

Can the Olive Genome Be a Miracle for Human DNA?

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Article

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TITLE

Can the Olive Genome Be a Miracle for Human DNA?

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ABSTRACT

In this project, it is aimed to compare the olive genome, one of the fruits of the Mediterranean region, to the human genome. We started plant-human genomic studies with olive on the hypothesis that whether we could consume the benefits of carbohydrates, proteins, fats, as well as genomic bioavailability. Many studies from past to present have shown positive effects of olives on cardiovascular diseases and some cancer pathways. In terms of both scientific and religious resources, olive is an important plant in many areas. In our project, we compared the olive genome with the human genome in Pubmed database. We detected pathological or non-pathological variations of the matching regions in the human genome. We investigated whether these variations were found in the olive genome as wild type and whether there were regions suitable for cutting in terms of restriction enzymes. In the data obtained, the presence of cardiovascular and cancer-related genes of the matching regions suggests a possible bioavailability. In the ongoing projects, it is aimed to compare the genomes of plants other than olive with the human genome.

Keywords Olive, genome, CALM1, CALM3, BRAF, SDHA, BRMS1L

INTRODUCTION

Olive, which is one of the fruits of the Mediterranean region, has managed to become an indispensable part of the tables from past to present. Both the mention of its name in religious books and its examination in terms of cardiovascular diseases in many scientific articles emphasize the importance of olive many times. It is reported that olive and olive oil consumption is associated with a decrease in the incidence and mortality of cardiovascular

diseases such as heart failure, atrial fibrillation and atherosclerosis. [1] Olive oil diet has antioxidant properties [2], anti-inflammatory [3] and anti-carcinogenic properties [4]. Based on the verse of the Qur'an, figs and olives mentioned in Surah Tin, it is aimed to examine the possible effects of olives sworn on in the Qur'an from a genetic perspective. Is there any genomic bioavailability of plants besides carbohydrate, fat, protein? We know that our microbiota has restriction enzymes that can cut the genome of the digested food from many different regions. So, could the genome of a food be cut into our enteric flora and presented to us? Starting from here, we compared the human genome with the olive genome in our project. We detected pathological or non-pathological variations of the matching regions in the human genome. We investigated whether these variations were found in the olive genome.

METRIALS AND METDHODS

- The olive genome sequence in the Pubmed genome database was mapped to the human genome on the NucleotidBlast site.
- Variations of the matching regions were searched in databases such as Pubmed, PolyPhen-2, Exac.browser to find deletion sites and SNPs causing pathogenicity.
- In addition, the restriction enzymes found in the olive genome matching regions were determined using the NEB site.

RESULTS

- When the olive genome is examined from Pubmed Genome, it is known to have 23 chromosomes. [8]
- In the comparison of olive and human genomes, we detected 73-100 percent matches in 67 genes. (Table 2, 3)
- Matching genes are found in cancer (BRAF, BRMS1L, SDHA) and calmodulin (CALM1, CALM3) related genes.

- There is a possibility that the matching region by the restriction enzymes may be appropriately removed

(Figure 5)

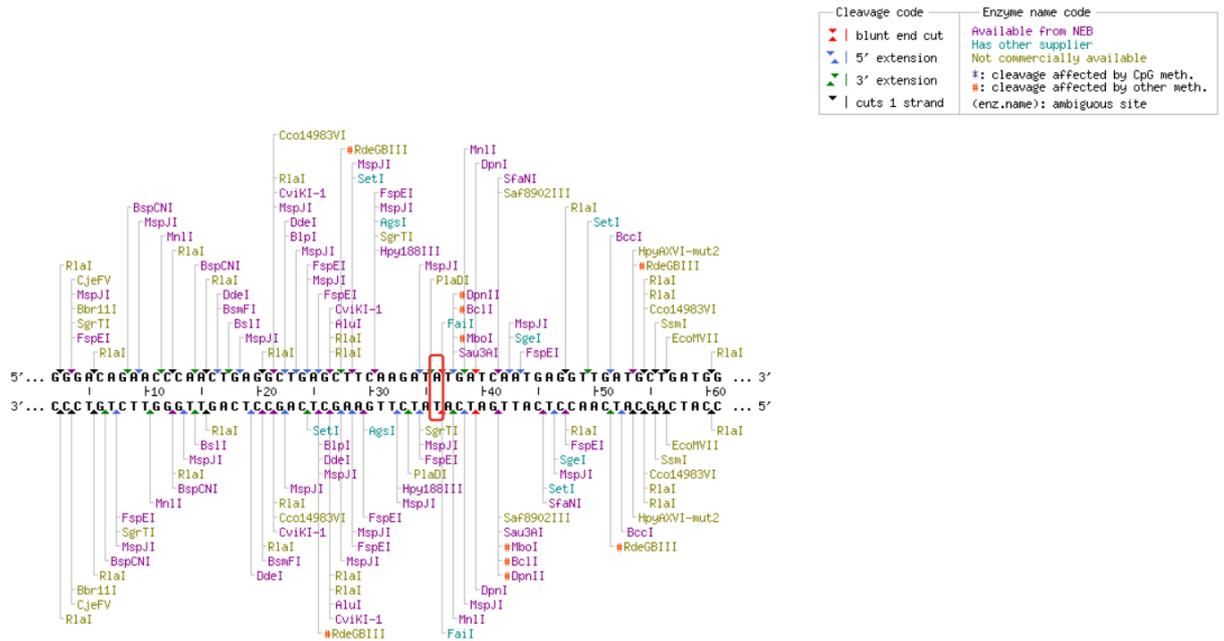


Figure 5. Restriction enzyme cleavage sites located in the proximal positions of the pathological rs267607276 SNP (circled in red) in the region matching the CALM1 gene.

