

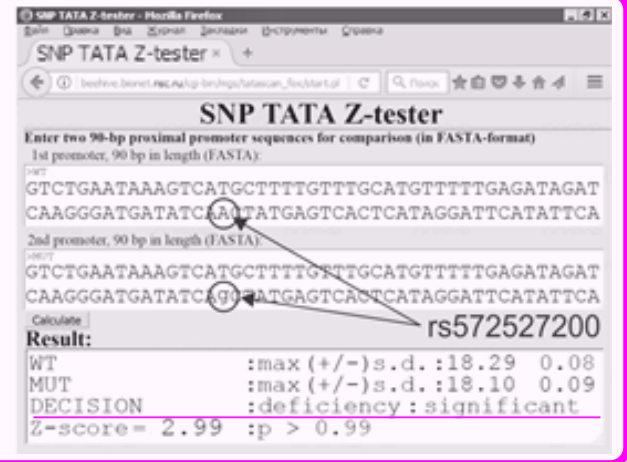
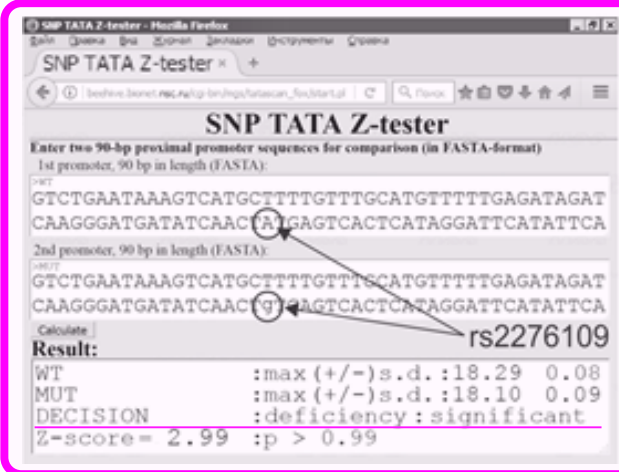
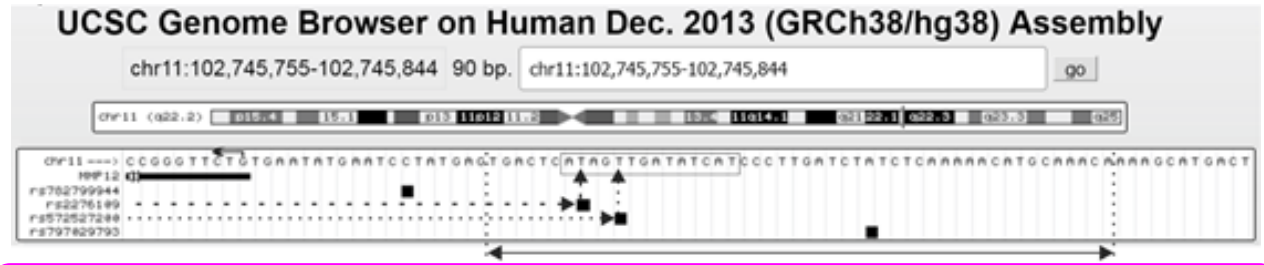
**Candidate SNP markers of rheumatoid arthritis changing the affinity of TATA-binding protein for the human gene promoters expo disruptive selection of immunoactivative and immunosuppressive genes that provoke and prevent this disorder, respectively, as if it could be a self-domestication syndrome**

*Klimova N, Chadaeva I, Oshchepkova E, Ponomarenko M, Oshchepkov D, Kozlov# V  
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*We made a genome-wide prognosis of candidate SNP markers for rheumatoid arthritis (RA), because that lifestyle and living conditions define a half of the RA risks and genetic susceptibility to RA do for another half (Nair et al., 2017)*



**Deficiency → less destructive rheumatoid arthritis**



**Both non-annotated rs2276109 and rs572527200 can cause MMP12 deficiency, which is a clinically proven physiological marker for less destructive rheumatoid arthritis (Liu et al., 2001)**

