

Identification of genomic variants using the SILE Method

Extension of the Research module &
Focus on the Brugada Syndrome



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- Other Genes
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- Conclusions
- Future Works



01 Introduction

INTRODUCTION

I) Objectives

- 1) **Evaluation** of SILE Method applied to Brugada Syndrome
- 2) **Improvement** of the Research module of SILE
- 3) **Evaluation** of the Improvement

II) SILE Method

S: Search
I: Identification

L: Load
E: Exploitation

III) Brugada Syndrome

Diagnosis

Treatment

IV) Genomics Concepts

DNA
Chromosomes
Genes

Variations
Genotype
Phenotype

Genomics data are **scattered** in many data sources

Each of them containing **different** information about different genes and variants

Goal: collect as many relevant data as possible

There is **no** protocol / **method** for searching and identifying relevant information

SILE method to **integrate** all the relevant information in the same place

S

Research and selection of genomic data sets to have quality data

I


- **Filter** information gathered
- Discart non-relevant and duplicates
- Keep only variations that have sufficiently relevant evidence
- Manually **solve inconsistencies**


L

- Platform based on the CSHG (Conceptual Schema of the Human Genome)
- **Validation** carried out by the platform

E

- **Extract knowledge** from the information stored
- Platform to **visualize** data
- Comparison between genetic variations





Global Variome shared LOVD
SCN5A (sodium channel, voltage-gated, t

Curator: Global Variome, with Curator vacancy

Genes
Transcripts
Variants
Individuals
Diseases
Screenings
Subm

The SCN5A gene homepage

General information	
Gene symbol	SCN5A
Gene name	sodium channel, voltage-gated, type V, alpha subunit
Chromosome	3
Chromosomal band	p21
Imprinted	Not imprinted
Genomic reference	LRG_289
Transcript reference	NM_198056.2
Exon/intron information	NM_198056.2 exon/intron table
Associated with diseases	ATFB10 , BRGDA1 , CMD1E , LQT3 , PFHB1A , SIDS , SSS1 , VF1
Citation reference(s)	-
Refseq URL	Genomic reference sequence
Curators (1)	Global Variome, with Curator vacancy
Total number of public variants reported	1639
Unique public DNA variants reported	981
Individuals with public variants	1509
Hidden variants	52
Download all this gene's data	Download all data
Notes	Establishment of this gene variant database (LSDB) was supported by the European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement No 200754 - the GEN2PHEN project.
Date created	April 29, 2010
Date last updated	November 30, 2021
Version	SCN5A:211130

LOVD (Leiden Open Variation Database)

Open source database containing information about genomic variations

More than 23,000 different genes

Follows the recommendations of **HGVS** (Human Genome Variation Society)

6 categories:

Genes

Transcripts

Variants

Individuals

Diseases

Screenings

BRUGADA

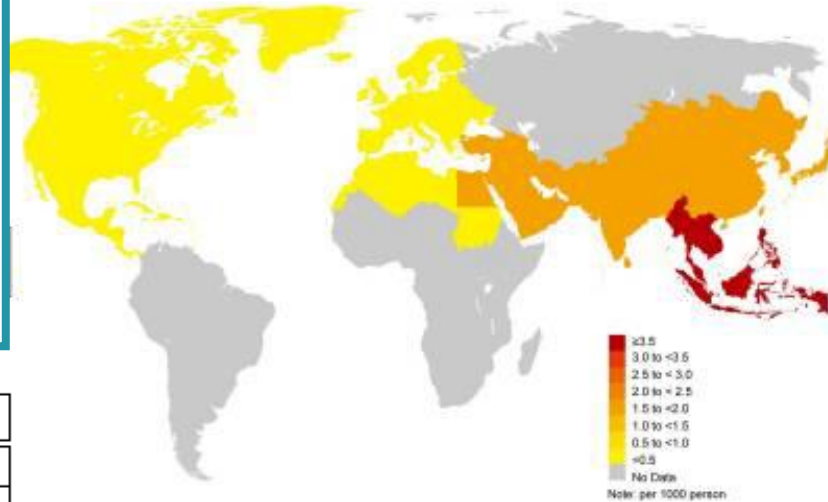
DIAGNOSIS

Rare **cardiac arrhythmia**

If left untreated can cause fainting, difficult breathing and high risk of **sudden cardiac death**, usually when sleeping

Can be caused by **mutation** in one gene:

Types	Associated Genes
Brugada syndrome 1 (BRGDA1)	SCN5A
Brugada syndrome 2 (BRGDA2)	GPD1L
Brugada syndrome 3 (BRGDA3)	CACNA1C
Brugada syndrome 4 (BRGDA4)	CACNB2
Brugada syndrome 5 (BRGDA5)	SCN1B
Brugada syndrome 6 (BRGDA6)	KCNE3
Brugada syndrome 7 (BRGDA7)	SCN3B
Brugada syndrome 8 (BRGDA8)	HCN4
Brugada syndrome 9 (BRGDA9)	KCND3



Globally affect 0,5 per 1000
In **Southeast Asia** 3,7 per 1000

TREATMENT

Symptomatic:

Implantation of Implantable Cardioverter-defibrillator (only treatment effective)

Asymptomatic:

Individual risk assessment
Consider other risk factors (age, sex, external)

