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Title: Specificity of genetic predisposition to tuberculosis in native and immigrant Siberian populations

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Body: There is a difference in prevalence of tuberculosis (TB) among ethnically divergent Siberian populations with highest rates of disease among aboriginal Asian populations. Given the similar environment, differential genetic background can be responsible for distinguished TB liability in native and immigrant Siberian populations. We addressed this issue in a study of common polymorphisms of twelve immune-response modifying genes in Siberian populations of Russians (304 patients, 265 controls), Tuvinians (238 patients, 263 controls), and Yakuts (150 patients, 135 controls). Both ethnic specific and common association between the genes and TB were identified. The rs12756687 (PIAS3), rs3760903 (PIASY), rs167769 (STAT6), rs1024611 (MCP1), and rs2069705 (IFNG) polymorphisms were associated with TB in Russians. The rs7572482 (STAT4), rs3760903 (PIASY), and rs167769 (STAT6) were linked to disease in Tuvinians. The rs16967593 (STAT5B), rs3760903 (PIASY), rs17880053 (IFNGR2), rs1024611 (MCP1) were associated with TB in Yakuts. The PIASY gene was associated with TB in all studied populations suggesting it as a cosmopolitan TB gene. However, while in Russians the common allele was protective against the disease (OR=0.67, P = 1E-6), in Tuvinians and Yakuts it increased the risk of TB (OR = 1.41, P = 0.032; OR = 1.67, P = 0.035, respectively). STAT6 gene common allele was protective in Russians and predisposing in Tuvinians; while in case of MCP1 gene, common allele was predisposing in Russians and protective in Yakuts. This finding suggests specificity in allelic effects predisposing to TB in Asians and Russians of Siberia. Molecular mechanisms of these inverse effects are to be investigated.