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Association of vitamin D receptor single nucleotide polymorphisms with late onset Alzheimer's disease in the Greek population.

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PURPOSE / OBJECTIVES

In the last few years the effect of vitamin D has been studied in chronic neurodegenerative diseases such as Alzheimer's disease, as it has been observed that its molecular mechanisms of action are involved in the development mechanisms of the disease such as the formation of amyloid b, cell toxicity and inflammation of neural cells[1,2,3].
Study primary objective was to investigate potential association of the single nucleotide variations TaqI, BsmI and FokI of the *VDR* gene with the development of **Late onset Alzheimer's disease (LOAD)** in a Southeastern Caucasians cohort. Secondary, to evaluate associations of these variations to *APOE* e4 allele and the neuropsychology Mini–Mental State Examination (MMSE) and Frontal Assessment Battery (FAB) assessments.

MATERIALS & METHODS

The cohort included 90 confirmed LOAD patients (median age 74 years, range 51-92 years, male 48.9% - female 51.1%, median MMSE score 21, median FAB score 10) and 103 unmatched healthy controls (median age 57 years, range 51-90 years, male 49.5% - female 50.5%).

Blood samples were analyzed to determine the genotypes of TaqI (rs731236), BsmI (rs1544410) and FokI (rs2228570). After DNA extraction and Polymerase Chain Reaction (PCR), BsmI and FokI SNPs were genotyped using the RFLP method. Genotypes of TaqI were determined using LightSNiP (SimpleProbe®) real time PCR (rtPCR) assay **(Figure 1)**.

RESULTS

The frequencies (%) of TaqI TT, TC and CC genotypes in controls/patients was 34.0/48.9, 47.6/41.1 and 18.4/10.0 respectively **(Table 1)**. A statistically significant difference was observed for TaqI C allele (TT vs CT+CC, OR 0.54, 95% CI 0.30-0.96, p=0.035), for TaqI TT genotype (CC+TC vs TT, OR 1.86, 95% CI 1.04-3.32, p=0.035) and for TaqI CC genotype in relation to MMSE score <21 in the patient's group (CC vs TC+TT, OR 0.128, 95% CI 0.015-10.72, p=0.036).

Vitamin D Receptor Gene TaqI polymorphism is associated with Alzheimer's disease in the Greek population

TaqI C allele might protect from Alzheimer's disease

Homozygous TaqI CC AD patients face milder cognitive impairment

RESULTS (continued)

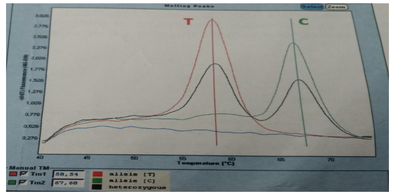

Figure 1. Melting curves of LightSNiP real time PCR assay for the TaqI rs731236 polymorphism.

TaqI rs731236 association with AD (n=193)					
Model	**Genotype**	**Controls n(%)**	**AD n(%)**	**OR (95% CI)**	**p value**
Codominant	CC	19 (18.4%)	9 (10%)	1.00	0.064
	TC	49 (47.6%)	37 (41.1%)	1.59 (0.65-3.92)	
	TT	35 (34%)	44 (48.9%)	2.65 (1.07-6.59)	
Dominant	CC	19 (18.4%)	9 (10%)	1.00	
	TC/TT	84 (81.5%)	81 (90%)	2.04 (0.87-4.76)	0.092
Recessive	CC/TC	68 (66%)	46 (51.1%)	1.00	
	TT	35 (34%)	44 (48.9%)	**1.86 (1.04-3.32)**	**0.035**

Table 1. Frequencies of TaqI genotypes in the different inheritance models.

REFERENCES

1. Landel V, Millet P, Baranger K, Loriod B, Féron F. Vitamin D Interacts With Esr1 and Igf1 to Regulate Molecular Pathways Relevant to Alzheimer's Disease. Mol Neurodegener, 2016;11:22.
2. Gezen-Ak D, Atasoy IL, Candaş E, Alaylioglu M, Yılmazer S, Dursun E. Vitamin D Receptor Regulates Amyloid Beta 1-42 Production With Protein Disulfide Isomerase A3. ACS Chem Neurosci, 2017;8(10):2335-2346.
3. Gezen-Ak D, Dursun E. Molecular Basis of Vitamin D Action in Neurodegeneration: The Story of a Team Perspective. Hormones, 2019;18(1):17-21.

SUMMARY/CONCLUSION

TaqI TT increases the risk of developing LOAD by 1.86 times.

TaqI C allele might act protectively with 46% lower risk of developing the disease. TaqI CC patients have 87% less likelihood of severe cognitive impairment based on MMSE score.

No association of the investigated polymorphisms was observed with FAB score or the presence of APOE e4 allele.