Scientific Research Institute for Medical Problems of the North

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Ficoline-3 and MASP-2 gene variants in Russian Arctic populations

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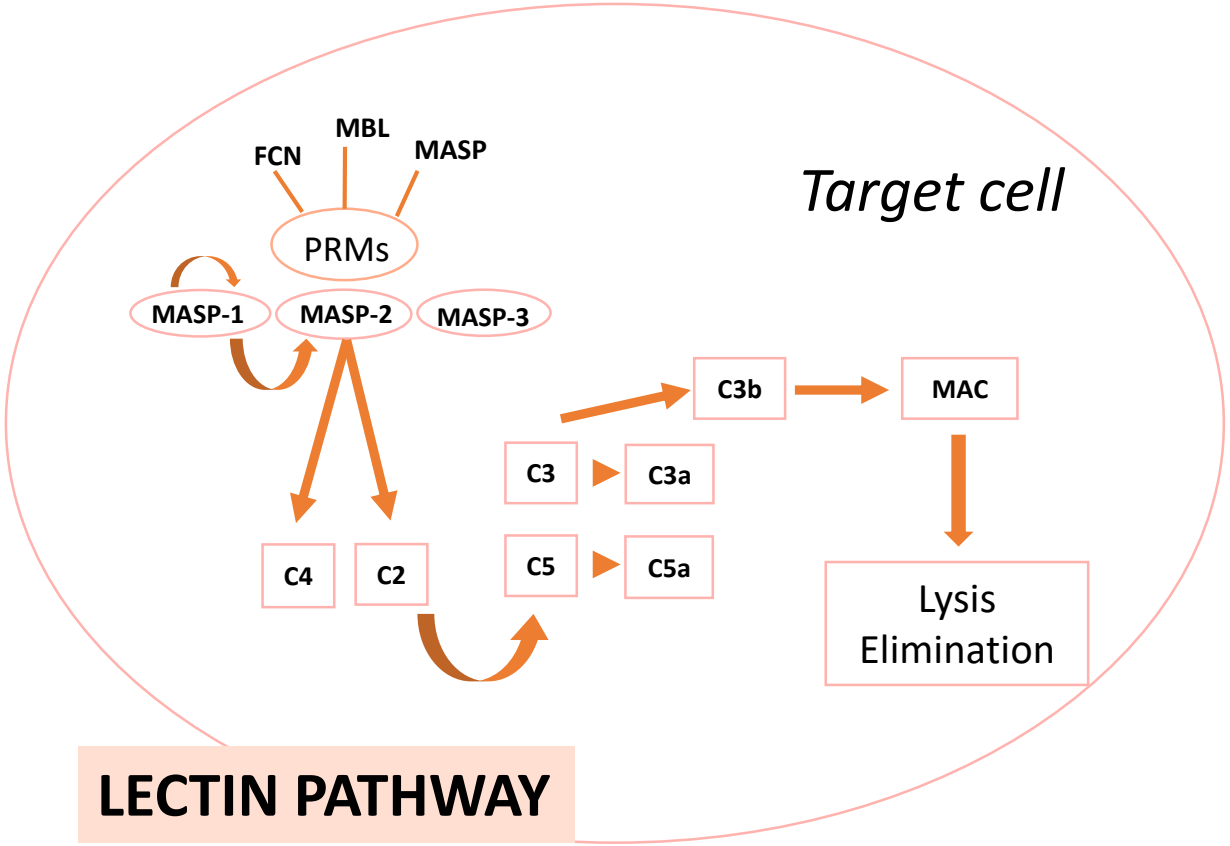
Motivation and Aim

- Ficolin-3 and MASP-2 – the key participants in the lectin pathway of complement activation
- The *FCN3* rs28357092 mutation is associated with low ficolin-3 levels in plasma
- Mutation in *MASP2* rs72550870 is associated with impaired protein binding to lectins



Aim: to reveal ethnic differences in the distribution of allelic gene variants for the lectin pathway components of complement activation between the indigenous populations of the Arctic territory of Siberia and Caucasoids

Methods and Algorithms

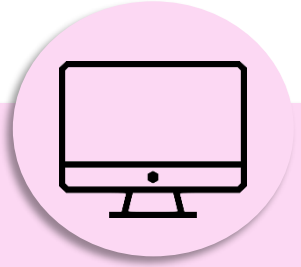
Materials

Newborn children of:

- indigenous Arctic ethnic groups: Nenets, Dolgan-Nganasans, mixed population, n=678
- Russians, n=302

Analysis

Genotyping of *FCN3* rs28357092 and *MASP2* rs72550870 was carried out by RT-PCR



Results

Allele and genotype frequencies were compared using an online calculator, the χ^2 test

The *FCN3* genotype frequency in newborns of different ethnic populations, n (%)

Genotype / allele	Nenets, n=323	Dolgan-Nganasans, n=138	Mixed population, n=217	Caucasoids, n=302	p
GG	292 (100.0)	128 (99.2)	199 (98.0)	291 (96.4)	1/3=0.02 1/4<0.001
G/del	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	-
del/del	0 (0.0)	1 (0.8)	4 (2.0)	10 (3.3)	1/3=0.02 1/4=0.002
del*	0 (0.0)	2 (0.8)	8 (2.0)	21 (3.5)	1/3<0.001 1/4<0.001 2/3=0.02 2/4=0.003

- The prevalence of GG homozygotes in all the studied populations
- The heterozygous genotype G/del rs28357092 was found to take place in only one Russian child

The *MASP2* genotype frequency in newborns of different ethnic populations, n (%)

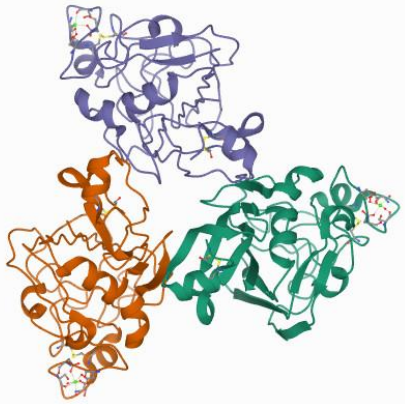
Genotype / allele	Nenets, n=323	Dolgan-Nganasans, n=138	Mixed population, n=217	Caucasoids, n=302	p
AA	322 (99.7)	136 (98.6)	213 (98.2)	226 (93.4)	1/4<0.001 2/4=0.02 3/4=0.01
AG	1 (0.3)	2 (1.4)	4 (1.8)	16 (6.6)	1/4<0.001 2/4=0.02 3/4=0.01
GG	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-
G*	1 (0.2)	2 (0.7)	4 (0.9)	16 (3.3)	1/4<0.001 2/4=0.03 3/4=0.01

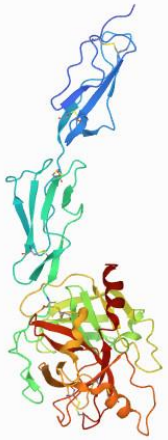
- The prevalence of AA homozygotes in all the studied populations
- The heterozygous AG rs72550870 genotype occurs occasionally in the Arctic populations compared with Russians

Conclusion

The genetic analysis results showed lower prevalence of genetic markers of ficolin-3 and MASP-2 deficiency in the indigenous populations of the Arctic territories compared to Russians

Crystal structure of the H-ficolin
(PDB ID 2J64),
DOI: 10.2210/pdb2j64/pdb





Crystal structure of the zymogen catalytic region of human MASP-2
(PDB ID 1ZJK),
DOI: 10.2210/pdb1ZJK/pdb