BRAF GENE FINDINGS

- BRAF plays a role in regulating the MAP kinase / ERK signaling pathway, which affects cell division, differentiation and secretion.
- 31/32 (97%) matches were found between olive genome and 32 bp of BRAF gene. (Figure 6)

Homo sapiens B-Raf proto-oncogene, serine/threonine kinase (BRAF), transcript variant 1, mRNA
 Sequence ID: [NM_004333.5](#) Length: 4560 Number of Matches: 1

Range 1: 127 to 158 [GenBank](#) [Graphics](#) [Next Match](#) [Previous Match](#)

Score	Expect	Identities	Gaps	Strand
54.7 bits(29)	3.3	31/32(97%)	0/32(0%)	Plus/Minus
Query 5800386	TGGCGGAGGCGGAGGCGGAGGCGGAGGCGGAG	5800417		
Sbjct 158	TGGGGGAGGCGGAGGCGGAGGCGGAGGCGGAGGCGGAG	127		

Figure 6. Matching region between olive genome and BRAF gene. 31/32 bp (97%) matches between olive genome and BRAF gene are shown.

- There are 9 SNPs and 9 deletions in the pubmed database in our region that matches the BRAF gene. (figure 7)

Homo sapiens succinate dehydrogenase complex flavoprotein subunit A (SDHA), transcript variant 3, mRNA
 Sequence ID: [NM_001330758.1](#) Length: 2547 Number of Matches: 2

Range 1: 587 to 678		GenBank	Graphics	Next Match	Previous Match
Score	Expect	Identities	Gaps	Strand	
87.9 bits(47)	4e-10	77/92(84%)	0/92(0%)	Plus/Minus	
Query	6554306	TTTCCAAAGTTTAGGCTTTGACCACCAAATGCACGCTGATAAATCTTCCCATCTTCGGTC			6554365
Sbjct	678	TTTCCAAAC TTGAGGCTCTGTCCACCAAATGCACGCTGATAAATCTTCCCATCTTCAGTT			619
Query	6554366	CTAGAGAATGGTAGCCATAATTTTCAAGCTC			6554397
Sbjct	618	CTGCTAAACGGCATGCCATAATTTTCTAGCTC			587

Range 2: 624 to 678		GenBank	Graphics	Next Match	Previous Match	First Match
Score	Expect	Identities	Gaps	Strand		
80.5 bits(43)	7e-08	51/55(93%)	0/55(0%)	Plus/Minus		
Query	6327075	TTTCCAAAGTTTAGGCTTTGACCACCAAATGCACGCTGATAAATCTTCCCATCTT				6327129
Sbjct	678	TTTCCAAAC TTGAGGCTCTGTCCACCAAATGCACGCTGATAAATCTTCCCATCTT				624

Figure 9. The matching region between the olive genome and the SDHA gene. A 77/92 bp (84%) match between the olive genome and the SDHA gene is shown. 2 matches are shown. Second match is a 51/55 bp (93%) region within the first match.

- There are 33 SNPs and 4 deletions in the pubmed database in our region matching SDHA gene. (Figure 10)

