, B., Semela, D., Dufour, J.F., Heim, M.H., Moradpour, D., Cerny, A., Malinverni, R., Hirsch, H., Martinetti, G., Suppiah, V., Stewart, G., Booth, D.R., George, J., Casanova, J.L., Brechot, C., Rice, C.M., Talal, A.H., Jacobson, I.M., Bourliere, M., Theodorou, I., Poynard, T., Negro, F., Pol, S., Bochud, P.Y., Abel, L., Swiss Hepatitis C Cohort Study Group, International Hepatitis C Genetics Consortium, French ANRS HC EP 26 Genoscan Study Group, 2012. Genome-wide association study identifies variants associated with progression of liver fibrosis from HCV infection. Gastroenterology 143 (1244-52.e1-12).
Pearson, T.A., Manolio, T.A., 2008. How to interpret a genome-wide association study. JAMA 299, 1335–1344.
Picard, C., Fieschi, C., Altare, F., Al-Jumaah, S., Al-Hajjar, S., Feinberg, J., Dupuis, S., Soudais, C., Al-Mohsen, I.Z., Genin, E., Lammas, D., Kumararatne, D.S., Leclerc, T., Rafii, A., Frayha, H., Murugasu, B., Wah, L.B., Sinniah, R., Loubser, M., Okamoto, E., Al-Ghonaium, A., Tufenkeji, H., Abel, L., Casanova, J.L., 2002. Inherited interleukin-12 deficiency: IL12B genotype and clinical phenotype of 13 patients from six kindreds. Am. J. Hum. Genet. 70, 336–348.
Plummer, F.A., Ball, T.B., Kimani, J., Fowke, K.R., 1999. Resistance to HIV-1 infection among highly exposed sex workers in Nairobi: what mediates protection and why does it develop? Immunol. Lett. 66, 27–34.
Png, E., Thalamuthu, A., Ong, R.T., Snippe, H., Boland, G.J., Seielstad, M., 2011. A genome-wide association study of hepatitis B vaccine response in an Indonesian population reveals multiple independent risk variants in the HLA region. Hum. Mol. Genet. 20, 3893–3898.
Popejoy, A.B., Fullerton, S.M., 2016. Genomics is failing on diversity. Nature 538, 161–164.
Price, A.L., Patterson, N.J., Plenge, R.M., Weinblatt, M.E., Shadick, N.A., Reich, D., 2006. Principal components analysis corrects for stratification in genome-wide association studies. Nat. Genet. 38, 904–909.
Prokunina-Olsson, L., Muchmore, B., Tang, W., Pfeiffer, R.M., Park, H., Dickensheets, H., Hergott, D., Porter-Gill, P., Mumy, A., Kohaar, I., Chen, S., Brand, N., Tarway, M., Liu, L., Sheikh, F., Astemborski, J., Bonkovsky, H.L., Edlin, B.R., Howell, C.D., Morgan, T.R., Thomas, D.L., Rehermann, B., Donnelly, R.P., O'Brien, T.R., 2013. A variant upstream of IFNL3 (IL28B) creating a new interferon gene IFNL4 is associated with impaired clearance of hepatitis C virus. Nat. Genet. 45, 164–171.
Quintana-Murci, L., 2016. Understanding rare and common diseases in the context of human evolution. Genome Biol. 17, 225.
Rasmussen, A.L., Okumura, A., Ferris, M.T., Green, R., Feldmann, F., Kelly, S.M., Scott, D.P., Safronetz, D., Haddock, E., LaCasse, R., Thomas, M.J., Sova, P., Carter, V.S., Weiss, J.M., Miller, D.R., Shaw, G.D., Korth, M.J., Heise, M.T., Baric, R.S., de Villena, F.P., Feldmann, H., Katze, M.G., 2014. Host genetic diversity enables Ebola hemorrhagic fever pathogenesis and resistance. Science 346, 987–991.
Raszek, M.M., Guan le, L., Plastow, G.S., 2016. Use of genomic tools to improve cattle health in the context of infectious diseases. Front. Genet. 7, 30.