GENOMICS CONCEPTS

HUMAN GENOME:
DNA and RNA

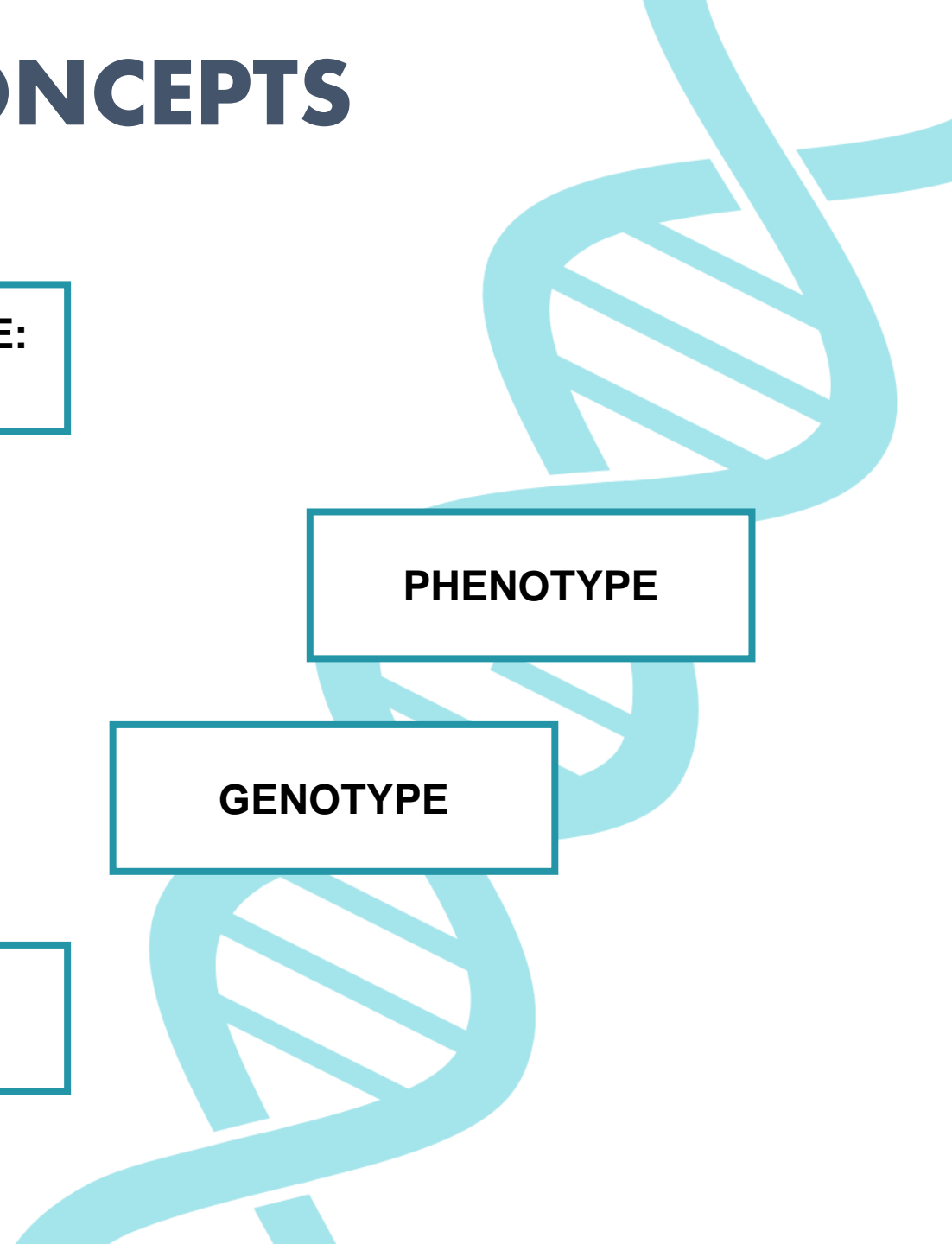
CHROMOSOMES

PHENOTYPE

GENES

GENOTYPE


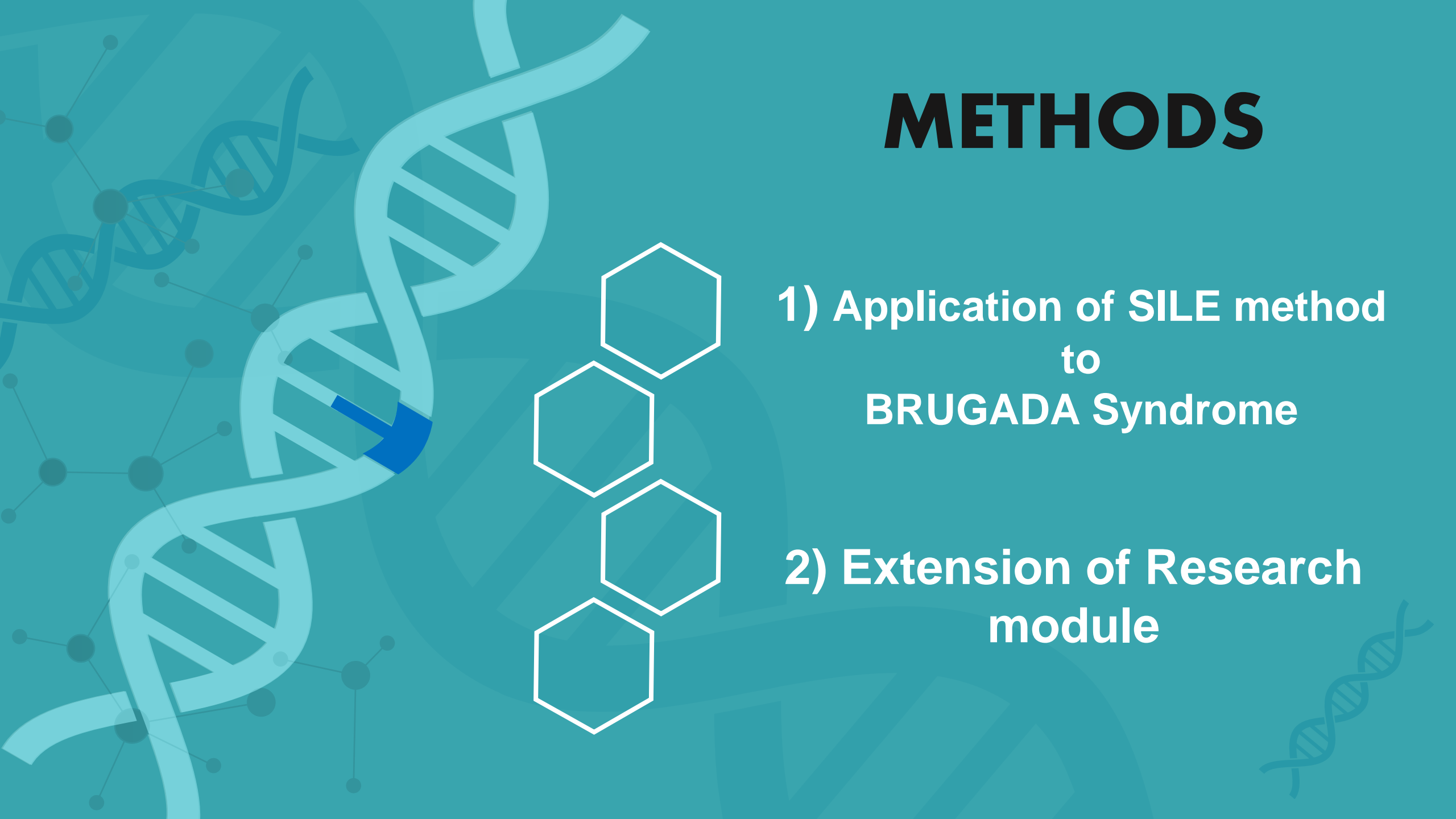
VARIATIONS





02 Methods

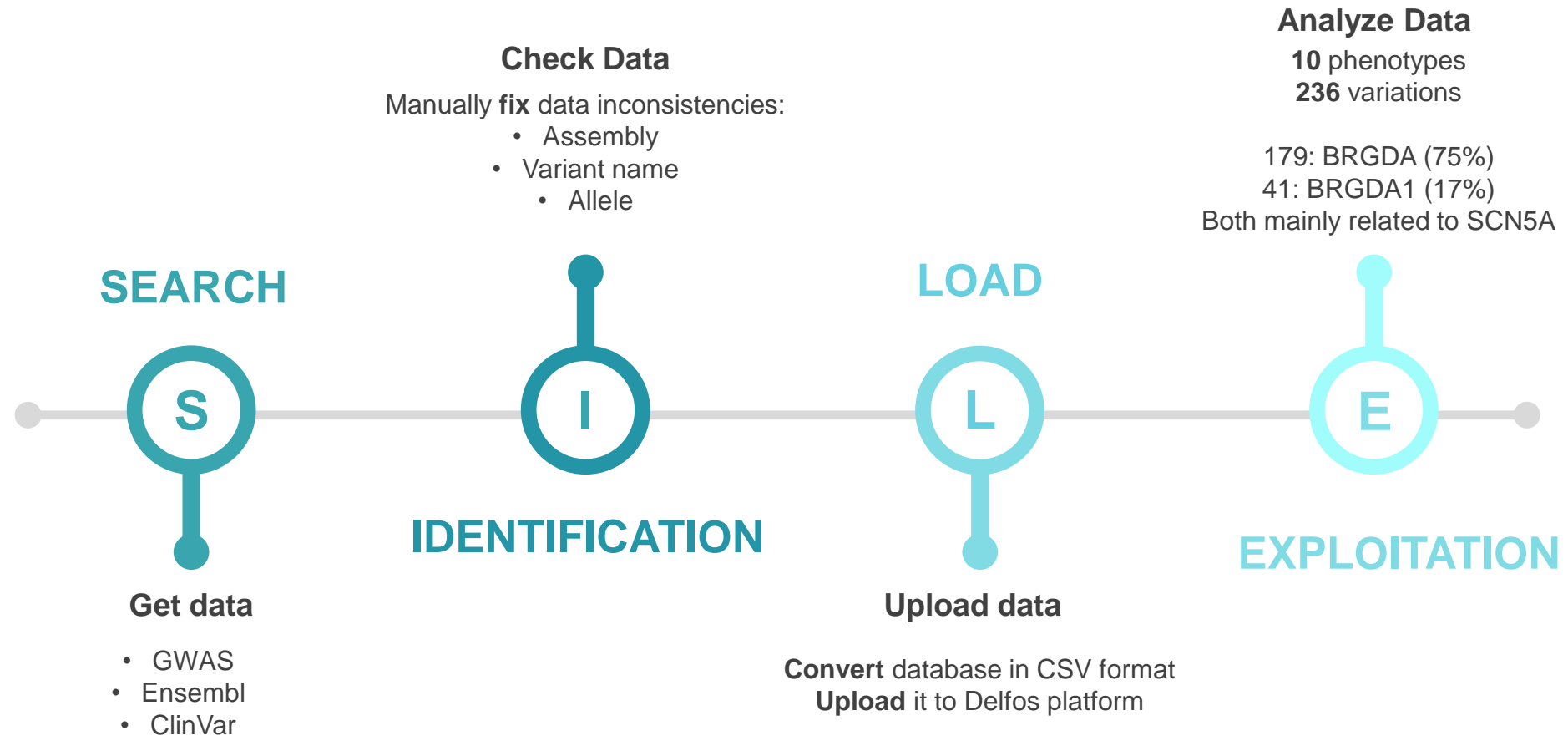
METHODS



**1) Application of SILE method
to
BRUGADA Syndrome**

**2) Extension of Research
module**

SILE TO BRUGADA



SILE TO BRUGADA

Brugada Syndrome	
Chromosome Affected	Chr3: 38.649.686 - 38.548.060
Gene affected	SCN5A
Number of variations for the phenotype	179
Evidence of variations	171 limited, 8 moderate
Most common type of variation	Single nucleotide variant