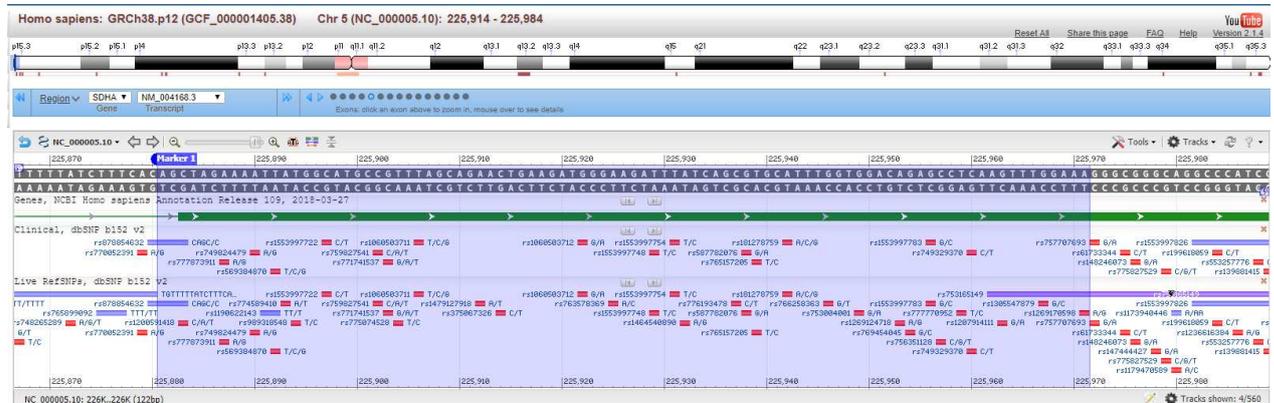


Figure 10. SNPs reported in the Pubmed database in the region matching the SDHA gene. The Marker 1 region indicated in blue indicates the region that matches the SDHA gene. This region is among the nucleotides 225,880-222,971 (92b) in the Human genome 7. Chromosome, GRCh38p.12. The direction of the arrows in the green line The olive genome shows the direction of the 3'-5' DNA sequence. The red regions indicated by the Rs numbers indicate the SNPs reported in the Pubmed database and the purple lines with longer lines indicate the deletion areas reported. The data obtained were investigated on 2018-03-27.

- Most SNPs present are Missense Variants, leading to pathologies such as Hereditary cancer-predisposing syndrome, Mitochondrial complex II deficiency, Paragangliomas 5 and one of their wild types are found in the olive genome. [12] [13] (Uncertain-Significance related SNPs are rs1560987595, rs1560987595, rs749824479, rs569384870, rs1553997722, rs759827541, rs1060503711, rs1060503712, rs763578369, rs1553997748, rs1553997754, rs587782076, rs1553997783)

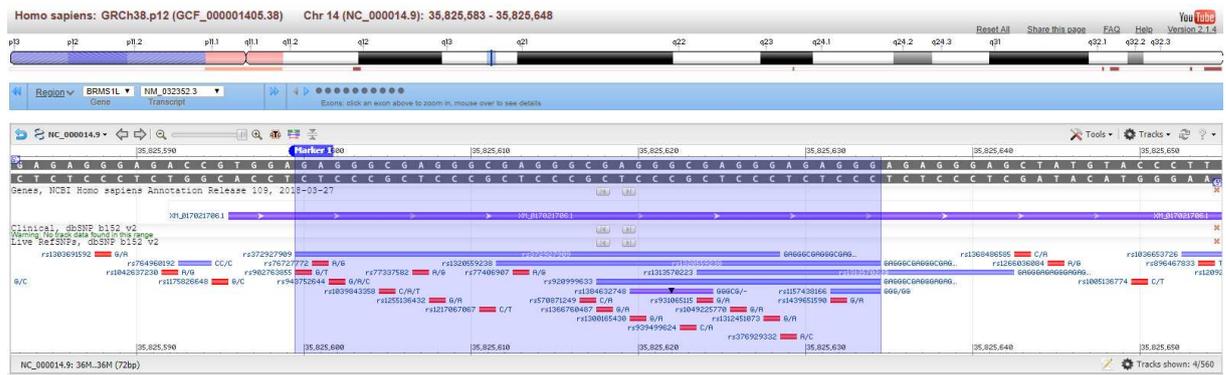


Figure 13. SNPs reported in the Pubmed database at the region matching the BRMS1L gene. The Marker 1 region indicated in blue indicates the region that matches the BRMS1L gene. This region is among the nucleotides 35,825,600 - 35,825,634 (35bc) in Human genome 14 Chromosome, GRCh38p.12. The direction of the arrows in the purple line The olive genome shows the direction of the 3'-5 'DNA sequence. The red regions indicated by the Rs numbers indicate the SNPs reported in the Pubmed database and the purple lines with longer lines indicate the deletion areas reported. The data obtained were investigated on 2018-03-27.

- The wild type of most of the SNP-containing regions is found in the olive genome.
 - There are many candidate regions for restriction enzymes in the 39 bp region where we found a match.
- (Figure 14)



Linear Sequence: unnamed sequence

Display: - All commercial restriction enzymes

GC=77%, AT=23%

Cleavage code	Enzyme name code
▬ blunt end cut	Available from NEB
▬ 5' extension	Has other supplier
▬ 3' extension	Not commercially available
▬ cuts 1 strand	*: cleavage affected by CpG methylation
	#: cleavage affected by other methylation (enz. name): ambiguous site

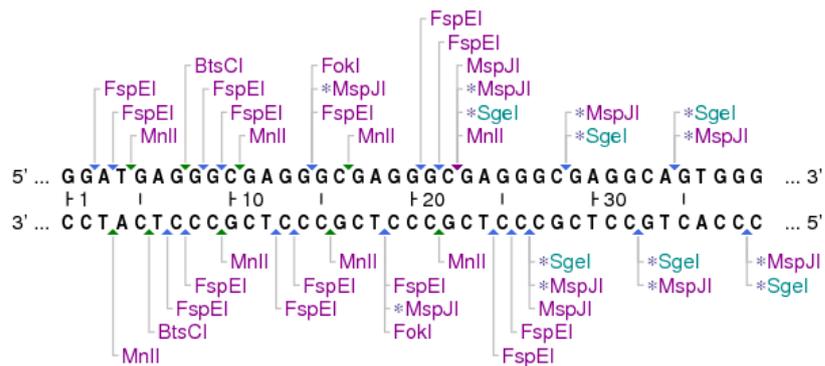


Figure 14. Restriction enzymes in the NEB database of the region matching the BRMS1L gene.