Rauch, A., Kutalik, Z., Descombes, P., Cai, T., Di Iulio, J., Mueller, T., Bochud, M., Battegay, M., Bernasconi, E., Borovicka, J., Colombo, S., Cerny, A., Dufour, J.F., Furrer, H., Gunthard, H.F., Heim, M., Hirschel, B., Malinverni, R., Moradpour, D., Mullhaupt, B., Witteck, A., Beckmann, J.S., Berg, T., Bergmann, S., Negro, F., Telenti, A., Bochud, P.Y., Swiss Hepatitis C Cohort Study, Swiss HIV Cohort Study, 2010. Genetic variation in IL28B is associated with chronic hepatitis C and treatment failure: a genome-wide association study. Gastroenterology 138, 1338–1345 (1345.e1-7).
Richardson, I.W., Berry, D.P., Wiencko, H.L., Higgins, I.M., More, S.J., McClure, J., Lynn, D.J., Bradley, D.G., 2016. A genome-wide association study for genetic susceptibility to *Mycobacterium bovis* infection in dairy cattle identifies a susceptibility QTL on chromosome 23. Genet. Sel. Evol. 48 (19-016-0197-x).
Rubicz, R., Yolken, R., Drigalenko, E., Carless, M.A., Dyer, T.D., Bauman, L., Melton, P.E., Kent Jr., J.W., Harley, J.B., Curran, J.E., Johnson, M.P., Cole, S.A., Almasy, L., Moses, E.K., Dhurandhar, N.V., Kraig, E., Blangero, J., Leach, C.T., Goring, H.H., 2013. A genome-wide integrative genomic study localizes genetic factors influencing antibodies against Epstein-Barr virus nuclear antigen 1 (EBNA-1). PLoS Genet. 9, e1003147.
Sahana, G., Guldbrandtsen, B., Thomsen, B., Lund, M.S., 2013. Confirmation and fine-mapping of clinical mastitis and somatic cell score QTL in Nordic Holstein cattle. Anim. Genet. 44, 620–626.
Salie, M., van der Merwe, L., Moller, M., Daya, M., van der Spuy, G.D., van Helden, P.D., Martin, M.P., Gao, X.J., Warren, R.M., Carrington, M., Hoal, E.G., 2014. Associations between human leukocyte antigen class I variants and the *Mycobacterium tuberculosis* subtypes causing disease. J Infect Dis 209, 216–223.
Sanchez-Juan, P., Bishop, M.T., Aulchenko, Y.S., Brandel, J.P., Rivadeneira, F., Struchalin, M., Lambert, J.C., Amouyel, P., Combarros, O., Sainz, J., Carracedo, A., Uitterlinden, A.G., Hofman, A., Zerr, I., Kretzschmar, H.A., Laplanche, J.L., Knight, R.S., Will, R.G., van Duijn, C.M., 2012. Genome-wide study links MTMR7 gene to variant Creutzfeldt-Jakob risk. Neurobiol. Aging 33 (1487.e21-1487.e28).
Sanchez-Juan, P., Bishop, M.T., Kovacs, G.G., Calero, M., Aulchenko, Y.S., Ladogana, A., Boyd, A., Lewis, V., Ponto, C., Calero, O., Poleggi, A., Carracedo, A., van der Lee, S.J., Strobel, T., Rivadeneira, F., Hofman, A., Haik, S., Combarros, O., Berciano, J., Uitterlinden, A.G., Collins, S.J., Budka, H., Brandel, J.P., Laplanche, J.L., Pocchiari, M., Zerr, I., Knight, R.S., Will, R.G., van Duijn, C.M., 2015. A genome wide association study links glutamate receptor pathway to sporadic Creutzfeldt-Jakob disease risk. PLoS One 10, e0123654.
Sanders, A.E., Sofer, T., Wong, Q., Kerr, K.F., Agler, C., Shaffer, J.R., Beck, J.D., Offenbacher, S., Salazar, C.R., North, K.E., Marazita, M.L., Laurie, C.C., Singer, R.H., Cai, J., Finlayson, T.L., Divaris, K., 2017. Chronic periodontitis genome-wide association study in the Hispanic Community Health Study/Study of Latinos. J. Dent. Res. 96, 64–72.