Brugada Syndrome 1	
Chromosome Affected	Chr3: 38.649.686 - 38.548.060
Gene affected	SCN5A
Number of variations for the phenotype	41
Evidence of variations	7 limited, 34 moderate
Most common type of variation	Single nucleotide variant

1 variation for BRGDA2, BRGDA7, BRGDA8, BRGDA9

2 variations for BRGDA3, BRGDA5

7 variations for "Brugada Syndrome (Shorter-than-normal QT interval)"

1 variation for "Spontaneous Brugada pattern ECG"

EXTENSION SITE

The SCN5A gene homepage

General information

Gene symbol	SCN5A
Gene name	sodium channel, voltage-gated, type V, alpha subunit
Chromosome	3
Chromosomal band	p21
Imprinted	Not imprinted
Genomic reference	LRG_289
Transcript reference	NM_198056.2
Exon/intron information	NM_198056.2 exon/intron table
Associated with diseases	ATFB10 , BRGDA1 , CMD1E , LQT3 , PFHB1A , SIDS , SSS1 , VF1
Citation reference(s)	-
Refseq URL	Genomic reference sequence
Curators (1)	Global Variome, with Curator vacancy
Total number of public variants reported	1639
Unique public DNA variants reported	981
Individuals with public variants	1509
Hidden variants	52
Download all this gene's data	Download all data
Notes	

Date created
Date last updated
Version

All individuals with variants in gene SCN5A

766 entries on 8 pages. Showing entries 1 - 100.

Individual ID	ID_report	Reference	Remarks	Gen
00004251	-	PubMed: Riuro. 2014	-	-
00004252	-	PubMed: Riuro. 2014	-	-
00004253	-	PubMed: Riuro. 2014	5-generation family, 3 affecteds, 2 unaffected carriers (3985G>A)	-
00004254	-	PubMed: Riuro. 2014	-	-
00016929	-	PubMed: Riuro. 2014	3-generation family, 3 affecteds	-
00029639	-	-	-	F
00029640	-	-	-	M
00047336	-	Fam823	2-generation family, 2 carriers (1M, 1F)	-
00047337	-	Fam136	2-generation family, 2 carriers (2F)	F
00047338	-	Fam399	2-generation family, 3 carriers (3M)	M
00047339	-	Fam427	2-generation family, 3 carriers (1M, 2F)	-
00047340	-	F61.537U	3-generation family, 3 carriers (1M, 2F)	-
00047342	-	F61.537T	3-generation family, 4 carriers (1M, 3F)	-

Transcript #00018523 (NM_198056.2, SCN5A gene)

Transcript name	transcript variant 1
Gene name	SCN5A (sodium channel, voltage-gated, type V, alpha subunit)
Chromosome	3
Transcript - NCBI ID	NM_198056.2
Transcript - Ensembl ID	-
Protein - NCBI ID	NP_932173.1
Protein - Ensembl ID	-
Protein - Uniprot ID	-
Exon/intron information	Exon/intron information table: HTML , Txt
Remarks	-

Variants

1639 entries on 17 pages. Showing entries 1 - 100.

Affects function	Exon	DNA change (cDNA)	RNA change	Protein
?	-	c.-53+1G>A	r.spl?	
-?	-	c.-53+114_-53+116dup	r.(=)	
-?	-	c.-52-153A>C	r.(=)	
-?	-	c.-6_-4del	r.(?)	
+	17	c.(2851_2853)?	r.(?)	
+	23	c.4213G>Y	r.(?)	
+	28	c.5851G>Y	r.(?)	
-?	-	c.5851G>Y	r.(?)	
+	8	c.951G>Y	r.(?)	
-?	1_28	c.=	r.3229_3231del	
+	2	c.3G>A	r.(?)	
?	-	c.4G>A	r.(?)	
?	-	c.23C>A	r.(?)	

Rselenium library used for:

Transcripts, Individuals,
Screenings

All diseases associated with gene SCN5A

8 entries on 1 page. Showing entries 1 - 8.

ID	Abbreviation	Name	OMIM ID	Inheritance	In
03516	ATFB10	fibrillation, atrial, familial, type 10	614022	-	
00118	BRGDA1	Brugada syndrome, type 1 (BRGDA-1)	601144	AD	
02343	CMD1E	cardiomyopathy, dilated, type 1E (CMD-1E)	601154	AD	
00407	LQT3	QT syndrome, long, type 3 (LQT-3)	603830	AD	
01217	PFHB1A	heart block, progressive, familial, type 1A (PFHB1A, heart block, nonprogressive)	113900	AD	
02087	SIDS	death, sudden, syndrome, infant (SIDS)	272120	AR	
02765	SSS1	sinus, sick, syndrome, type 1, autosomal recessive	608567	AR	
			8829	-	

All screenings for gene SCN5A

693 entries on 7 pages. Showing entries 1 - 100.

Screening ID	Individual ID	Template	Technique	Tissue	Remarks
0000004166	00004238	DNA	SEQ	-	-
0000004167	00004239	DNA	SEQ	-	-
0000004168	00004240	DNA	SEQ	-	-
0000004169	00004241	DNA	SEQ	-	-
0000004170	00004242	DNA	SEQ	-	-
0000004171	00004243	DNA	SEQ	-	-
0000004172	00004244	DNA	SEQ	-	-
0000004173	00004245	DNA	SEQ	-	-
0000004174	00004246	DNA	SEQ	-	-
0000004175	00004247	DNA	SEQ	-	-
0000004176	00004248	DNA	SEQ	-	-
0000004177	00004249	DNA	SEQ	-	-
0000004178	00004250	DNA	SEQ	-	-
0000004179	00004251	DNA	SEQ	-	-

EXTENSION SITE

VARIANTS ON TRANSCRIPTS

SCREENINGS TO VARIANTS

All transcripts active for the CACNA1C gene

2 entries on 1 page. Showing entries 1 - 2.

100 per page [How to query](#)

ID	Chr	Name
00001160	12	transcript variant 18
00024102	12	transcript variant 1

Transcript #00018523 (NM_198056.2, SCN5A gene)

Transcript name	transcript variant 1
Gene name	SCN5A (sodium channel, voltage-gated, type V, alpha subunit)
Chromosome	3
Transcript - NCBI ID	NM_198056.2
Transcript - Ensembl ID	-
Protein - NCBI ID	NP_932173.1
Protein - Ensembl ID	-
Protein - Uniprot ID	-
Exon/intron information	Exon/intron information table: HTML , Txt
Remarks	-

Variants

1639 entries on 17 pages. Showing entries 1 - 100.

100 per page [Legend](#) [How to query](#) [« First](#) [« Prev](#) [1](#) [2](#) [3](#) [4](#) [5](#) [6](#) [7](#) [8](#) [9](#) [10](#) [11](#) ... [Next »](#) [Last »](#)

Affects function	Exon	DNA change (cDNA)	RNA change	Protein
?	-	c.-53+1G>A	r.spl?	p.?
-?	-	c.-53+114_-53+116dup	r.(=)	p.(=)
-?	-	c.-52-153A>C	r.(=)	p.(=)
-?	-	c.-6_-4del	r.(?)	p.(=)
+	17	c.(2851_2853)?	r.(?)	p.(Asp951*)
+	23	c.4213G>Y	r.(?)	p.(Val1405Leu)
+	28	c.5851G>Y	r.(?)	p.(Val1951Leu)

id	transcriptid	VariantOnTranscript/DNA	VariantOnTranscript/RNA	VariantOnTranscript/Protein	VariantOnTranscript/Exon
1	0000519573	00018523	c.-53+1G>A	r.spl?	p.?
2	0000608615	00018523	c.-53+114_-53+116dup	r.(=)	p.(=)
3	0000608614	00018523	c.-52-153A>C	r.(=)	p.(=)
4	0000297945	00018523	c.-6_-4del	r.(?)	p.(=)
5	0000164726	00018523	c.(2851_2853)?	r.(?)	p.(Asp951*)
6	0000164872	00018523	c.4213G>Y	r.(?)	p.(Val1405Leu)
7	0000165023	00018523	c.5851G>Y	r.(?)	p.(Val1951Leu)
8	0000470179	00018523	c.5851G>Y	r.(?)	p.(Val1951Leu)
9	0000164705	00018523	c.951G>Y	r.(?)	p.(Lys317Asn)
10	0000242392	00018523	c.=	r.3229_3231del	p.Gln1077del
11	0000164641	00018523	c.3G>A	r.(?)	p.(?)
12	0000519571	00018523	c.4G>A	r.(?)	p.(Ala2Thr)
13	0000519570	00018523	c.23G>A	r.(?)	p.(Arg8Gln)

All screenings for gene SCN5A

693 entries on 7 pages. Showing entries 1 - 100.