CALM3 GENE FINDINGS

- 79% (293/369) matches were found between the olive genome and 369 bp in 3rd, 4th, 5th and 6th exons of the CALM 3 gene. (Figure 15)

Homo sapiens calmodulin 3 (CALM3), transcript variant 3, mRNA

Sequence ID: [NM_001329922.1](#) Length: 2227 Number of Matches: 1

Range 1: 218 to 586		GenBank	Graphics	Next Match	Previous Match
Score	Expect	Identities	Gaps	Strand	
261 bits(141)	3e-62	293/369(79%)	0/369(0%)	Plus/Plus	
Query	30652542	ATCACTACTAAGGAGCTTGGGACTGTGATGCGTTCTCTGGGACAGAACCCAACCGAGGCC			30652601
Sbjct	218	ATCACCACCAAGGAGTTGGGGACAGTGATGAGATCCCTGGGACAGAACCCACTGAAGCA			277
Query	30652602	GAGCTTCAAGATATGATTAATGAGGTTGATGCCGATGGGAATGGGACAATTGACTTCCCA			30652661
Sbjct	278	GAGCTGCAGGATATGATCAATGAGGTGGATGCAGATGGGAACGGGACCATTGACTTCCCG			337
Query	30652662	GAGTTCCTCAACTTGATGGCCAGAAAGATGAAGGACACAGACTCCGAGGAGGAGCTCAA			30652721
Sbjct	338	GAGTTCCTGACCATGATGGCCAGAAAGATGAAGGACACAGACAGTGAAGGAGGAGATCCGA			397
Query	30652722	GAAGCTTTCCGGTTTTTGGACAAGGACAAAATGGTTTCATTTCTGCAGCTGAACTCCGC			30652781
Sbjct	398	GAGGCGTTCCGTGTCTTTGACAAGGATGGGAATGGCTACATCAGCGCCGAGAGCTGCGT			457
Query	30652782	CATGTCATGACAAATCTTGGTGAAGCTTACAGACGAGGAGGTTGATGAGATGATTCTGA			30652841
Sbjct	458	CACGTAATGACGAACCTGGGGGAGAAGCTGACCGATGAGGAGGTGGATGAGATGATCAGG			517
Query	30652842	GAGGCTGATGTGGATGGCGATGGGAGATTAACATGAGGAGTTTGTCAAGATCATGATG			30652901
Sbjct	518	GAGGCTGACATCGATGGAGATGGCCAGGCAATTATGAAGAGTTTGTACAGATGATGACT			577
Query	30652902	GCCAAGTGA			30652910
Sbjct	578	GCAAAGTGA			586

Figure 15. Mapping region between olive genome and CALM 3 gene. 293/369 bp (79%) matches between the olive genome and the CALM3 gene are shown.

- There are 62 SNPs and 1 deletion in the pubmed database in our region that matches CALM3 gene. (Figures 16, 17, 18, 19)

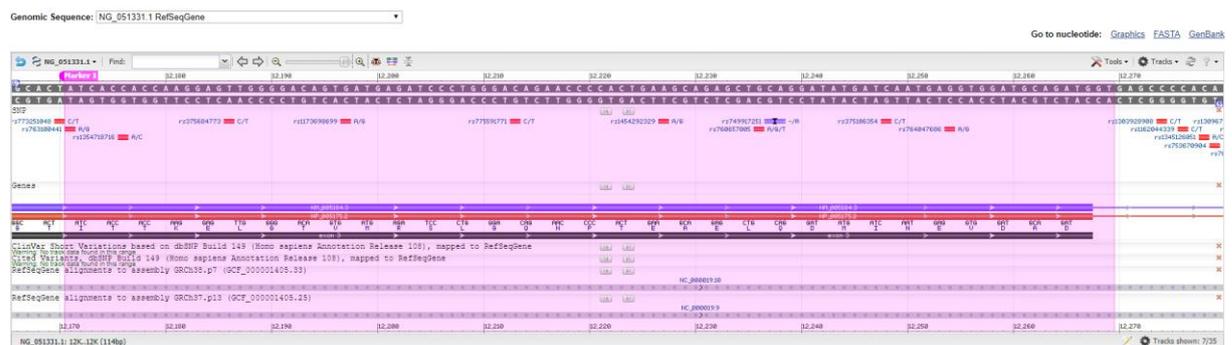


Figure 16. SNPs reported in the Pubmed database in the region matching the 3rd exon of the CALM3 gene. The Marker 1 region indicated in pink indicates the region that matches the SDHA gene. This region is between nucleotides 12,171 - 12,269 in the human genome 19. Chromosome, GRCh37.p13. Direction of arrows in the purple line The olive genome shows the direction of the 5'-3 Zeytin DNA sequence. The red regions indicated by the Rs numbers indicate the SNPs reported in the Pubmed database and the purple lines with longer lines indicate the deletion areas reported. The data obtained were investigated on 2018-03-27.

