# Study of serotonin transporter gene polymorphism Stin2 in two Siberian indigenous populations

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## INTRODUCTION

Serotonin (5-hydroxytryptamine, 5-HT) → emotions, mood, sleep, appetite, and cognitive processes.

Dysfunction of serotonin system → mental disorders (depression, suicidal behavior, excessive aggression, anxiety, addiction, obsessive-compulsive disorder, attention deficit/hyperactivity disorder and autism).

Serotonin transporter (5-HTT, SERT) → reuptake of 5-HT from the synaptic cleft → modulation of serotonergic neurotransmission.

5-HTT is the target for selective serotonin reuptake inhibitors (SSRIs), which are used to treat depression, anxiety, ADHD and other emotional and behavioral disorders.

Gene SLC6A4 → 5-HTT protein.

VNTR polymorphism Stin2 in intron 2 of the SLC6A4 gene:
9, 10 or 12 copies of a 16–17 bp repeat (Stin2.9, Stin2.10 and Stin2.12 alleles respectively).

Stin2 polymorphism → 5-HTT expression and response to transcription factors → association with anxiety, depression, alcohol dependence, suicidal behavior, obsessive-compulsive disorder.

Allele frequencies for Stin2 polymorphism have been studied in different populations, including Russians and other people living in Russian Federation.

To date, there was no information about these polymorphisms in Tundra Nenets and Nganasans inhabiting north Siberia.

The aim of the present study was to investigate Stin2 allele frequencies in the samples of Tundra Nenets and Nganasans.

## METHODS

Blood samples were collected during expeditions to Yamalo-Nenets Autonomous Okrug and Taymyrsky Dolgano-Nenetsky District from 1988 to 2009.

Genomic DNA was extracted from peripheral blood using standard phenol–chloroform method. Genotyping was performed using PCR and gel electrophoresis.

Correspondence of genotype frequencies to the Hardy-Weinberg equilibrium was assessed using Pearson's chi-squared ($\chi 2$) criterion. Differences in allele frequencies between the populations were estimated using a $\chi 2$ test.

## RESULTS AND DISCUSSION

Genotype counts and allele frequencies for STin2 are shown in Table 1. The distribution of genotypes was in accordance with Hardy-Weinberg equilibrium in the samples of Nenets ($p=0.065$) and Nganasans ($p=0.771$). We did not find carriers of the 9-repeat allele in either of the two samples.

Both indigenous populations studied have higher frequencies of Stin2.12 allele compared to Russians (60% for the published Russian sample, $p<0.001$).

The data obtained are consistent with the uniform geographic gradient of STin2 alleles, with low frequency of the STin2.10 allele in East Asia and its increase towards west. The information on the Stin2 allele frequency in indigenous populations may be further used in personalized medicine in order to choose the optimal treatment options for psychiatric disorders.

TABLE I. GENOTYPE AND ALLELE DISTRIBUTION FOR STIN2.

| **Population** | | **Genotype count** | | | **Alleles, %** | |
|---|---|---|---|---|---|---|
| | ***N*** | ***12/12*** | ***12/10*** | ***10/10*** | ***12*** | ***10*** |
| Nenets | 179 | 88 | 82 | 9 | 72.1 | 27.9 |
| Nganasans | 109 | 86 | 23 | 0 | 89.4 | 10.6 |

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