100 per page [Legend](#) [How to query](#) [« First](#) [« Prev](#)

Screening ID	Individual ID	Template
0000004166	00004238	DNA
0000004167	00004239	DNA
0000004168	00004240	DNA
0000004169	00004241	DNA
0000004170	00004242	DNA
0000004171	00004243	DNA
0000004172	00004244	DNA
0000004173	00004245	DNA
0000004174	00004246	DNA
0000004175	00004247	DNA
0000004176	00004248	DNA
0000004177	00004249	DNA
0000004178	00004250	DNA
0000004179	00004251	DNA

Screening #0000004166

Individual ID	00004238
Template	DNA
Technique	SEQ
Tissue	-
Remarks	-
Variants found?	1
Owner name	Anna Iglesias
Database submission license	No license selected
Created by	Anna Iglesias

Genes screened

Symbol	Gene	Chr
KCNE1	potassium voltage-gated channel, Isk-related family, member 1	21
KCNE2	potassium voltage-gated channel, Isk-related family, member 2	21
KCNH2	potassium voltage-gated channel, subfamily H (eag-related), member 2	7
KCNQ1	potassium voltage-gated channel, KQT-like subfamily, member 1	11
S100A1	S100 calcium binding protein A1	1
SCN5A	sodium channel, voltage-gated, type V, alpha subunit	3

Variants found

1 entry on 1 page. Showing entry 1.

100 per page [Legend](#) [How to query](#)

Chr	Allele	Effect	Classification method	Clinical classification
11	Paternal (confirmed)	+/?	-	pathogenic

screeningid	variantid
1	0000309522
2	0000309541
3	0000309542
4	0000309542
5	0000309807
6	0000309807
7	0000310440
8	0000310441
9	0000329184
10	0000329322

EXTENSION SILE

INDIVIDUALS TO DISEASES

All individuals with variants in gene SCN5A

766 entries on 8 pages. Showing entries 1 - 100.

100 per page [Legend](#) [How to query](#) [« First](#) [< Prev](#) **1** [2](#) [3](#) [4](#) [5](#) [6](#) [7](#) [8](#) [Next >](#) [Last](#)

Individual ID	ID_report	Reference	Remarks	Gender
00004251	-	PubMed: Riuro 2014	-	-
00004252	-	PubMed: Riuro 2014	-	-
00004253	-	PubMed: Riuro 2014	5-generation family, 3 affecteds, 2 unaffected carriers (3985G>	-
00004254	-	PubMed: Riuro 2014	-	-
00016929	-	PubMed: Riuro 2014	3-generation family, 3 affect	-
00029639	-	-	-	-
00029640	-	-	-	-
00047336	-	Fam823	2-generation family, 2 carrie 1F)	-
00047337	-	Fam136	2-generation family, 2 carrie	-
00047338	-	Fam399	2-generation family, 3 carrie	-
00047339	-	Fam427	2-generation family, 3 carrie 2F)	-
00047340	-	F61.537U	3-generation family, 3 carrie 2F)	-
00047342	-	F61.537T	3-generation family, 4 carrie 3F)	-

Individual #00029639

ID_report	-
Reference	-
Remarks	-
Gender	F
Consanguinity	no
Country	Belgium
Population	white
Age at death	-
VIP	0
Data_av	-
Treatment	-
Panel size	1
Diseases	BRGDA, myotonia congenita, autosomal domin
Owner name	Uschi Peeters
Database submission license	No license selected
Created by	Uschi Peeters

- Starts from Individuals page
- Delete all the rows without “disease”
- Make a list taking only “Individuals ID” column
- Goes en each Individual page
- Takes Disease ID from each “href” and associate it with the individuals list

	individualid	diseaseid
1	00004251	00407
2	00004252	00407
3	00004253	00407
4	00004254	00407
5	00016929	00407
6	00029639	00407
7	00029640	00407
8	00047336	00407
9	00047337	00407
10	00047338	00407
11	00047339	00407
12	00047340	00407
13	00047342	00407
14	00047343	00407

EXTENSION SITE

PHENOTYPE

	individualid	diseaseid
1	00004251	00407
2	00004252	00407
3	00004253	00407
4	00004254	00407
5	00016929	00407
6	00029639	00407
7	00029640	00407
8	00047336	00407
9	00047337	00407
10	00047338	00407
11	00047339	00407
12	00047340	00407

Phenotypes

Brugada syndrome (BRGDA) (BRGDA) + Add phenotype for this disease

Phenotype ID	Phenotype details	Diagnosis/Initial	Diagnosis/Definite	Inheritance
0000034680	asymptomatic Brugada syndrome	-	-	Familial

	id	diseaseid	individualid	Phenotype/Inheritance	Phenotype/Age	Phenotype/Additional	Phenotype
1	0000015290	00407	00004251	-	Isolated (sporadic)	-	-
2	0000015291	00407	00004252	-	Isolated (sporadic)	-	-
3	0000015292	00407	00004253	-	Familial, autosomal dominant	-	-
4	0000015293	00407	00004254	-	Isolated (sporadic)	-	-
5	0000015296	00407	00016929	-	Familial, autosomal dominant	-	-
6	0000034680	00407	00029639	-	Familial	-	-
7	0000034679	00407	00029640	-	Familial	-	-
8	0000035743	00407	00047336	-	Familial	-	-
9	0000035744	00407	00047337	-	Familial	-	-
10	0000035746	00407	00047338	-	Familial	-	-
11	0000035747	00407	00047339	-	Familial	-	-
12	0000035751	00407	00047340	-	Familial	-	-
13	0000034668	00407	00047342	-	Familial, autosomal dominant	-	-
14	0000035753	00407	00047343	-	Familial, autosomal dominant	-	-
15	0000034743	00407	00047469	-	Unknown	-	-

- Start from the Individual ID list obtained before
- Goes in each Individual page and takes data from Phenotypes table
- Merges the obtained db with “individual to disease”

EXTENSION SILE

SCREENINGS TO GENES

All screenings for gene SCN5A

693 entries on 7 pages. Showing entries 1 - 100.

Screening ID	Individual ID	Template	Technique	Tissue
0000004166	00004238	DNA	SEQ	-
0000004167	00004239	DNA	SEQ	-
0000004168	00004240	DNA	SEQ	-
0000004169	00004241	DNA	SEQ	-
0000004170	00004242	DNA	SEQ	-
0000004171	00004243	DNA	SEQ	-
0000004172	00004244	DNA	SEQ	-
0000004173	00004245	DNA	SEQ	-
0000004174	00004246	DNA	SEQ	-
0000004175	00004247	DNA	SEQ	-
0000004176	00004248	DNA	SEQ	-
0000004177	00004249	DNA	SEQ	-
0000004178	00004250	DNA	SEQ	-
0000004179	00004251	DNA	SEQ	-

Screening #0000004166

Individual ID	00004238
Template	DNA
Technique	SEQ
Tissue	-
Remarks	-
Variants found?	1
Owner name	Anna Iglesias
Database submission license	No license selected
Created by	Anna Iglesias

Genes screened

Symbol	Gene	Chr	Band	Transc
KCNE1	potassium voltage-gated channel, Isk-related family, member 1	21		
KCNE2	potassium voltage-gated channel, Isk-related family, member 2	21		
KCNH2	potassium voltage-gated channel, subfamily H (eag-related), member 2	7		
KCNQ1	potassium voltage-gated channel, KQT-like subfamily, member 1	11		
S100A1	S100 calcium binding protein A1	1		
SCN5A	sodium channel, voltage-gated, type V, alpha subunit	3		


screeningid	geneid
1	0000004166 KCNE1
2	0000004166 KCNE2
3	0000004166 KCNH2
4	0000004166 KCNQ1
5	0000004166 S100A1
6	0000004166 SCN5A
7	0000004167 KCNE1
8	0000004167 KCNE2
9	0000004167 KCNH2
10	0000004167 KCNQ1
11	0000004167 SCN5A

- Start from the Screenings table
- Goes in each Screening page and takes data from Genes Screened table
- Keeps only Screening ID and Gene ID

EXTENSION SILE

VARIANTS ON GENOME

All variants in the SCN5A gene

 The variants shown are described using the NM_198056.2 transcript reference sequence.