Schaefer, A.S., Richter, G.M., Nothnagel, M., Manke, T., Dommisch, H., Jacobs, G., Arlt, A., Rosenstiel, P., Noack, B., Groessner-Schreiber, B., Jepsen, S., Loos, B.G., Schreiber, S., 2010. A genome-wide association study identifies GLT6D1 as a susceptibility locus for periodontitis. Hum. Mol. Genet. 19, 553–562.
Schneider, M.C., Prosser, B.E., Caesar, J.J., Kugelberg, E., Li, S., Zhang, Q., Quoraishi, S., Lovett, J.E., Deane, J.E., Sim, R.B., Roversi, P., Johnson, S., Tang, C.M., Lea, S.M., 2009. Neisseria meningitidis recruits factor H using protein mimicry of host carbohydrates. Nature 458, 890–893.
Semenza, J.C., 2010. Strategies to intervene on social determinants of infectious diseases. Euro Surveill. 15, 32–39.
Settles, M., Zanella, R., McKay, S.D., Schnabel, R.D., Taylor, J.F., Whitlock, R., Schukken, Y., Van Kessel, J.S., Smith, J.M., Neibergs, H., 2009. A whole genome association analysis identifies loci associated with *Mycobacterium avium* subsp. paratuberculosis infection status in US holstein cattle. Anim. Genet. 40, 655–662.
Shaffer, J.R., Feingold, E., Wang, X., Lee, M., Tcuenco, K., Weeks, D.E., Weyant, R.J., Crout, R., McNeil, D.W., Marazita, M.L., 2013. GWAS of dental caries patterns in the permanent dentition. J. Dent. Res. 92, 38–44.
Shi, Y., Li, L., Hu, Z., Li, S., Wang, S., Liu, J., Wu, C., He, L., Zhou, J., Li, Z., Hu, T., Chen, Y., Jia, Y., Wang, S., Wu, L., Cheng, X., Yang, Z., Yang, R., Li, X., Huang, K., Zhang, Q., Zhou, H., Tang, F., Chen, Z., Shen, J., Jiang, J., Ding, H., Xing, H., Zhang, S., Qu, P., Song, X., Lin, Z., Deng, D., Xi, L., Lv, W., Han, X., Tao, G., Yan, L., Han, Z., Li, Z., Miao, X., Pan, S., Shen, Y., Wang, H., Liu, D., Gong, E., Li, Z., Zhou, L., Luan, X., Wang, C., Song, Q., Wu, S., Xu, H., Shen, J., Qiang, F., Ma, G., Liu, L., Chen, X., Liu, J., Wu, J., Shen, Y., Wen, Y., Chu, M., Yu, J., Hu, X., Fan, Y., He, H., Jiang, Y., Lei, Z., Liu, C., Chen, J., Zhang, Y., Yi, C., Chen, S., Li, W., Wang, D., Wang, Z., Di, W., Shen, K., Lin, D., Shen, H., Feng, Y., Xie, X., Ma, D., 2013. A genome-wide association study identifies two new cervical cancer susceptibility loci at 4q12 and 17q12. Nat. Genet. 45, 918–922.
Shirvani-Dastgerdi, E., Schwartz, R.E., Ploss, A., 2016. Hepatocarcinogenesis associated with hepatitis B, delta and C viruses. Curr. Opin. Virol. 20, 1–10.
Shrestha, S., Irvin, M.R., Taylor, K.D., Wiener, H.W., Pajewski, N.M., Haritunians, T., Delaney, J.A., Schambelan, M., Polak, J.F., Arnett, D.K., Chen, Y.D., Grunfeld, C., 2010. A genome-wide association study of carotid atherosclerosis in HIV-infected

men. AIDS 24, 583–592.