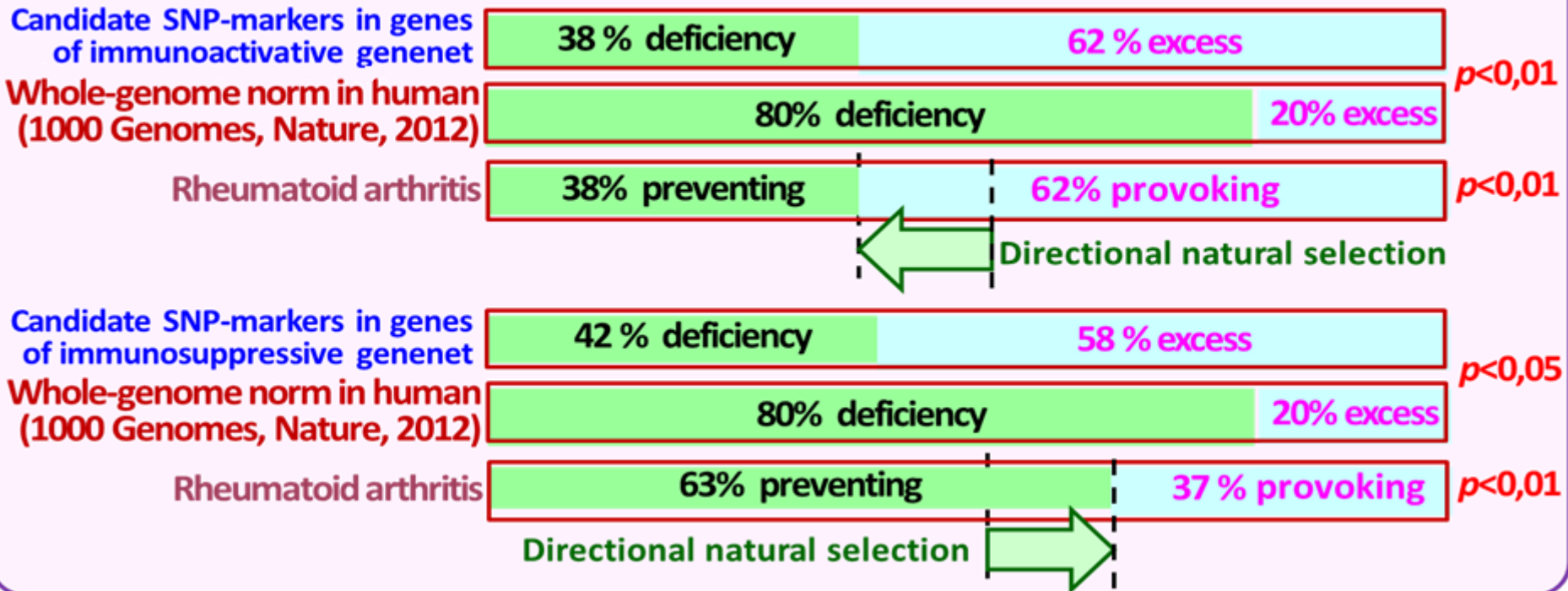
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We made a genome-wide prognosis of candidate SNP markers for rheumatoid arthritis (RA), because that lifestyle and living conditions define a half of the RA risks and genetic susceptibility to RA do for another half (Nair et al., 2017)

We tested **all 1939 SNPs** in question within promoters of **70 RA-related genes** in the human genome that yielded **526 SNPs altering significantly expression** of these genes.

The relative proportions of candidate SNP markers decrease and increase the affinity of the TBP–DNA



We found disruptive selection of immunoactivative and immunosuppressive genes that provoke and prevent rheumatoid arthritis, respectively, as if it could be a self-domestication syndrome

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**We confirmed our predictions of rheumatoid arthritis (RA) as a self-domestication syndrome using the publically available RNA-seq data on the differentially expressed genes (DEGs) between foxes (*Vulpes vulpes*) of two unique outbred lines bred in aggressiveness and tameness as an animal model of human diseases (Hekman et al., 2018).**

<i>Gene</i>	RNA-seq		RA risk		Clinical physiological markers	
	$\log_2(\text{tame/aggress})$	$P_{\text{ADJ}}$	aggress	tame	Known phenotype	Reference
<i>Npy</i>	0,37	0,01	↓	↑	NPY excess can cause obesity as RA risk factor	Stofkova et al., 2009
<i>Esr2</i>	-0,32	0,05	↓	↑	ESR2-excess can suppress inflammation in RA	Armstrong et al., 2013
<i>Tgfb2</i>	0,53	0,01	↓	↑	TGFB2 excess can inhibit bone repair under inflammation	Um et al., 2018
<i>Il1r2</i>	-0,41	0,05	↓	↑	IL1R2 excess can reduce inflammation in RA	Ocsko et al., 2018
<i>Il9r</i>	0,44	0,05	↓	↑	IL9R excess can elevate inflammation in RA	Raychaudhuri et al., 2018
<b>TOTAL</b>			$N_{\text{Aggress}\downarrow} = 5; N_{\text{Aggress}\uparrow} = 0; N_{\text{Tame}\downarrow} = 0; N_{\text{Tame}\uparrow} = 5$			
<i>Pearson's <math>\chi^2</math>-test, <math>\chi^2</math> (significance)</i>			10.00 ( $P_{\chi^2} < 0.0025$ )			
<i>Fisher's exact test (significance)</i>			0.004 ( $P_{\text{FISHER}} < 0.05$ )			

**We thank Ministry of Higher Education and Science Project #0324-2019-0040-C-01 for its support for this study**