1639 entries on 17 pages. Showing entries 1 - 100.

100 per page [Legend](#) [How to query](#) [« First](#) [< Prev](#) [1](#) [2](#) [3](#) [4](#) [5](#) [6](#) [7](#) [8](#) [9](#) [10](#)

Effect	Exon	DNA change (cDNA)	RNA change	Protein
?./.	-	c.-53+1G>A	r.spl?	p.?
-?./.	-	c.-53+114_-53+116dup	r.(=)	p.(=)
-?./.	-	c.-52-153A>C	r.(=)	p.(=)
-?./.	-	c.-6_-4del	r.(?)	p.(=)
+?./.	17	c.(2851_2853)?	r.(?)	p.(Asp951*)
+?./.	23	c.4213G>Y	r.(?)	p.(Val1405Leu)
+?./.	28	c.5851G>Y	r.(?)	p.(Val1951Leu)

Variant #0000519573 (NC_000003.11:g.38691021C>T, SCN5A(NM_198056.2):c.-53+1G>A)

Chromosome	3
Allele	Unknown
Affects function (as reported)	Effect unknown
Affects function (by curator)	Not classified
Classification method	-
Clinical classification	VUS
DNA change (genomic) (Relative to hg19 / GRCh37)	g.38691021C>T
DNA change (hg38)	g.38649530C>T
Published as	-
ISCN	-
DB-ID	SCN5A_001301
Variant remarks	VKGL data sharing initiative Nederland
Reference	-
ClinVar ID	-
dbSNP ID	-
Origin	CLASSIFICATION record
Segregation	-
Frequency	-
Re-site	-
VIP	-
Methylation	-
Average frequency (gnomAD)	-
Owner	-
Database submission license	-
Created by	-

	id	allele	chromosome	owned_by	VariantOnGenome/DBID	VariantOnGenome/DNA
1	0000305372	3	10	03508	PDE6C_000083	g.(?_95372482)_(95372963_
2	0000305372	3	10	00000	PDE6C_000078	g.95372567C>T
3	0000305372	3	10	00000	PDE6C_000078	g.95372567C>T
4	0000305372	3	10	03508	PDE6C_000078	g.95372567C>T
5	0000305372	3	10	03508	PDE6C_000078	g.95372567C>T
6	0000305372	1	10	00000	PDE6C_000073	g.95372571_95372581del
7	0000305372	3	10	02330	PDE6C_000034	g.95372685C>T
8	0000305372	3	10	02325	PDE6C_000002	g.95372734G>A
9	0000305372	3	10	02327	PDE6C_000002	g.95372734G>A
10	0000305372	3	10	02330	PDE6C_000001	g.95372734G>T
11	0000305372	3	10	01943	PDE6C_000001	g.95372734G>T
12	0000305372	3	10	02327	PDE6C_000025	g.95372764C>T
13	0000305372	Both (homozygous)	10	00000	PDE6C_000084	g.95372786C>T

- Takes the whole variants table and also put the href in each row in a separate list
- Goes in each Variant page and takes data from the table
- Merges the two tables

EXTENSION SITE

RESEARCH BY PHENOTYPE

All diseases

10 entries on 1 page. Showing entries 1 - 10.

100 per page

[Legend](#) [How to query](#)

ID	Abbreviation	Name	OMIM ID	Inheritance	Individuals	Phenotypes	Associated with genes	Assoc
04170	BRGDA	Brugada syndrome (BRGDA)	-	-	120	98	SCN1B, SCN2B, SCN3B, SCN4B	-
00118	BRGDA1	Brugada syndrome, type 1 (BRGDA-1)	601144	AD	364	363	SCN5A	-
03055	BRGDA2	Brugada syndrome, type 2 (BRGDA-2)	611777	-	0	0	GPD1L	-
00680	BRGDA3	Brugada syndrome, type 3 (BRGDA-3)	611875	-	0	0	CACNA1C	-
03066	BRGDA4	Brugada syndrome, type 4 (BRGDA-4)	611876	-	0	0	CACNB2	-
01020	BRGDA5	Brugada syndrome, type 5 (BRGDA-5, conduction defect cardiac nonspecific)	612838	-	0	0	SCN1B	-
			613119	-	0	0	KCNE3	-
			613120	AD	0	0	SCN3B	-
			613123	-	0	0	HCN4	-
			616399	AD	0	0	KCND3	-

Disease #04170 (BRGDA (Brugada syndrome (BRGDA)))

Official abbreviation	BRGDA
Name	Brugada syndrome (BRGDA)
OMIM ID	-
Inheritance	-
Individuals reported having this disease	120
Phenotype entries for this disease	98
Associated with 4 genes	SCN1B, SCN2B, SCN3B, SCN4B
Associated tissues	-
Disease features	-
Remarks	-

Individuals

120 entries on 2 pages. Showing entries 1 - 100.

100 per page [Legend](#) [How to query](#) « First < Prev 1 2 Next > Last »

Individual ID	ID_report	Reference	Remarks	Gender	Consanguinity	Country
00022471	-	-	This patient is also diagnosed with sodium channel myotonia	M	no	Belgium
00028976	-	PubMed: Alleque 2015, Journal: Alleque 2015	-	F	-	Belgium
00028977	-	PubMed: Alleque 2015, Journal: Alleque 2015	-	M	-	United States
00028978	-	PubMed: Alleque 2015, Journal: Alleque 2015	-	M	-	United States
00028979	-	PubMed: Alleque 2015, Journal: Alleque 2015	-	-	-	-
00028980	-	PubMed: Alleque 2015, Journal: Alleque 2015	-	-	-	-

Variants

4 entries on 1 page. Showing entries 1 - 4.

100 per page

[Legend](#) [How to query](#)

Chr	Allele	Effect	Classification method	Clinical classification	DNA change (genomic) (hg19)
11	Unknown	?/.	-	VUS	g.123504959C>G
11	Unknown	?/.	-	VUS	g.123524411G>A
19	Unknown	?/.	-	VUS	g.35521779G>T
19	Unknown	?/.	-	VUS	g.35524824T>C

- Starts from the Disease page related to the Disease chosen
- Goes into each row and takes data from each individual table page
- Goes into each Individual page and takes data from variants table
- Merges Individuals and Variants tables

BRGDA & BRGDA1

EXTENSION SITE

RESEARCH BY PHENOTYPE

ID	Abbreviation	Individuals	Phenotypes	Associated with genes
04170	BRGDA	120	98	SCN1B, SCN2B, SCN3B, SCN4B
00118	BRGDA1	364	363	SCN5A
03055	BRGDA2	0	0	GPD1L
00680	BRGDA3	0	0	CACNA1C
03066	BRGDA4	0	0	CACNB2
01020	BRGDA5	0	0	SCN1B
03264	BRGDA6	0	0	KCNE3
03265	BRGDA7	0	0	SCN3B
03267	BRGDA8	0	0	HCN4
04540	BRGDA9	0	0	KCND3

All individuals with variants in gene CACNA1C

16 entries on 1 page. Showing entries 1 - 16.

100 per page

Legend

How to query

Individual ID	ID_report	Reference	Remarks
00000208	-	PubMed: Sun 2011, Journal: Sun 2011	-
00000209	-	PubMed: Sun 2011, Journal: Sun 2011	-
		PubMed: Allegue 2015, Journal: Allegue 2015	-
		PubMed: Allegue 2015, Journal: Allegue 2015	-
		-	-
		-	-
		-	-

Variants

4 entries on 1 page. Showing entries 1 - 4.