Simpson, K.W., Dogan, B., Rishniw, M., Goldstein, R.E., Klaessig, S., McDonough, P.L., German, A.J., Yates, R.M., Russell, D.G., Johnson, S.E., Berg, D.E., Harel, J., Bruant, G., McDonough, S.P., Schukken, Y.H., 2006. Adherent and invasive *Escherichia coli* is associated with granulomatous colitis in boxer dogs. Infect. Immun. 74, 4778–4792.
Sironi, M., Clerici, M., 2010. The hygiene hypothesis: an evolutionary perspective. Microbes Infect. 12, 421–427.
Smith, C.M., Proulx, M.K., Olive, A.J., Laddy, D., Mishra, B.B., Moss, C., Gutierrez, N.M., Bellerose, M.M., Barreira-Silva, P., Phuah, J.Y., Baker, R.E., Behar, S.M., Kornfeld, H., Evans, T.G., Beamer, G., Sassetti, C.M., 2016. Tuberculosis susceptibility and vaccine protection are independently controlled by host genotype. MBio 7. http://dx.doi.org/10.1128/mBio.01516-16.
Sobota, R.S., Stein, C.M., Kodaman, N., Scheinfeldt, L.B., Maro, I., Wieland-Alter, W., Igo Jr., R.P., Magohe, A., Malone, L.L., Chervenak, K., Hall, N.B., Modongo, C., Zetola, N., Matee, M., Joloba, M., Froment, A., Nyambo, T.B., Moore, J.H., Scott, W.K., Lahey, T., Boom, W.H., von Reyn, C.F., Tishkoff, S.A., Sirugo, G., Williams, S.M., 2016. A locus at 5q33.3 confers resistance to tuberculosis in highly susceptible individuals. Am. J. Hum. Genet. 98, 514–524.
Sodeland, M., Kent, M.P., Olsen, H.G., Opsal, M.A., Svendsen, M., Sehested, E., Hayes, B.J., Lien, S., 2011. Quantitative trait loci for clinical mastitis on chromosomes 2, 6, 14 and 20 in Norwegian Red cattle. Anim. Genet. 42, 457–465.
Staeheli, P., Grob, R., Meier, E., Sutcliffe, J.G., Haller, O., 1988. Influenza virus-susceptible mice carry Mx genes with a large deletion or a nonsense mutation. Mol. Cell. Biol. 8, 4518–4523.
Sun, Q., Yang, J., Xing, G., Sun, Q., Zhang, L., He, F., 2008. Expression of GSDML associates with tumor progression in uterine cervix cancer. Transl. Oncol. 1, 73–83.
Suppiah, V., Moldovan, M., Ahlenstiel, G., Berg, T., Weltman, M., Abate, M.L., Bassendine, M., Spengler, U., Dore, G.J., Powell, E., Riordan, S., Sheridan, D., Smedile, A., Fragomeli, V., Muller, T., Bahlo, M., Stewart, G.J., Booth, D.R., George, J., 2009. IL28B is associated with response to chronic hepatitis C interferon-alpha and ribavirin therapy. Nat. Genet. 41, 1100–1104.
Sveinbjornsson, G., Gudbjartsson, D.F., Halldorsson, B.V., Kristinsson, K.G., Gottfredsson, M., Barrett, J.C., Gudmundsson, L.J., Blondal, K., Gylfason, A., Gudjonsson, S.A., Helgadottir, H.T., Jonasdottir, A., Jonasdottir, A., Karason, A., Kardum, L.B., Knezevic, J., Kristjansson, H., Kristjansson, M., Love, A., Luo, Y., Magnusson, O.T., Sulem, P., Kong, A., Masson, G., Thorsteinsdottir, U., Dembic, Z., Nejentsev, S., Blondal, T., Jonsdottir, I., Stefansson, K., 2016. HLA class II sequence variants influence tuberculosis risk in populations of European ancestry. Nat. Genet. 48, 318–322.
Tan, W., Xia, J., Dan, Y., Li, M., Lin, S., Pan, X., Wang, H., Tang, Y., Liu, N., Tan, S., Liu, M., He, W., Zhang, W., Mao, Q., Wang, Y., Deng, G., 2017. Genome-wide association study identi fi es HLA-DR variants conferring risk of HBV-related acute-on-chronic liver failure. Gut.