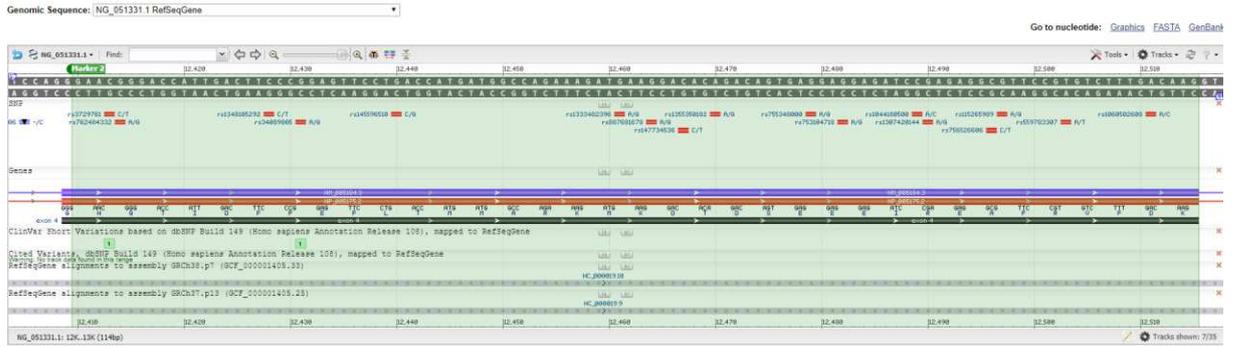


Figure 17. SNPs reported in the Pubmed database at the region matching the 4th exon of the CALM3 gene. This region is between nucleotides 12,410 - 12,515 in the Human genome 7. Chromosome, GRCh37.p13.

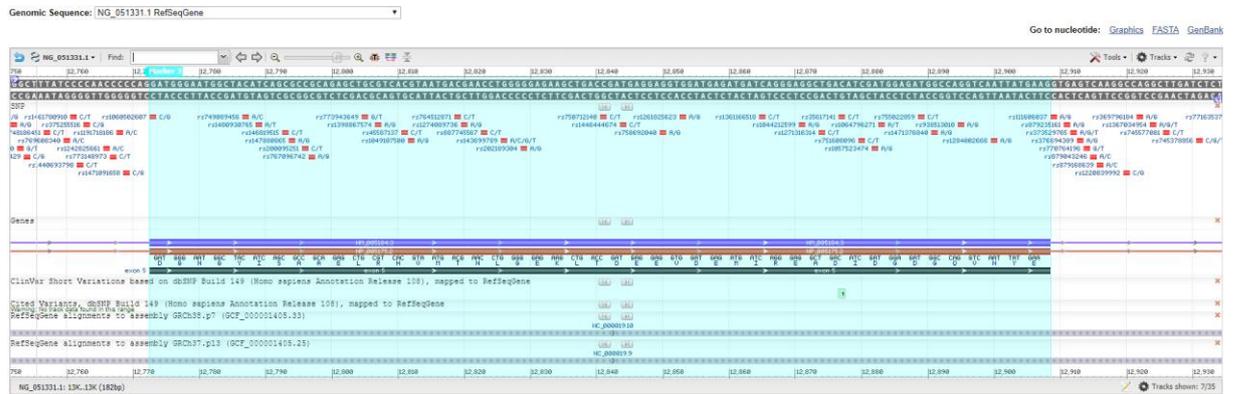


Figure 18. SNPs reported in Pubmed database in the region matching the 5th exon of the CALM3 gene.

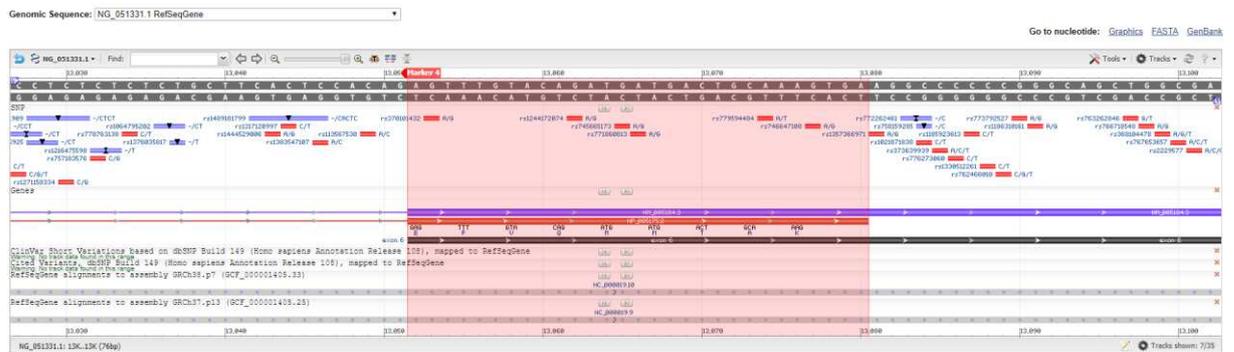


Figure 19. SNPs reported in the Pubmed database in the region matching the 6th exon of the CALM3 gene. This region is between the nucleotides 13,052 - 13,080 in the Human genome 7. Chromosome, GRCh37.p13.