100 per page

Legend

How to query

Chr	Allele	Effect	Classification method	Clinical classification	DNA change (genomic) (hg19)
11	Unknown	?/.	-	VUS	g.123504959C>G
11	Unknown	?/.	-	VUS	g.123524411G>A
19	Unknown	?/.	-	VUS	g.35521779G>T
19	Unknown	?/.	-	VUS	g.35524824T>C

Disease

CHTE

CHTE

OTHER GENES

BRGDA

BRGDA

SUD

BRGDA

BRGDA

SUD

- Takes the list of the Associated Genes from each row who has Individuals = 0
- Goes in each Individuals page associated with each gene in the list
- Goes into each Individual page and takes data from variants table
- Merges Individuals and Variants tables
- Filter the obtained table by the column "Disease" by taking only the related ones



03

Validation of the Solutions

BRGDA & BRGDA1

BRGDA:

From 120 individuals, 420 variations data

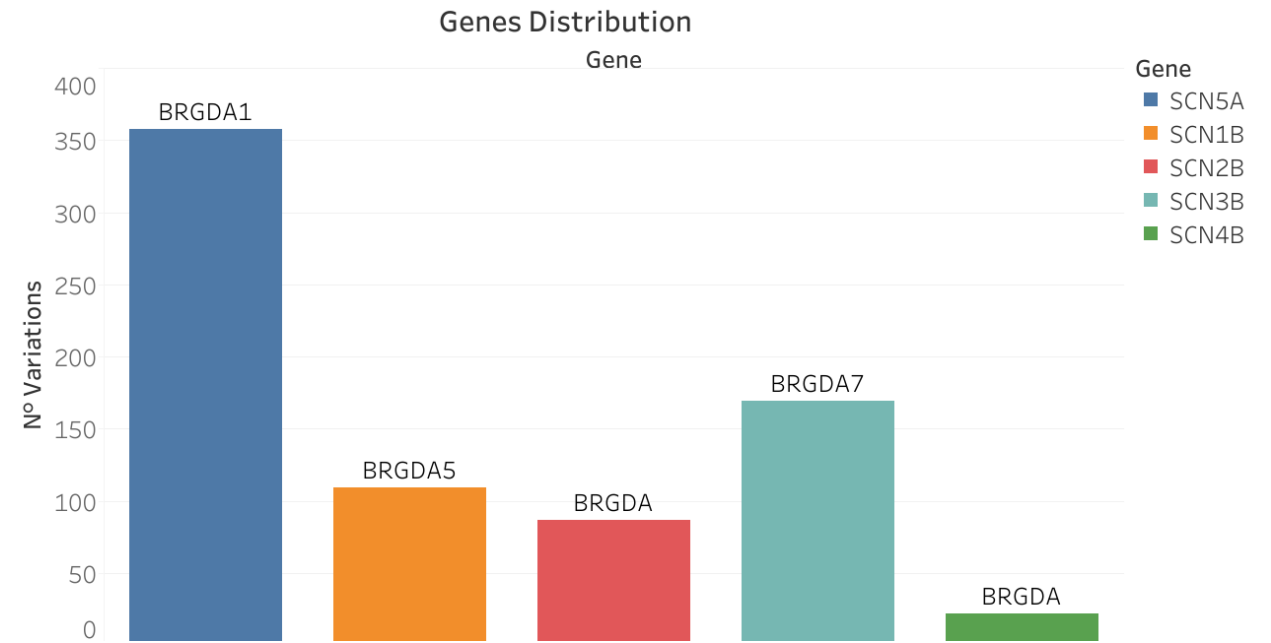
Study of *Peeters* on 74 unrelated individuals

[**SCN1B**, SCN2B, **SCN3B**, SCN4B]

BRGDA 1:

From 364 individuals, 366 variations data

Genes Distribution



BRGDA & BRGDA1

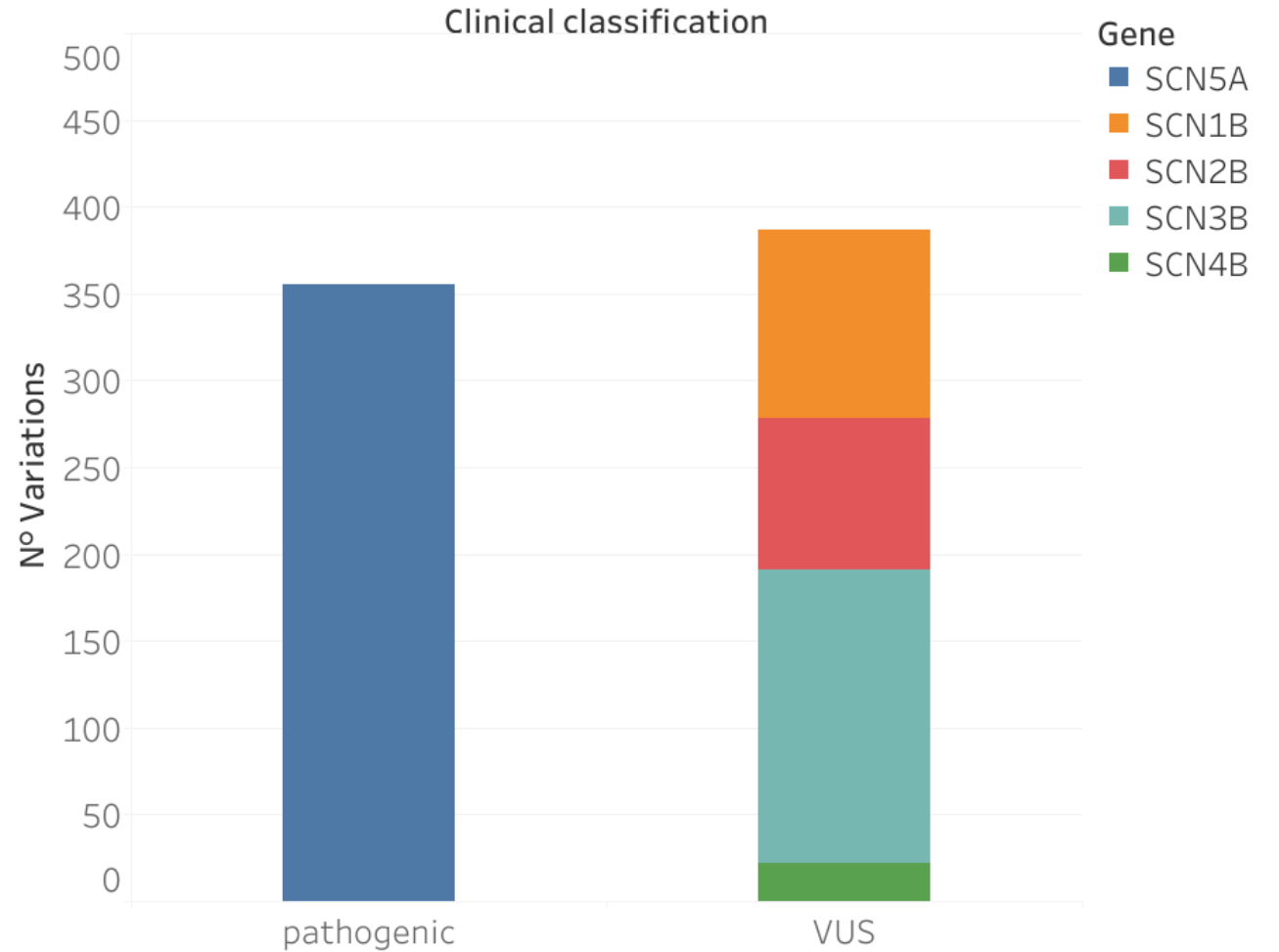
BRGDA:

Totality of observations classified as
“VUS”
(Variant of Uncertain Significance)

BRGDA 1:

Totality of observations classified as
“pathogenic”

