LRP5 GENE SINGLE NUCLEOTIDE POLYMORPHISMS AND OSTEOPOROSIS IN CHILDREN WITH PRIMARY GLOMERULONEPHRITIS TREATED WITH GLUCOCORTICOIDS

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INTRODUCTION

* Glucocorticoids, standard therapy in idiopathic nephrotic syndrome-important risk factor for decrease in bone mineral concentration (BMD) by inhibiting the replication of osteoblasts, apoptosis stimulation and the inhibition of collagen I synthesis.
* LRP5—Wnt signaling pathway proteins coreceptor involved through the RANK-RANKL in regulation of the osteoblasts function.
* *LRP5* is included to the osteoporosis phenotype genes group and its selected single nucleotide polymorphisms can be responsible for BMD decrease in patients with steroidotherapy.

AIM OF THE STUDY

* The aim of our study was to analyze twelve single nucleotide polymorphisms (SNP) of gene *LRP5* potentially associated with osteoporosis risk in children with routine steroidotherapy in the course of the idiopathic nephrotic syndrome.

PATIENTS AND METHODS

* The study group was composed of 40 children with idiopathic nephrotic syndrome under the age of twelve years old , 14 with osteoporosis and 26 with normal bone mass density.
* The control group consists of 102 healthy individuals at the same age not treated with glucocorticoids.
* Odds ratio value (OR) was based on frequencies of selected twelve single nucleotide polymorphisms (SNP) potentially associated with osteoporosis risk in analysis of coding regions of gene *LRP5*.

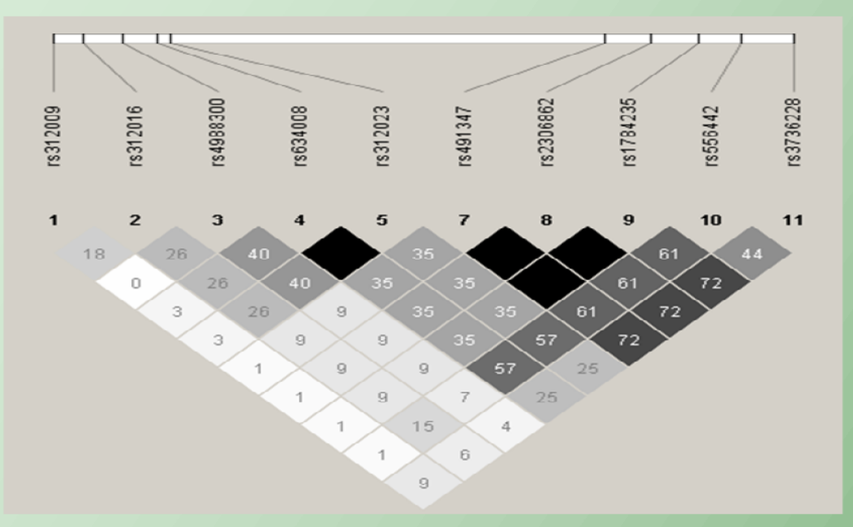
LRP5 SNP	nt	gene location
rs3736228	C/T	Exon 18, Ala 1330 Val
rs491347	A/G	Intron 7
rs312009	C/T	5'UTR
rs556442	A/G	Exon 15, Val 1119 Val
rs1784235	C/T	Intron 13
rs41494349	A/G	Exon 2, Gln 89 Arg
rs2306862	C/T	Exon 10, Asn 740 Asn
rs3736229	C/T	Exon 19, Asp 1363 Asp
rs312016	C/T	Intron 1
rs4988300	G/T	Intron 1
rs634008	C/T	Intron 1
rs312023	A/G	Intron 1

RESULTS:

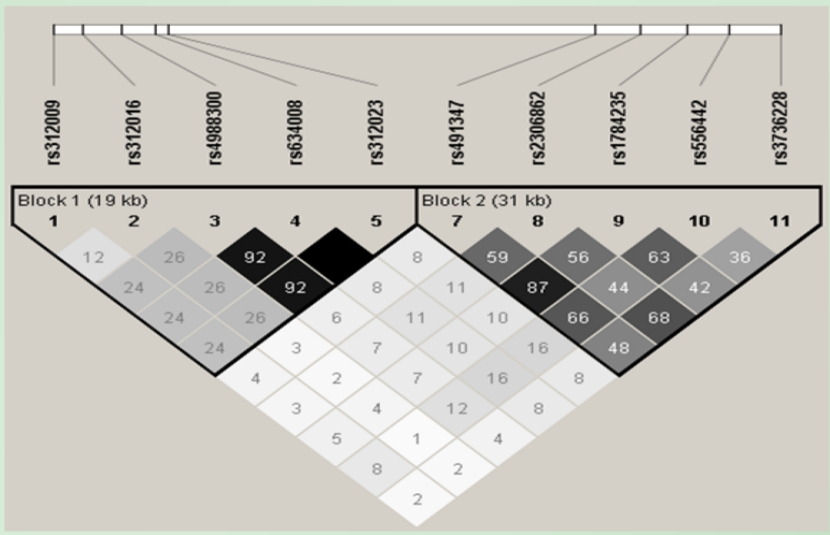
* The results showed not significant differences in OR value among the three groups.
* However there were found the important differences in the gene structure.
* Based on Gabriel algorithm we proved that the degree of interdependence between pairs of SNP 7,8 and 9 in children with nephrotic syndrome and osteoporosis was higher than in the other two groups.
* The SNPs 3,4 and 5 form the haplotype block based on linkage disequilibrium in children with nephrotic syndrome and without osteoporosis that is not observed in other groups.