- Three of the matching SNLs were pathologically demonstrated on Pubmed. (rs1060502608 [14], rs1064796271 [15], rs1555814427 [7])
- The wild type form of most of the regions with SNP is found in the olive genome.
- There are many candidate regions for restriction enzymes in the 369 bp region where we found a match. (Figure 20)

Linear Sequence: unnamed sequence

Display: - NEB single cutter restriction enzymes
 - Main non-overlapping, min. 100 aa ORFs
 GC=48%, AT=52%

Cleavage code	Enzyme name code
▬ blunt end cut	Available from NEB
▬ 5' extension	Has other supplier
▬ 3' extension	Not commercially available
▬ cuts 1 strand	*: cleavage affected by CpG methylation
	#: cleavage affected by other methylation
	(enz. name): ambiguous site

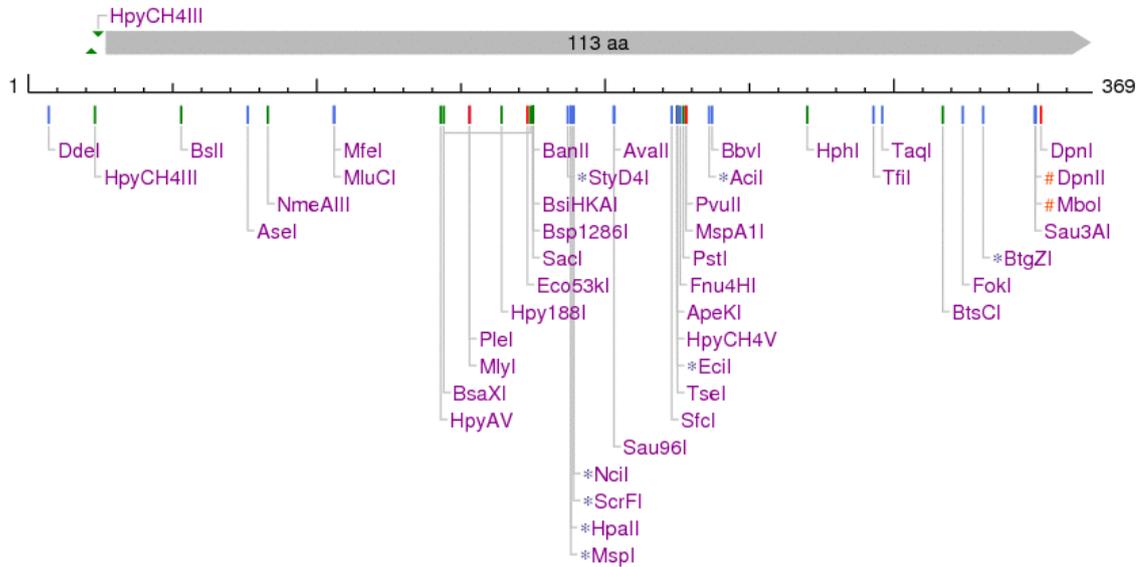


Figure 20. Restriction enzymes in the NEB database of the region matching the CALM 3 gene.

CONCLUSION AND DISCUSSION

As a result of our comparison between olive genome and human genome, we found matches in 67 genes. (Genes summary table). We focus our attention on cancer (BRAF, BRMS1L, SDHA) and cardiovascular system (CALM1, CALM3...) related genes. We carried out a summary study on Pubmed about the functions of these genes and then compiled the reported mutation analyzes of these genes on the site 'Exac.browser' and searched for the presence of matching regions in the matching genes in olive. As can be expected, hundreds of mutations have been reported for each gene, but some of them have also led to very serious pathologies (Pathogenic Variants table). Human deletions or snps in the matching regions on the CALM3, SDHA, BRAF, BRMS1L and CALM1 gene are reported to cause pathological conditions. The wild type of these regions is found in the olive genome and there are many restriction enzymes capable of cutting these matching regions from the appropriate regions. We have seen that many restriction enzymes available today allow us to cut off our matching gene region from appropriate sites. Based on this, we concluded that the use of non-pathological sequencing from the genome of the olives that we consume can benefit individuals with mutations. Considering all this, we

have come to the conclusion that GMO products may perhaps deprive living beings of this natural therapy by causing the genome that is treating us to be pathological, leading to even worse outcomes. In particular, can the olive genome be used for the repair of mutagenized genes as a guide DNA chain used in the cell repair mechanism? From another point of view, can genetic bioavailability also have an impact on explaining the idiopathic concept underlying many diseases that are still unclear? According to this hypothesis, can specific diets having common regions and genes involved in pathogenesis be included in our future treatment plans? With these matches, can we approach the relationship between diet and disease from a different perspective?

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- [12] Date of access: 2018.12.22 https://www.ncbi.nlm.nih.gov/snp/rs777873911#clinical_significance
- [13] Date of access: 2018.12.22 <https://www.ncbi.nlm.nih.gov/clinvar/variation/486403/#supporting-observations>
- [14] Date of access: 2018.12.22 <https://www.ncbi.nlm.nih.gov/clinvar/RCV000475293.1/>
- [15] Date of access: 2018.12.22 <https://www.ncbi.nlm.nih.gov/clinvar/RCV000484148.1/>

ATTACHMENTS

Table 2. Matching regions between olive genome and human genome. The number of chromosomes of the olive genome and which gene overlaps in the human genome are shown in the table. The pairings examined on the genes show matches ranging from 29 to 1259 bp with a similarity of 72% to 100%.

