



Genetics Ircd With Tb

Sophia Berniece Georghiou



Genetics Ircd With Tb:

International Research Centers Directory, 1984 **Organizations Master Index** Denise M. Allard, 1987 *Genetics of Tuberculosis Resistance* Rafal Sebastian Sobota, 2015 **Exploring Tuberculosis Genetics** Noemi Borsay Hall, 2016

Pulmonary tuberculosis disease TB caused by infection with *Mycobacterium tuberculosis* Mtb remains a major public health threat globally with a high burden in Sub Saharan Africa In this study we explored the stages of TB pathogenesis with a focus on two groups of individuals those who have active TB disease and those who remain uninfected despite prolonged exposure to an index case with active TB disease These latter individuals who appear to persistently resist Mtb infection are referred to as resisters RSTR From data collected through The Kawempe Community Health Study in Kampala Uganda a household contact study with a two year period of follow up we conducted regression analyses focusing on these two outcomes of interest as well as structural equation modeling of the interferon gamma IFN γ immune response First both TB and RSTR were tested for association with 546 haplotype tagging SNPs representing 29 candidate genes The RSTR phenotype was then the focus of an annotated SNP based regression analysis focusing on 305 SNPs within 17 genes shown to be differentially expressed in RSTRs and those with a positive tuberculin skin test We then used structural equation modeling to incorporate human genetics Mtb lineage and IFN γ response to three different Mtb antigens in modeling the latent variable IFN γ immune response Through these analyses we were able to detect associations with TB disease in IL1B TICAM2 NOD1 and NOD2 Interestingly SNPs within NOD1 NOD2 and TICAM2 also showed association with the RSTR phenotype The RSTR focused annotated SNP analysis also identified suggestive associations within the COLEC10 and HDAC4 genes COLEC10 HDAC4 and NOD1 had not been known to previously show an association with susceptibility to TB disease or with resistance to infection with Mtb The NOD1 association is novel both with TB disease and with RSTR and is therefore of special interest Future genetic association analysis should focus on these novel associations with RSTR and TB in order to develop a more effective vaccine and identify drug targets for faster acting effective TB treatments Genetics of Susceptibility to Tuberculosis Agnes Abiola Oluwatoyin Awomoyi, 2000 **Genetic Epidemiologic of the Response to *Mycobacterium Tuberculosis*** Natascha Remus, 2008 Tuberculosis TB remains a major global public health threat and host genetic factors are known to modulate the outcome of exposure to M tuberculosis We studied the genes NRAMP1 which has been associated with TB susceptibility in several ethnic groups and IL12RB1 that plays a major role in Mendelian Susceptibility to Mycobacterial Disease MSMD and found no evidence for association with pulmonary TB in an adult Moroccan population Thus complex susceptibility to TB disease in this population seems to be governed by other mechanisms than Mendelian susceptibility in children which might explain the different clinical presentations and physiopathological pathways in these different age groups We then analysed familial correlations of the immune response to infection studying the tuberculin skin test TST size and IFN γ production of PBMC s after stimulation with mycobacterial antigens in a

population from a low to moderate incidence region near Paris Val de Marne We observed strong familial correlations for the TST and after restriction of the study population to non infected individuals correlations for the ESAT6 trait were borderline significant $p = 0.047$ These studies have both scientific implications as they will enhance understanding of immune mechanisms controlling infection and medical implications as they will open the way for new preventive and therapeutic strategies *Genetic Susceptibility of Tuberculosis* Christian Søbørg,2004 **Genomic and Co-Evolutionary**

Determinants of Clinical Severity in Active Tuberculosis Patients Michael Lyon McHenry,2021 Tuberculosis TB is a major public health problem causing more deaths globally than any other pathogen prior to COVID19 It is also the leading cause of death among people infected with human immunodeficiency virus HIV Susceptibility to TB can be influenced by human genetic variation However factors underlying variation in TB severity are less well studied Clinical severity is an important phenotype that encompasses prognosis patient experience and risk of mortality Thus it is important to study severity as it can help us better understand patients quality of life disease experience and to predict survival among TB patients receiving treatment There is also evidence that MTB genetic variation as delineated by phylogenetic lineage can affect TB disease severity when considered simultaneously with human genetic variations and the interaction between the two Many genetic studies of TB stop short of linking these genetic effects to biological function The proposed study will address these fundamental gaps by 1 studying the genomic underpinnings of active TB severity using a meaningful replicable and validated clinical phenotype 2 demonstrating evidence of co evolution between humans and MTB on a population level how it affects severity and 3 bridging the gap between genetic variants and immunological function by studying gene expression in the macrophage response The overall goal is to examine how genomic variation in humans and MTB impact the immunological response to active TB disease and how this correlates with clinical severity Gene Xpert Testing of Stool Sample for the Diagnosis of Tb in Children Seble Haile Welday,Gunturu Revathi,Andrew Nyerere Kimangá,2016-04-15