LRP5 gene structure

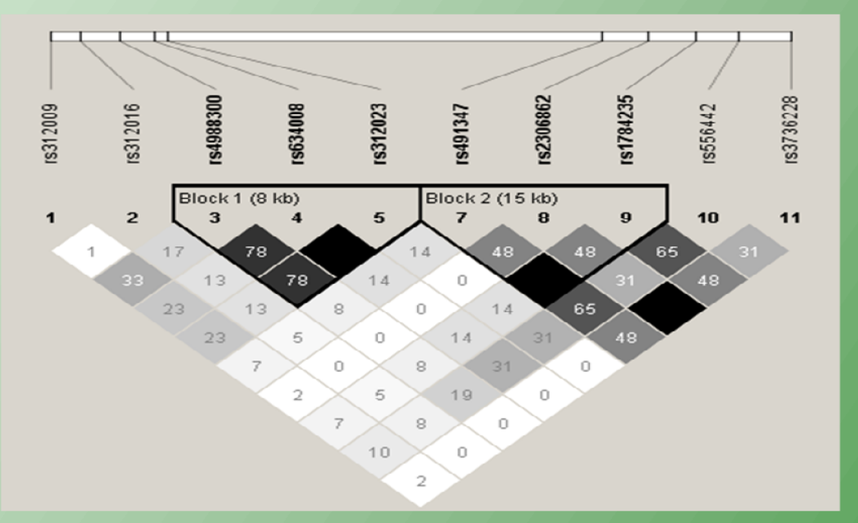
Nephrotic syndrome and osteoporosis group 1



Control group 3



Nephrotic syndrome without osteoporosis group 2



Lp.	Nazwa SNP	Częstość alleli			Częstość genotypów		
		Grupa badana Z score<-1,00	Grupa badana Z score>-1,00	Grupa kontrolna	Grupa badana Z score<-1,00	Grupa badana Z score>-1,00	Grupa kontrolna
1	rs3736228	C: 0,90 T: 0,10	C: 0,89 T: 0,11	C: 0,87 T: 0,13	CC: 0,79 TT: 0,00 CT: 0,21	CC: 0,85 TT: 0,00 CT: 0,15	CC: 0,77 TT: 0,03 CT: 0,20
2	rs491347	A: 0,86 G: 0,14	A: 0,79 G: 0,21	A: 0,77 G: 0,23	AA: 0,72 GG: 0,00 AG: 0,28	AA: 0,58 GG: 0,00 AG: 0,42	AA: 0,59 GG: 0,06 AG: 0,35
3	rs312009	C: 0,57 T: 0,43	C: 0,50 T: 0,50	C: 0,74 T: 0,26	CC: 0,36 TT: 0,21 CT: 0,43	CC: 0,23 TT: 0,23 CT: 0,54	CC: 0,57 TT: 0,08 CT: 0,35
4	rs556442	A: 0,79 G: 0,21	A: 0,71 G: 0,29	A: 0,72 G: 0,28	AA: 0,57 GG: 0,00 AG: 0,43	AA: 0,50 GG: 0,04 AG: 0,46	AA: 0,55 GG: 0,10 AG: 0,35
5	rs1784235	C: 0,14 T: 0,86	C: 0,21 T: 0,79	C: 0,26 T: 0,74	CC: 0,00 TT: 0,72 CT: 0,28	CC: 0,00 TT: 0,58 CT: 0,42	CC: 0,08 TT: 0,56 CT: 0,36
6	rs2306862	C: 0,86 T: 0,14	C: 0,88 T: 0,12	C: 0,84 T: 0,16	CC: 0,71 TT: 0,00 CT: 0,29	CC: 0,77 TT: 0,00 CT: 0,23	CC: 0,71 TT: 0,04 CT: 0,25
7	**rs312016**	**C: 0,64 T: 0,36**	**C: 0,85 T: 0,15**	**C: 0,73 T: 0,27**	**CC: 0,36 TT: 0,07 CT: 0,57**	**CC: 0,70 TT: 0,00 CT: 0,30**	**CC: 0,55 TT: 0,09 CT: 0,36**
8	rs4988300	G: 0,68 T: 0,32	G: 0,52 T: 0,48	G: 0,55 T: 0,45	GG: 0,43 TT: 0,07 GT: 0,50	GG: 0,23 TT: 0,19 GT: 0,58	GG: 0,35 TT: 0,24 GT: 0,41
9	rs634008	C: 0,32 T: 0,68	C: 0,42 T: 0,58	C: 0,46 T: 0,54	CC: 0,07 TT: 0,43 CT: 0,50	CC: 0,19 TT: 0,35 CT: 0,46	CC: 0,24 TT: 0,33 CT: 0,43
10	rs312023	A: 0,68 G: 0,32	A: 0,58 G: 0,42	A: 0,56 G: 0,44	AA: 0,43 GG: 0,07 AG: 0,50	AA: 0,35 GG: 0,19 AG: 0,46	AA: 0,34 GG: 0,22 AG: 0,44

SNP rs312016	Gene variants		
Control group	**CT/TT**	**CC**	**CT/TT/CC**
ZN+Z-score≤-1,00	**9(23%)**	**5(13%)**	**14(35%)**
ZN+Z-score≥-1,00	**8(20%)**	**18(45%)**	**26(65%)**
total	**17(43%)**	**23(58%)**	**40(100%)**

P=0,0525; OR=4,050

CONCLUSIONS

* The size of the study groups decides that was not statistically important differences between them. However analyzing LRP5 gene structure we suggest it is likely a correlation between the selected SNPs, their haplotypes and the risk of osteoporosis regardless of the steroids bone effect.

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