Matching Genes	MATCHING (BP-RATE)	Matching Localization (Bp / Chromosome)	Number of SNPs and Deletions	SEQUENCE ID
CALM1	125/149 (84%)	90,401,255 - 90,401,403 (149bp) (GRCh38.p12) human genome 14 Chr.	19 SNPs	NM_006888.4
CALM3	293/369 (79%)	12,171 - 12,269 12,410 - 12,515 12,773 - 12,908 13,052 - 13,080 (GRCh37.p13) 19. Chromosome	62 SNPs / 1 del.	NM_001329922.1
BRAF	31/32(97%)	140,924,771 –140,924,802 (32bp) (GRCh38.p12) 7. Chromosome	9 SNPs / 9 del	NM_004333.5
SDHA	77/92(84%)	225,880-222,971 (92bp) (GRCh38.p12) 7. Chromosome	33 SNPs / 4 del.	NM_001330758.1
BRMS1L	36/39(92%)	35,825,600 - 35,825,634 (35bp) (GRCh38.p12) 14. Chromosome	17 SNPs / 6 del.	XM_017021706.1

Table 3.

OLIVE GENOM	MATCHING GEN	MATCHING (BP-RATE)	SEQUENCE ID
1. CHROMOSOME	CALM3	293/369(79%)	NM_001329922.1
	TUBB8P12	270/371(73%)	NM_001358689.1
	HSP90AB1	67/80(84%)	NM_001271972.1
	DDX27	31/31(100%)	NM_017895.7
	STAM2	33/35(94%)	XR_001738586.1
	MEF2C-AS1	29/29(100%)	NR_136222.1
2. CHROMOSOME	UBC	887/1140(78%)	NM_021009.6
	HSPA1L	964/1323(73%)	NM_005527.3
	HSPA6	901/1259(72%)	NM_002155.4
	ACTA1	299/374(80%)	NM_001100.3
	ACTB	310/397(78%)	NM_001101.4
	POTEM	288/372(77%)	NM_001145442.1

	POTEF	201/246(82%)	NM_001099771.2
	POTEI	199/245(81%)	XM_017004732.2
	POTEE	193/236(82%)	XM_017004161.2
	POTEJ	198/245(81%)	NM_001277083.1
	LINC02250	30/30(100%)	XR_931996.2
	SIPA1L3	29/29(100%)	NM_015073.2
3. CHROMOSOME	UBC	300/368(82%)	NM_021009.6
	PPP1CC	251/340(74%)	XM_011538505.3
	FUS	36/39(92%)	XM_005255233.5
4. CHROMOSOME	(NO MATCHED TRANSCRIPT FOUND)		
5. CHROMOSOME	NISCH	28/28(100%)	NM_007184.3
6. CHROMOSOME	LINC02250	100%	XR_931996.2
	LOC105376278	97%	XR_001746939.2
	NTN5	100%	XM_017026274.1
7. CHROMOSOME	ACTA1	294/361(81%)	NM_001100.3
	ACTB	296/370(80%)	NM_001101.4
	POTEF	291/372(78%)	
	POTEM	284/364(78%)	NM_001145442.1
	POTEI	286/368(78%)	NM_001277406.1
	POTEE	286/368(78%)	NM_001083538.1
	POTEJ	284/368(77%)	NM_001277083.1
	TUBB8P12	299/398(75%)	NM_001358689.1
	H3.Y	78/94(83%)	NM_001355258.1
	LCN10	36/37(97%)	NM_001001712.2
8. CHROMOSOME	ATP5F1B	163/209(78%)	NM_001686.3
	BRMS1L	36/39(92%)	XM_017021706.1
	ANKRD26	38/42(90%)	XM_017015929.1
9. CHROMOSOME	(NO MATCHED TRANSCRIPT FOUND)		
10. CHROMOSOME	UBC	727/921(79%)	NM_021009.6
	ACTG1	292/375(78%)	NM_001199954.1
	LOC100130331	288/378(76%)	NR_027247.2
	SCO1	39/41(95%)	NM_004589.3
	LINC02250	29/29(100%)	XR_931996.2
11. CHROMOSOME	MAGOH2P	60/69(87%)	NR_049723.1
12. CHROMOSOME	PSMC5	95/120(79%)	XR_934508.2
	CALM1	86%	NM_006888.4
	MLLT3	100%	NM_004529.3