Genetic Basis for Aminoglycoside Resistance in Mycobacterium Tuberculosis ,2017 Tuberculosis is a remerging and drug resistant infectious disease caused by Mycobacterium tuberculosis Mtb While the majority of tuberculosis TB incidences are susceptible cases a growing proportion of cases are drug resistant Drug resistance is usually stratified into mono resistance Multi Drug Resistance MDR Extensively Drug Resistance XDR and Total Drug Resistance TDR TB Mono resistance is when a strain is resistant to only one anti TB drug MDR TB strains are those resistant to the two most potent first line drugs Isoniazid INH and Rifampin RIF Additional resistance to fluoroquinolone group of drugs and to at least one injectable aminoglycoside is defined as XDR TB TDR is not as well defined and is usually understood to be the group of isolates that are resistant to most common anti TB drugs The Global Consortium for Drug resistant TB Diagnostics GCDD was funded by the National Institute of Health NIH to develop a rapid molecular test for the diagnosis of resistance to seven popular first and second line drugs namely Isoniazid INH Rifampicin RIF Ethambutol ETH Pyrazinamide PZA Amikacin AMK Kanamycin KAN

Capreomycin CAP Moxifloxacin MOX and Ofloxacin OFX This thesis project involved the study of the GCDD genomes for a better understanding of the mechanism of resistance to three aminoglycoside drugs AMK KAN CAP The project's primary aim was the identification of potential new mechanisms of resistance for those isolates that lack the expected mutations in the known genes Through identification of potential new gene markers we may be able to find a better more efficient and accurate diagnostic method for TB

Ri Im/Tb Genetics Hartwell,1999-08-01 *Human Genetic Susceptibility to Tuberculosis* Marlo Miller,2007

Association Between {221}-Chemokine Gene Polymorphisms and Tuberculosis Sok-Fan Chu, 2017-01-26 This dissertation Association Between 221 Chemokine Gene Polymorphisms and Tuberculosis by Sok fan Chu was obtained from The University of Hong Kong Pokfulam Hong Kong and is being sold pursuant to Creative Commons Attribution 3.0 Hong Kong License The content of this dissertation has not been altered in any way We have altered the formatting in order to facilitate the ease of printing and reading of the dissertation All rights not granted by the above license are retained by the author

Abstract Abstract of thesis entitled Association between Chemokine Gene Polymorphisms and Tuberculosis Submitted by Chu Sok Fan for the Degree of Master of Philosophy at the University of Hong Kong in August 2005 Tuberculosis TB is a chronic infectious disease caused by Mycobacterium tuberculosis MTB It has been estimated that one third of the human populations are infected with MTB TB is a significant public health burden accounting for 8.8 million new cases and 1.7 million deaths worldwide in 2003 Hong Kong is a place of intermediate burden of TB with a notification rate of around 110 per 100 000 persons Since only 10% of the infected individuals develop clinical disease in their lifetime host genetic factors may contribute to the interpersonal differences in the outcome of infections Chemokines are small chemotactic cytokines that mediate the migration of inflammatory cells to form a characteristic histological structure known as granuloma in TB The genes of chemokines a sub family of chemokines are clustered at chromosome 17q11.2 in humans Family based genome wide studies have shown the linkage of the chemokine locus to susceptibility to TB This study focused on the three most intensively studied members of chemokines including CCL2 monocyte chemotactic protein 1 MCP 1 CCL3 macrophage inflammatory protein 1 MIP 1 and CCL5 regulated upon activation normal T cell expressed and secreted RANTES which had been associated with complex diseases We hypothesized that the genetic polymorphisms regulating the transcription of these genes might contribute to TB susceptibility Five reported functional single nucleotide polymorphisms SNPs in the chemokine genes were investigated MCP 1 2518 A/G RANTES 403 G/A RANTES 28 C/G RANTES In1 1 T/C MIP 1 459 C/T Five hundred forty seven patients and four hundred sixty two controls were genotyped for the SNPs by polymerase chain reaction restriction fragment length polymorphism and the genotype and allele frequencies were compared between the two groups of subjects Linkage disequilibrium LD between each SNP within the same gene was measured The frequencies of CCL5 haplotypes were estimated by the expectation maximization algorithm and those of the combined genotypes of the three CCL5 SNPs were determined for patients with TB and controls Although

