



Genetic Evidence for Cancer Immune Surveillance

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BACKGROUND

The immune system is involved in the control of cancer as the cancer immunoediting concept outlines

As a direct application, cancer immunotherapy has evolved to a powerful treatment option

The evidence for cancer immunoprevention also exists. Cancer is increased among immunosuppressed or immunodeficient people and occult cancer rates are high in autopsies of otherwise healthy people

METHODS

Given the amount of data on genetic correlations with immune parameters including immune cell counts, phenotype and cytokine levels and unbiased GWAS data in cancer, we explored associations of immune system-related SNPs with cancer susceptibility to test whether there is genetic evidence for cancer immunoprevention

We used GRASP and PhenoScanner databases to explore disease associations of immune regulatory gene variants

DATA SOURCE

Genetic Variants Regulating Immune Cell Levels in Health and Disease

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Large-Scale Exome-wide Association Analysis Identifies Loci for White Blood Cell Traits and Pleiotropy with Immune-Mediated Diseases

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The Genetic Architecture of the Human Immune System: A Bioresource for Autoimmunity and Disease Pathogenesis

Mario Roederer,^{1,7,*} Lydia Quaye,^{2,7} Massimo Mangino,^{2,4,7} Margaret H. Beedall,¹ Yolanda Mahnke,^{1,5} Pratip Chattopadhyay,¹ Isabella Tosi,^{3,4} Luca Napolitano,³ Manuela Terranova Barberio,³ Cristina Menni,² Federica Villanova,^{3,4} Paola Di Meglio,^{3,6} Tim D. Spector,^{2,8,*} and Frank O. Nestle^{3,4,8}

Differential Effects of Environmental and Genetic Factors on T and B Cell Immune Traits

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Host and Environmental Factors Influencing Individual Human Cytokine Responses

Rob ter Horst,^{1,14} Martin Jaeger,^{1,14} Sanne P. Smeekens,¹ Marije Oosting,¹ Morris A. Swertz,² Yang Li,² Vinod Kumar,² Dimitri A. Diavatopoulos,³ Anne F.M. Jansen,¹ Heidi Lemmers,¹ Helga Toenhake-Dijkstra,¹ Antonius E. van Herwaarden,⁴ Matthijs Janssen,¹² Renate G. van der Molen,⁴ Irma Joosten,⁴ Fred C.G.J. Sweep,⁴ Johannes W. Smit,^{1,5} Romana T. Netea-Maier,^{1,5} Mieke M.J.F. Koenders,⁶ Ramnik J. Xavier,^{7,8,9} Jos W.M. van der Meer,¹ Charles A. Dinarello,^{1,10} Norman Pavelka,^{1,11} Cisca Wijmenga,^{2,13} Richard A. Netea,^{1,8} Leo A.B. Joosten,^{1,*} and Mihai G. Netea^{1,15,*}

RESULTS

The screening of SNPs correlating with immune parameters revealed no cancer associations at the genome-wide statistical significance level

SNPs in or around immunoregulatory genes (IL, IFN, CC, CXCL, CCR, CXCR) revealed the statistically most significant associations with cancer susceptibility for skin, colorectal, breast, prostate, lung, bladder and liver cancers, and T-ALL with SNPs in or around *CXCR2*, *CCR4*, *CD163L1*, *CD300E*, *CD226*, *CTLA4*, *IFNG*, *IL1A1*, *IL1RAP*, *IL6*, *IL12RB2*, *IL16*, *IL17RC*, *IL18*, *IRF4*, *IRF8*, *IRFBP2* and *PTPN22*

RESULTS

Previously reported associations with cancer risk in candidate gene studies revealed GWAS associations with cancer, including lymphoma, melanoma, breast and lung cancer, although not the same ones as initially reported

We also screened the HLA region cancer associations for their involvement with the immune system. A small proportion of them were due to immunoregulatory gene variants or eQTL effects on classical HLA genes

CONCLUSIONS

This study did not reveal overwhelming evidence for a genetic component in cancer immune surveillance

This observation is in line with known stronger influence of the environment on the immune system

If immunoregulatory gene variants are involved in cancer immune surveillance, it is probably due to epistatic effects rather than individual variant effects

See also



Cancer Immunoprevention and Public Health

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RESULTS

GARLIC: GWAS-based Prediction Toolkit for Connecting Diseases and Cell Types



Welcome to GARLIC Viewer!

Show values for all diseases and traits ☐

Show values for all cell types ☐

DNase-seq regulatory map:

T_Reg

Disease/Trait name:

Colorectal cancer

Show

Clear

$p = 0.0360196398000000$

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Enabling the democratization of the genomics
revolution with a fully integrated web-based
bioinformatics platform

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A. Bishop-Lilly^{3,4}, Yan Xu¹, Sanaa Ahmed¹, Shihai Feng¹, Vishwesh P. Mokashi³ and Patrick
S.G. Chain^{1,*}

RESULTS

DNase-seq regulatory map:

T_Reg

Disease/Trait name:

Melanoma

Show

Clear

$p = 0.0163798362000000$

DNase-seq regulatory map:

T_Reg

Disease/Trait name:

Esophageal cancer (squamous cell)

Show

Clear

$p = 0.0127798722000000$

DNase-seq regulatory map:

T_Reg

Disease/Trait name:

Hodgkin's lymphoma

Show

Clear

$p = 0.0005199948000000$

DNase-seq regulatory map:

T_Reg

Disease/Trait name:

Lung adenocarcinoma

Show

Clear

$p = 0.0420495795000000$