Tanaka, Y., Nishida, N., Sugiyama, M., Kurosaki, M., Matsuura, K., Sakamoto, N., Nakagawa, M., Korenaga, M., Hino, K., Hige, S., Ito, Y., Mita, E., Tanaka, E., Mochida, S., Murawaki, Y., Honda, M., Sakai, A., Hiasa, Y., Nishiguchi, S., Koike, A., Sakaida, I., Imamura, M., Ito, K., Yano, K., Masaki, N., Sugauchi, F., Izumi, N., Tokunaga, K., Mizokami, M., 2009. Genome-wide association of IL28B with response to pegylated interferon-alpha and ribavirin therapy for chronic hepatitis C. Nat. Genet. 41, 1105–1109.
Tanaka, Y., Kurosaki, M., Nishida, N., Sugiyama, M., Matsuura, K., Sakamoto, N., Enomoto, N., Yatsuhashi, H., Nishiguchi, S., Hino, K., Hige, S., Itoh, Y., Tanaka, E., Mochida, S., Honda, M., Hiasa, Y., Koike, A., Sugauchi, F., Kaneko, S., Izumi, N., Tokunaga, K., Mizokami, M., 2011. Genome-wide association study identified ITPA/DDRGK1 variants reflecting thrombocytopenia in pegylated interferon and ribavirin therapy for chronic hepatitis C. Hum. Mol. Genet. 20, 3507–3516.
Thompson, A.J., Clark, P.J., Singh, A., Ge, D., Fellay, J., Zhu, M., Zhu, Q., Urban, T.J., Patel, K., Tillmann, H.L., Naggie, S., Afdhal, N.H., Jacobson, I.M., Esteban, R., Poordad, F., Lawitz, E.J., McCone, J., Shiffman, M.L., Galler, G.W., King, J.W., Kwo, P.Y., Shianna, K.V., Noviello, S., Pedicone, L.D., Brass, C.A., Albrecht, J.K., Sulkowski, M.S., Goldstein, D.B., McHutchison, J.G., Muir, A.J., 2012. Genome-wide association study of interferon-related cytopenia in chronic hepatitis C patients. J. Hepatol. 56, 313–319.
Thons, C., Senff, T., Hydes, T.J., Manser, A.R., Heinemann, F.M., Heinold, A., Heilmann, M., Kim, A.Y., Uhrberg, M., Scherbaum, N., Lauer, G.M., Khakoo, S.I., Timm, J., 2017. HLA-Bw4 80(T) and multiple HLA-Bw4 copies combined with KIR3DL1 associate with spontaneous clearance of HCV infection in people who inject drugs. J. Hepatol. 67, 462–470.
Thorven, M., Grahn, A., Hedlund, K.O., Johansson, H., Wahlfrid, C., Larson, G., Svensson, L., 2005. A homozygous nonsense mutation (428G → A) in the human secretor (FUT2) gene provides resistance to symptomatic norovirus (GGII) infections. J. Virol. 79, 15351–15355.
Thye, T., Vannberg, F.O., Wong, S.H., Owusu-Dabo, E., Osei, I., Gyapong, J., Sirugo, G., Sisay-Joof, F., Enimil, A., Chinbuah, M.A., Floyd, S., Warndorff, D.K., Sichali, L., Malema, S., Crampin, A.C., Ngwira, B., Teo, Y.Y., Small, K., Rockett, K., Kwiatkowski, D., Fine, P.E., Hill, P.C., Newport, M., Lienhardt, C., Adegbola, R.A., Corrah, T., Ziegler, A., African TB Genetics Consortium, Wellcome Trust Case Control Consortium, Morris, A.P., Meyer, C.G., Horstmann, R.D., Hill, A.V., 2010. Genome-wide association analyses identifies a susceptibility locus for tuberculosis on chromosome 18q11.2. Nat. Genet. 42, 739–741.