	LOC101927188	100%	NR_126040.1
	BHMG1	100%	NM_001310124.1
	FDFT1	100%	NM_001287750.1
13. CHROMOSOME	SDHA	77/92(84%)	NM_001330758.1
	LOC220729	84%	NR_003266.2
	SDHAP2	82%	NR_003265.3
	SDHAP1	83%	NR_003264.2
	DIEXF	100%	NM_014388.6
	TMEM9B	100%	NM_020644.2
	CYTIP	100%	NM_004288.4
14. CHROMOSOME	ACTB	324/403(80%)	NM_001101.4
	ACTA1	308/380(81%)	NM_001100.3
		286/364(79%)	
	POTEM	286/364(79%)	NM_001145442.1
	POTEF	313/405(77%)	NM_001099771.2
	POTEI	78%	NM_001277406.1
	POTEE	78%	NM_001083538.1
	POTEJ	77%	NM_001277083.1
	H3.Y	79%	NM_001355258.1
	LINC02250	100%	XR_931996.2
	WDR26	97%	NM_025160.6
	ASH1L	100%	NM_018489.2
	LOC403312	100%	NM_001301851.1
15. CHROMOSOME	UBC	723/906(80%)	NM_021009.6
		725/918(79%)	
	HIST1H3G	307/385(80%)	NM_003534.2
	TUBA1C	282/369(76%)	NM_032704.4
	TUBA1B	282/369(76%)	NM_006082.2
	UBB	189/234(81%)	NM_018955.3
	PPP1CC	250/340(74%)	NM_002710.3
	SIPA1L3	38/41(93%)	NM_015073.2
	PLEKHG1	35/37(95%)	NM_001029884.2
16. CHROMOSOME	(NO MATCHED TRANSCRIPT FOUND)		
17. CHROMOSOME	IGHMBP2	29/29(100%)	XM_017017671.2
	BRAF	31/32(97%)	NM_004333.5
	IGHMBP2	29/29(100%)	NM_002180.2

18. CHROMOSOME	HIST1H3F	84%	NM_021018.2
	H3F3A	81%	NM_002107.4
	H3F3AP4	81%	NR_002315.1
19. CHROMOSOME	FDFT1	29/29(100%)	NM_001287750.1
	SUPT20HL2	28/28(100%)	NM_001136233.2
20. CHROMOSOME	EEF1A1	361/450(80%)	NM_001402.5
	TNFRSF10D	28/28(100%)	NM_003840.4
21. CHROMOSOME	STK4	37/38(97%)	NM_006282.4
	HOXB6	37/38(97%)	NM_018952.4
22. CHROMOSOME	PSMC1	74/85(87%)	NM_002802.2
	CALN1	29/29(100%)	NM_031468.3
23. CHROMOSOME	CGN	28/28(100%)	NM_020770.2
EX CHROMOSOME	(NO MATCHED TRANSCRIPT FOUND)		

Tablo 4 Possible pathogenic / pathogenic variations reported in matching regions.

Pathogenic Variants		Position	Alleles	Clinical Significance	Gene : Consequence	Publication (PMID)	Olive match
Gene	SNPs						
CALM1	rs267607276	chr14:90401385 (GRCh38.p12)	NM_001363670.1:c.164A>G NM_001363670.1:c.164A>T	Pathogenic	Asn55Ser / Asn55Ile	23040497	A
SDHA	rs1560987595	chr5: 225886 (GRCh38)	NM_004168.4:c.460G>A	No Data	Glu154Lys	No Data	G
	rs749824479	chr5:225890 (GRCh38.p12)	NM_004168.4:c.464A>G	Uncertain significance	Asn155Ser	No Data	A
	rs569384870	chr5:225892 (GRCh38.p12)	NM_004168.4:c.466T>C	Uncertain significance	Tyr156His	No Data	T
	rs1553997722	chr5: 225897 (GRCh38)	NM_004168.4:c.471C>T	Uncertain significanc	Synonymous Gly109=	No Data	G (-)
	rs759827541	chr5:225902 (GRCh38.p12)	NM_004168.4:c.476C>A	Uncertain significanc	Pro159Gln	No Data	C
	rs1060503711	chr5:225906 (GRCh38.p12)	NM_004168.4:c.480T>C / T>G	Uncertain significanc	Phe160=/ Phe160Leu	No Data	C (-)
	rs1060503712	chr5:225922 (GRCh38.p12)	NM_004168.4:c.496G>A	Uncertain significanc	Gly166Arg	No Data	G
	rs763578369	chr5: 225925 (GRCh38)	NM_004168.4:c.499A>C	Uncertain significanc	Lys167Gln	No Data	A
	rs1553997748	chr5: 225929 (GRCh38)	NM_004168.4:c.503T>C	Uncertain significanc	Ile168Thr	No Data	T
	rs1553997754	chr5: 225931 (GRCh38)	NM_004168.4:c.505T>C	Uncertain significanc	Tyr121His	No Data	T
	rs587782076	chr5: 225938 (GRCh38)	NM_004168.4:c.512G>A	Uncertain significanc	Arg123His	No Data	G
	rs1553997783	chr5: 225956 (GRCh38)	NM_004168.4:c.530G>C	Uncertain significanc	Ser129Thr	No Data	G
CALM3	rs1060502608	chr19:46608584 (GRCh38.p12)	NM_005184.4:c.281A>C	Pathogenic (Clinvar acesion) RCV000475293.1	Asp94Ala	No Data	A
	rs1064796271	chr19:46608956 (GRCh38.p12)	NM_005184.4:c.396T>A	Pathogenic (RCV000484148.1)	Asp132Glu	No Data	T