we did not find any significant differences in the genotype and allele frequencies of the individual SNPs of the chemokine genes between patients and controls a substantial difference in the LD pattern of SNPs in the CCL5 gene was observed between patients with TB and controls Furthermore we found a significant difference in the distribution of CCL5 haplotypes between patients and controls DOI 10.5353/th.b3573613 Subjects Tuberculosis Genetic aspects Chemokines Granuloma Genetic polymorphisms

Association of Killer Immunoglobulin-like Receptor (KIR) Genes with Tuberculosis Disease in Two Canadian Cohorts Kali Braun, 2013 In Canada and more specifically in Canadian born Aboriginals and foreign born populations high incidence of tuberculosis TB causes significant morbidity and mortality The presence or absence of specific killer immunoglobulin like receptor KIR genes individually or in conjunction may be associated with tuberculosis active latent or uninfected disease status as well as ethnicity of an individual It is hypothesized that the differences in KIR profiles gene frequencies and or haplotypes in Canadian born Aboriginal Canadian born non Aboriginal and foreign born individuals elicits a differential activation or inhibition profile resulting in differential cytokine expression and eventually contributes to the outcome of TB infection In this study we examined the enrichment or depletion of KIR genes in different ethnic populations in Manitoba with special focus on active latent and uninfected TB status In addition we sought to explore the statistical correlation between TB status and inhibitory stimulatory KIR haplotypes

Mutations in the GyrA and GyrB Genes of Fluoroquinolone-resistant Mycobacterium Tuberculosis from TB Patients in Thailand Pannamthip Pitaksajakul, Mahāwitthayālai Mahidon, Mahāwitthayālai Mahidon. Faculty of Tropical Medicine, 2004

Gene Expression Profiling Meta-analysis Reveals Novel Gene Signatures and Pathways Shared Between Tuberculosis and Rheumatoid Arthritis Mohamed Tarek Badr, Georg Häcker, 2019 Abstract Tuberculosis TB is among the leading causes of death by infectious diseases An epidemiological association between Mycobacterium tuberculosis infection and autoimmune diseases like rheumatoid arthritis RA has been reported but it remains unclear if there is a causal relationship and if so which molecular pathways and regulatory mechanisms contribute to it Here we used a computational biology approach by global gene expression meta analysis to identify candidate genes and pathways that may link TB and RA Data were collected from public expression databases such as NCBI GEO Studies were selected that analyzed mRNA expression in whole blood or blood cell populations in human case control studies at comparable conditions Six TB and RA datasets 41 active TB patients 33 RA patients and 67 healthy controls were included in the downstream analysis This approach allowed the identification of deregulated genes that had not been identified in the single analysis of TB or RA patients and that were co regulated in TB and RA patients compared to healthy subjects The genes encoding TLR5 TNFSF10 TRAIL PPP1R16B TIMAP SIAH1 PIK3IP1 and IL17RA were among the genes that were most significantly deregulated in TB and RA Pathway enrichment analysis revealed T cell receptor signaling pathway Toll like receptor signaling pathway and virus defense related pathways among the pathways most strongly associated with both diseases The identification of a common gene signature and pathways

substantiates the observation of an epidemiological association of TB and RA and provides clues on the mechanistic basis of this association Newly identified genes may be a basis for future functional and epidemiological studies **Genetic**