Thye, T., Owusu-Dabo, E., Vannberg, F.O., van Crevel, R., Curtis, J., Sahiratmadja, E., Balabanova, Y., Ehmen, C., Muntau, B., Ruge, G., Sievertsen, J., Gyapong, J., Nikolayevskyy, V., Hill, P.C., Sirugo, G., Drobniewski, F., van de Vosse, E., Newport, M., Alisjahbana, B., Nejentsev, S., Ottenhoff, T.H., Hill, A.V., Horstmann, R.D., Meyer, C.G., 2012. Common variants at 11p13 are associated with susceptibility to tuberculosis. Nat. Genet. 44, 257–259.
Timmann, C., Thye, T., Vens, M., Evans, J., May, J., Ehmen, C., Sievertsen, J., Muntau, B., Ruge, G., Loag, W., Ansong, D., Antwi, S., Asafo-Adjei, E., Nguah, S.B., Kwakye, K.O., Akoto, A.O., Sylverken, J., Brendel, M., Schuldt, K., Loley, C., Franke, A., Meyer, C.G., Agbenyega, T., Ziegler, A., Horstmann, R.D., 2012. Genome-wide association study indicates two novel resistance loci for severe malaria. Nature 489, 443–446.
Trachtenberg, E., Bhattacharya, T., Ladner, M., Phair, J., Erlich, H., Wolinsky, S., 2009. The HLA-B/-C haplotype block contains major determinants for host control of HIV. Genes Immun. 10, 673–677.
Troyer, J.L., Nelson, G.W., Lautenberger, J.A., Chinn, L., McIntosh, C., Johnson, R.C., Sezgin, E., Kessing, B., Malasky, M., Hendrickson, S.L., Li, G., Pontius, J., Tang, M., An, P., Winkler, C.A., Limou, S., Le Clerc, S., Delaneau, O., Zagury, J.F., Schuitemaker, H., van Manen, D., Bream, J.H., Gomperts, E.D., Buchbinder, S., Goedert, J.J., Kirk, G.D., O'Brien, S.J., 2011. Genome-wide association study implicates PARD3B-based AIDS restriction. J Infect Dis 203, 1491–1502.
Ulveling, D., Le Clerc, S., Cobat, A., Labib, T., Noirel, J., Laville, V., Coulonges, C., Carpentier, W., Nalpas, B., Heim, M.H., Poynard, T., Cerny, A., Pol, S., Bochud, P.Y., Dabis, F., Theodorou, I., Levy, Y., Salmon, D., Abel, L., Dominguez, S., Zagury, J.F., HEPAVIH ANRS CO13 Cohort Study Group, Swiss Hepatitis C Cohort Study Group, French ANRS HC EP 26 Genoscan Study Group, 2016. A new 3p25 locus is associated with liver fibrosis progression in human immunodeficiency virus/hepatitis C virus-coinfected patients. Hepatology 64, 1462–1472.
Um, J.W., Kaufman, A.C., Kostylev, M., Heiss, J.K., Stagi, M., Takahashi, H., Kerrisk, M.E., Vortmeyer, A., Wisniewski, T., Koleske, A.J., Gunther, E.C., Nygaard, H.B., Strittmatter, S.M., 2013. Metabotropic glutamate receptor 5 is a coreceptor for Alzheimer abeta oligomer bound to cellular prion protein. Neuron 79, 887–902.
Urabe, Y., Ochi, H., Kato, N., Kumar, V., Takahashi, A., Muroyama, R., Hosono, N., Otsuka, M., Tateishi, R., Lo, P.H., Tanikawa, C., Omata, M., Koike, K., Miki, D., Abe, H., Kamatani, N., Toyota, J., Kumada, H., Kubo, M., Chayama, K., Nakamura, Y., Matsuda, K., 2013. A genome-wide association study of HCV-induced liver cirrhosis in the Japanese population identifies novel susceptibility loci at the MHC region. J. Hepatol. 58, 875–882.
Vered, K., Durrant, C., Mott, R., Iraqi, F.A., 2014. Susceptibility to *Klebsiella pneumonaie* infection in collaborative cross mice is a complex trait controlled by at least three loci acting at different time points. BMC Genomics 15 (865-2164-15-865).
Verra, F., Mangano, V.D., Modiano, D., 2009. Genetics of susceptibility to *Plasmodium falciparum*: from classical malaria resistance genes towards genome-wide association studies. Parasite Immunol. 31, 234–253.
Vilhjalmsson, B.J., Nordborg, M., 2013. The nature of confounding in genome-wide association studies. Nat. Rev. Genet. 14, 1–2.
Visscher, P.M., Wray, N.R., Zhang, Q., Sklar, P., McCarthy, M.I., Brown, M.A., Yang, J., 2017. 10 years of GWAS discovery: biology, function, and translation. Am. J. Hum. Genet. 101, 5–22.
Vukcevic, D., Traherne, J.A., Naess, S., Ellinghaus, E., Kamatani, Y., Dilthey, A., Lathrop, M., Karlsen, T.H., Franke, A., Moffatt, M., Cookson, W., Trowsdale, J., McVean, G., Sawcer, S., Leslie, S., 2015. Imputation of KIR types from SNP variation data. Am. J. Hum. Genet. 97, 593–607.
Wang, Z., Sun, Y., Fu, X., Yu, G., Wang, C., Bao, F., Yue, Z., Li, J., Sun, L., Irwanto, A., Yu, Y., Chen, M., Mi, Z., Wang, H., Huai, P., Li, Y., Du, T., Yu, W., Xia, Y., Xiao, H., You, J., Li, J., Yang, Q., Wang, N., Shang, P., Niu, G., Chi, X., Wang, X., Cao, J., Cheng, X., Liu, H., Liu, J., Zhang, F., 2016. A large-scale genome-wide association and meta-analysis identified four novel susceptibility loci for leprosy. Nat. Commun. 7, 13760.
Wanga, V., Venuto, C., Morse, G.D., Acosta, E.P., Daar, E.S., Haas, D.W., Li, C., Shepherd, B.E., 2015. Genomewide association study of tenofovir pharmacokinetics and creatinine clearance in AIDS Clinical Trials Group protocol A5202. Pharmacogenet. Genomics 25, 450–461.
Wellcome Trust Case Control Consortium, 2007. Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. Nature 447, 661–678.
Wiegering, V., Kaiser, J., Tappe, D., Weissbrich, B., Morbach, H., Girschick, H.J., 2011. Gastroenteritis in childhood: a retrospective study of 650 hospitalized pediatric patients. Int. J. Infect. Dis. 15, e401–7.
Williams-Blangero, S., VandeBerg, J.L., Blangero, J., Correa-Oliveira, R., 2011. Genetic epidemiology of Chagas disease. Adv. Parasitol. 75, 147–167.
Wu, X., Lund, M.S., Sahana, G., Guldbrandtsen, B., Sun, D., Zhang, Q., Su, G., 2015. Association analysis for udder health based on SNP-panel and sequence data in Danish Holsteins. Genet. Sel. Evol. 47 (50-015-0129-1).
Yang, J., Zaitlen, N.A., Goddard, M.E., Visscher, P.M., Price, A.L., 2014. Advantages and pitfalls in the application of mixed-model association methods. Nat. Genet. 46, 100–106.
Yoon, W., Ma, B.J., Fellay, J., Huang, W., Xia, S.M., Zhang, R., Shianna, K.V., Liao, H.X., Haynes, B.F., Goldstein, D.B., NIAID Center for HIV/AIDS Vaccine Immunology, 2010. A polymorphism in the HCP5 gene associated with HLA-B*5701 does not restrict HIV-1 in vitro. AIDS 24, 155–157.
Zare, Y., Shook, G.E., Collins, M.T., Kirkpatrick, B.W., 2014. Genome-wide association analysis and genomic prediction of *Mycobacterium avium* subspecies paratuberculosis infection in US Jersey cattle. PLoS One 9, e88380.