Susceptibility Genes in Tuberculosis □□□, So-Kwan Florence Cheng, 2017-01-27 This dissertation Genetic Susceptibility Genes in Tuberculosis Mannose Binding Lectin and Interferon Gamma by So kwan Florence Cheng was obtained from The University of Hong Kong Pokfulam Hong Kong and is being sold pursuant to Creative Commons Attribution 3 0 Hong Kong License The content of this dissertation has not been altered in any way We have altered the formatting in order to facilitate the ease of printing and reading of the dissertation All rights not granted by the above license are retained by the author DOI 10 5353 th_b3122577 Subjects Mannose Lectins Interferon Tuberculosis Genetic aspects **Analysis of Genetic**

Variability Within the Beijing Lineage of Mycobacterium Tuberculosis Samuel Donato, 2011 Previous research has demonstrated that the DosR DosS two component signaling system is constitutively overexpressed in modern Beijing strains of Mycobacterium tuberculosis M tb It is hypothesized that constitutive overexpression of this regulatory system is related to the unique pathogenic properties reported for this important strain lineage Within this thesis we attempted to determine the cause of this overexpression phenotype We first compared known DosR signaling stimuli between different strains of M tb looking specifically at NO nitric oxide and redox reduction oxidation balance We demonstrated that there was no difference in endogenous NO production between strains but we showed that there was a significantly more reductive NADH NAD pool in modern Beijing strains To determine the specific factor responsible we transformed four independent strains of M tb with a DosR dependent XylE reporter and developed a novel colony screening assay to **Molecular Diagnostics for**

Drug-resistant Tuberculosis Sophia Berniece Georghiou, 2016 Background Rapid molecular diagnostics with their ability to quickly identify genetic mutations associated with drug resistance have great potential to curb the spread of drug resistant tuberculosis DR TB Unfortunately the technical and diagnostic performance of these technologies has yet to be thoroughly evaluated in diverse clinical environments and the reliability and clinical relevance of the tuberculosis TB resistance mutations identified by these assays has not been well characterized Methods These analyses use data from a multisite observational cohort study conducted by the Global Consortium for Drug Resistant TB Diagnostics GCDD Chapter 2 assesses the diagnostic performance of a pyrosequencing assay in this study and applies logistic regression to identify the variables associated with poor assay technical performance Chapter 3 presents the frequency and distribution of all TB resistance mutations identified between clinical sites Chapter 4 applies multivariate logistic regression to determine the associations between TB resistance mutations and patient mortality for the GCDD study cohort Results Chapter 2 found pyrosequencing assay performance to be high overall though sensitivity fluctuated between sites Smear negativity culture negativity site Moldova and sequencing of the rpoB gyrA and rrs genes were associated with poor assay technical performance Chapter 3 found inclusion of the ahpC and eis promoter gene regions to be critical for optimal test sensitivity for isoniazid resistance

detection in South Africa and kanamycin resistance detection in Moldova Chapter 4 found that the detection of a mutation associated with high level fluoroquinolone or kanamycin resistance was significantly associated with higher odds of patient mortality by 52 weeks Conclusions A DR TB diagnostic demonstrated excellent specificity in a large multisite study though performance was influenced by regional genetics and technical errors Findings of the high prevalence of low global frequency TB resistance mutations in specific sites emphasizes that these mutations may be important resistance markers in certain regions The observation that patients with high level gyrA and rrs resistance mutations had higher mortality odds provides strong evidence that certain high level resistance mutations are clinically relevant Together these findings underscore the potential for molecular diagnostics to replace conventional growth based diagnostics as predictors of phenotypic drug resistance and clinical outcome

Genetics Tb T/A SRUSTAD,

Decoding **Genetics Ircd With Tb**: Revealing the Captivating Potential of Verbal Expression

In an era characterized by interconnectedness and an insatiable thirst for knowledge, the captivating potential of verbal expression has emerged as a formidable force. Its capability to evoke sentiments, stimulate introspection, and incite profound transformations is genuinely awe-inspiring. Within the pages of "**Genetics Ircd With Tb**," a mesmerizing literary creation penned by a celebrated wordsmith, readers set about an enlightening odyssey, unraveling the intricate significance of language and its enduring impact on our lives. In this appraisal, we shall explore the book's central themes, evaluate its distinctive writing style, and gauge its pervasive influence on the hearts and minds of its readership.

http://www.pet-memorial-markers.com/data/publication/default.aspx/Glassmaking_Americas_First_Industry.pdf

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