Zeng, Z., Feingold, E., Wang, X., Weeks, D.E., Lee, M., Cuenco, D.T., Broffitt, B., Weyant, R.J., Crout, R., McNeil, D.W., Levy, S.M., Marazita, M.L., Shaffer, J.R., 2014. Genome-wide association study of primary dentition pit-and-fissure and smooth surface caries. Caries Res. 48, 330–338.
Zhang, F.R., Huang, W., Chen, S.M., Sun, L.D., Liu, H., Li, Y., Cui, Y., Yan, X.X., Yang, H.T., Yang, R.D., Chu, T.S., Zhang, C., Zhang, L., Han, J.W., Yu, G.Q., Quan, C., Yu, Y.X., Zhang, Z., Shi, B.Q., Zhang, L.H., Cheng, H., Wang, C.Y., Lin, Y., Zheng, H.F., Fu, X.A., Zuo, X.B., Wang, Q., Long, H., Sun, Y.P., Cheng, Y.L., Tian, H.Q., Zhou, F.S., Liu, H.X., Lu, W.S., He, S.M., Du, W.L., Shen, M., Jin, Q.Y., Wang, Y., Low, H.Q., Erwin, T., Yang, N.H., Li, J.Y., Zhao, X., Jiao, Y.L., Mao, L.G., Yin, G., Jiang, Z.X., Wang, X.D., Yu, J.P., Hu, Z.H., Gong, C.H., Liu, Y.Q., Liu, R.Y., Wang, D.M., Wei, D., Liu, J.X., Cao, W.K., Cao, H.Z., Li, Y.P., Yan, W.G., Wei, S.Y., Wang, K.J., Hibberd, M.L., Yang, S., Zhang, X.J., Liu, J.J., 2009. Genomewide association study of leprosy. N. Engl. J. Med. 361, 2609–2618.
Zhang, H., Zhai, Y., Hu, Z., Wu, C., Qian, J., Jia, W., Ma, F., Huang, W., Yu, L., Yue, W., Wang, Z., Li, P., Zhang, Y., Liang, R., Wei, Z., Cui, Y., Xie, W., Cai, M., Yu, X., Yuan, Y., Xia, X., Zhang, X., Yang, H., Qiu, W., Yang, J., Gong, F., Chen, M., Shen, H., Lin, D., Zeng, Y.X., He, F., Zhou, G., 2010. Genome-wide association study identifies 1p36.22 as a new susceptibility locus for hepatocellular carcinoma in chronic hepatitis B virus carriers. Nat. Genet. 42, 755–758.

Zhang, F., Liu, H., Chen, S., Low, H., Sun, L., Cui, Y., Chu, T., Li, Y., Fu, X., Yu, Y., Yu, G., Shi, B., Tian, H., Liu, D., Yu, X., Li, J., Lu, N., Bao, F., Yuan, C., Liu, J., Liu, H., Zhang, L., Sun, Y., Chen, M., Yang, Q., Yang, H., Yang, R., Zhang, L., Wang, Q., Liu, H., Zuo, F., Zhang, H., Khor, C.C., Hibberd, M.L., Yang, S., Liu, J., Zhang, X., 2011. Identification of two new loci at IL23R and RAB32 that influence susceptibility to leprosy. Nat. Genet. 43, 1247–1251.

Zignego, A.L., Wojcik, G.L., Cacoub, P., Visentini, M., Casato, M., Mangia, A., Latanich, R., Charles, E.D., Gragnani, L., Terrier, B., Piazzola, V., Dustin, L.B., Khakoo, S.I., Busch, M.P., Lauer, G.M., Kim, A.Y., Alric, L., Thomas, D.L., Duggal, P., 2014. Genome-wide association study of hepatitis C virus- and cryoglobulin-related vasculitis. Genes Immun. 15, 500–505.

Zuk, O., Schaffner, S.F., Samocha, K., Do, R., Hechter, E., Kathiresan, S., Daly, M.J., Neale, B.M., Sunyaev, S.R., Lander, E.S., 2014. Searching for missing heritability: designing rare variant association studies. Proc. Natl. Acad. Sci. U. S. A. 111, E455–64.