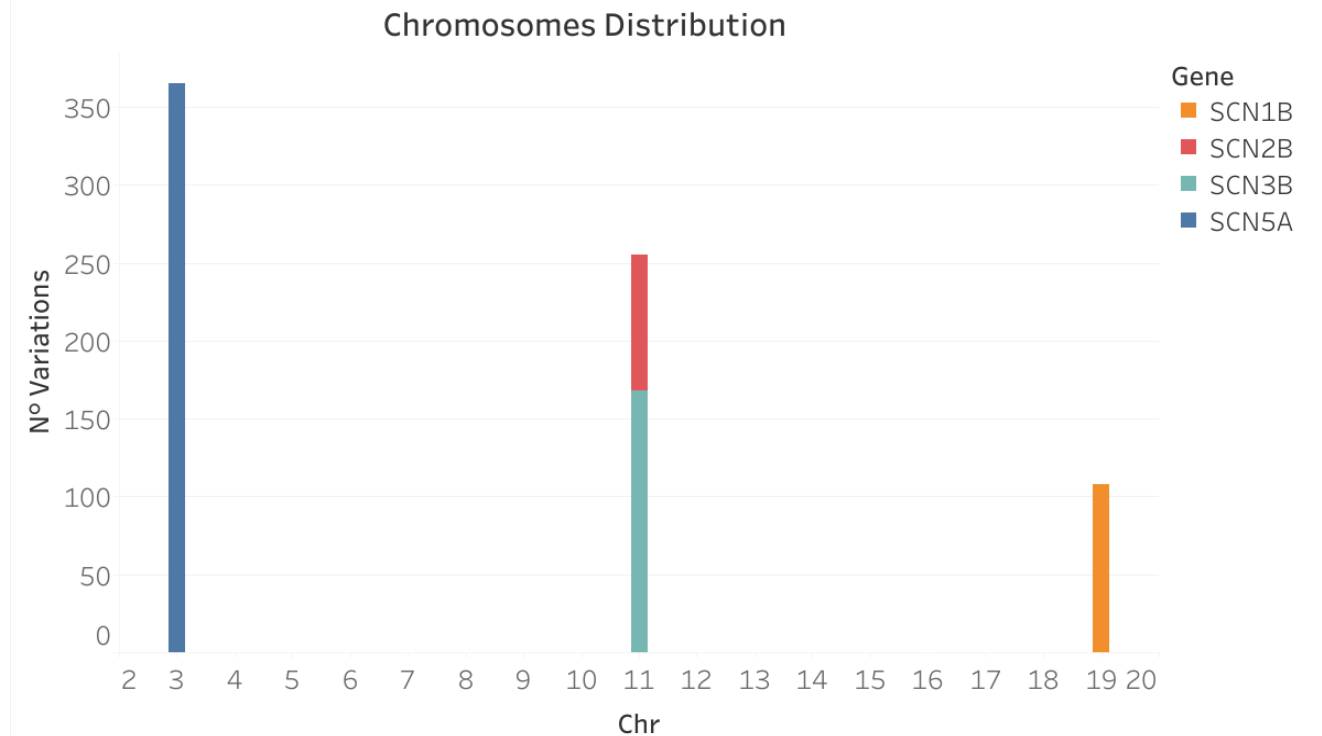
Clinical Classification



BRGDA & BRGDA1

- **SCN5A**, typically associated with BRGDA1, mutation in **chromosome 3**
- **SCN1B**, typically associated with BRGDA5, mutations in **chromosome 19**
- **SCN3B**, typically associated with BRGDA7, mutations in **chromosome 11**

Chromosomes Distribution



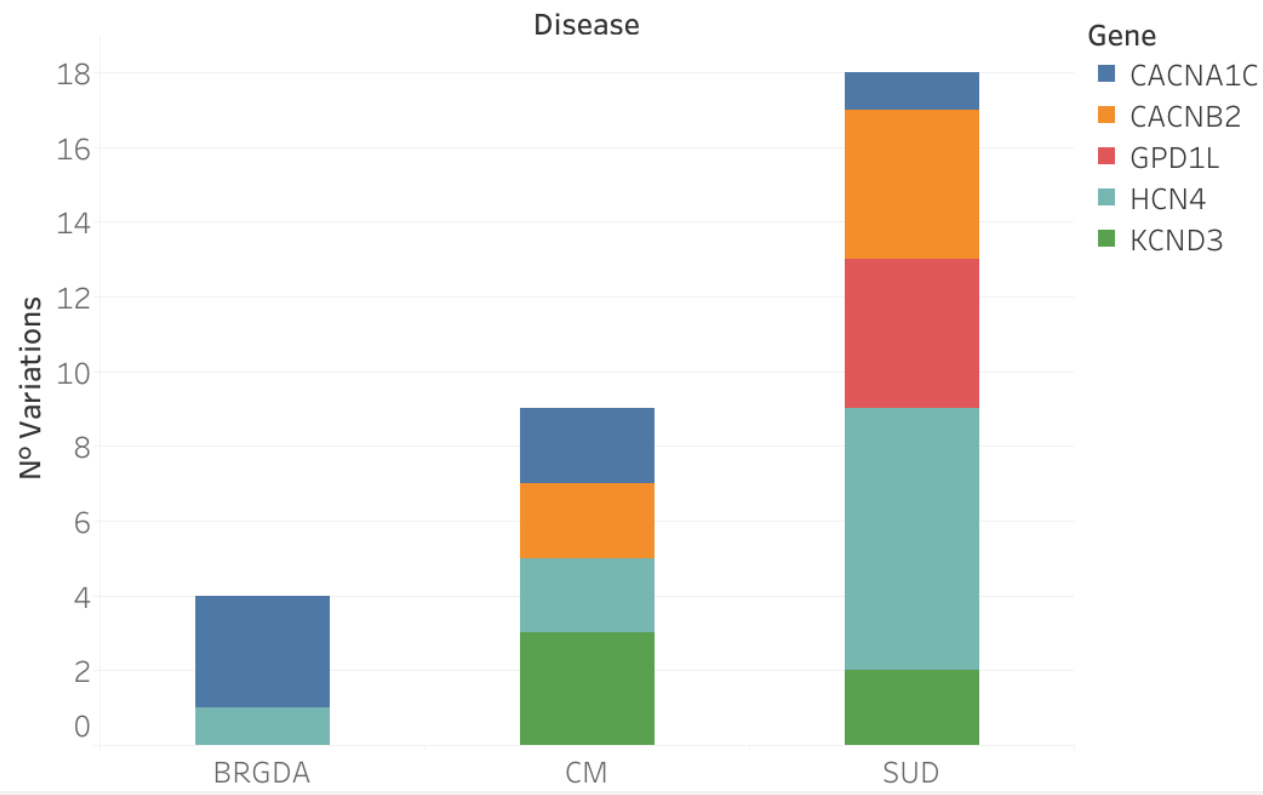
OTHER GENES

From the **921** variations obtained:

- **Deleted** the ones already present in the previous database by “individual ID”
- Selecting the ones **labeled** as:
 - **BRGDA**
 - **CM** (Cardiomyopathy), associated with strong arrhythmias
 - **SUD** (Sudden Unexplained Death), synonym of Brugada in *MedGen*

Resulting db composed by **31** variations

Diseases Distribution



OTHER GENES

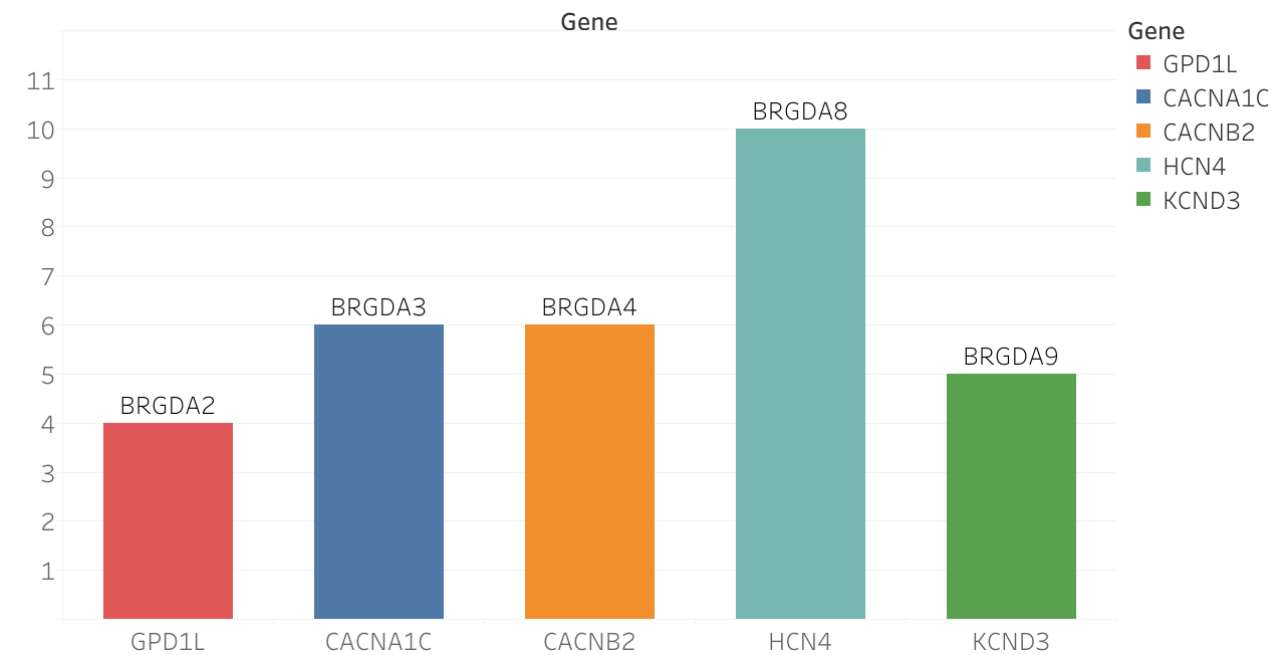
Variations in:

GPD1L (4)
CACNA1C (6)
CACNB (6)
HCN4 (10)
KCND3 (5)

Typically associated with:

BRGDA2
BRGDA3
BRGDA4
BRGDA8
BRGDA9

Genes Distribution



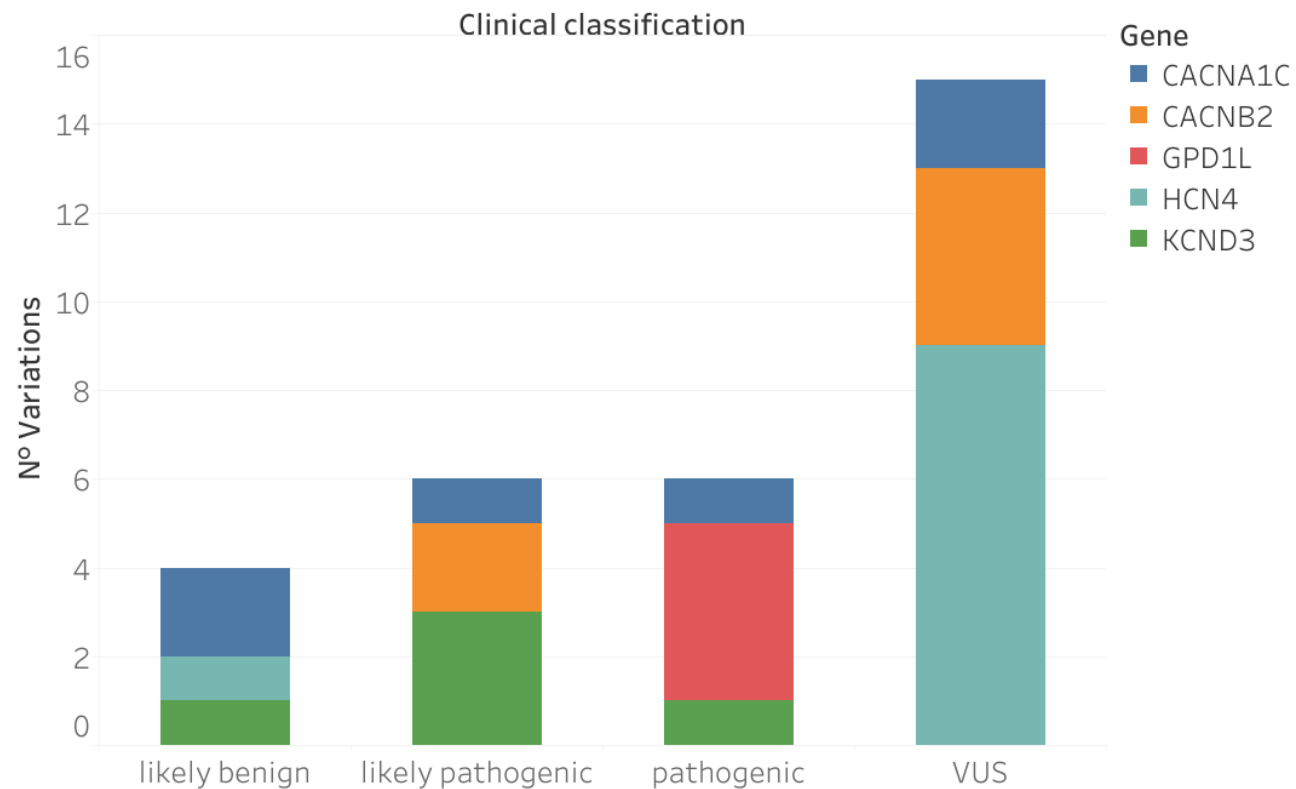
OTHER GENES

15 variations labeled as “VUS”

GPD1L labeled as “pathogenic” in all observations

KCND3 in the majority “likely pathogenic”

Clinical Classification



OTHER GENES

GPD1L, mutation in **chromosome 3** (BrS2)

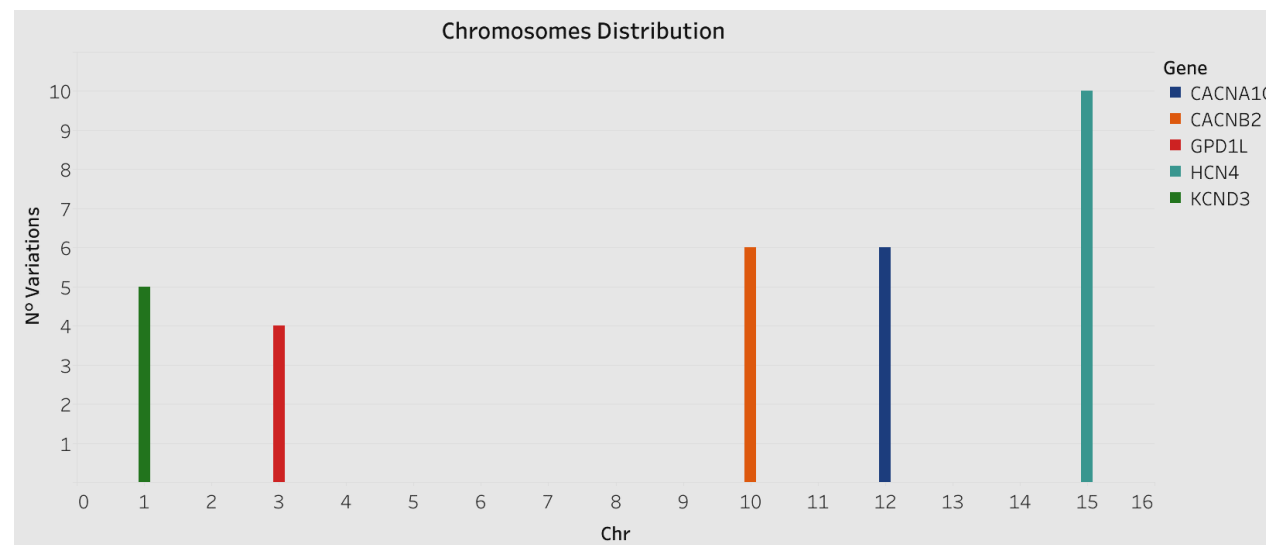
CACNA1C, mutation in **chromosome 12** (BrS3)

CACNB2, mutation in **chromosome 10** (BrS4)

HCN4, mutation in **chromosome 15** (BrS8)

KCND3, mutation in **chromosome 1** (BrS9)

Chromosomes Distribution



DISCUSSION

DOWNLOAD:

Download all this gene's data	Download all data
Notes	Establishment of this gene supported by the Leiden University Medical Center (LUMC) , Leiden, Nederland
Date created	May 03, 2013
Date last updated	September 17, 2021

PRO:

- Reduce **time** to collect data

CONS:

- Feature available for only a **small group** of the genes in LOVD
- **Lower quality** of data obtained:
 - Data in download file are updated manually, so most of the time the information present in it are different from the ones on the website
- **Can't obtain** the information present in “**Research by Phenotype**”, fundamental for the analysis carried out by PROS

DISCUSSION

TIME:

Library “***rvest***” only obtains data in the first table (**max 100**), even manually changing the url the result doesn’t change

- Usually variants, screenings and individuals have more than 100 entries

Library “***Rselenium***” overcomes the problem by **simulating the navigation** and clicking the button to take data from the subsequent tables

Screenings page, even in normal navigation, takes more time than others to load

No API available, so web scraping is the only way to obtain data for the moment

DATA:

Brugada Syndrome is a **rare** disease, the most common type is BRGDA1

Types from **BRGDA2 to BRGDA9** are even **more rare** so only few data are available and in most of the cases are labeled with the generic name
“BRGDA”



04

Conclusions

CONCLUSIONS

OBJECTIVES:

- 1) After applying **SILE** method to **Brugada** Syndrome, noticed a reduced presence of data
- 2) For this reason, another source of data has been **added** to the ones already present: the biological database **LOVD**
- 3) **Evaluated** the effectiveness of the extension of the research module by **applying** it to analysis of **Brugada** Syndrome

CONCLUSIONS

BRGDA1:

Most of the data obtained (**45%**) refers to the variations of **SCN5A** as “**pathological**”, which is associated with **BRGDA1** (most widespread type)

BRGDA:

Most of the data belonging to **BRGDA** has variations in genes SCN1B and SCN3B, generally associated to BRGDA5 and BRGDA7

- Clinical classification labeled as “VUS” (not yet possible to determine if pathological or benign)

OTHERS:

Variations of GPD1L, CACNA1C, CACNB2, HCN4, KCND3, labeled in LOVD as “**CM**” and “**SUD**”

Data kept because **generally associated** with BRGDA2, BRGDA3, BRGDA4, BRGDA8, BRGDA9

More accurate assesment in **following steps** and evaluation by **panel of experts** to take this decision and to evaluate the overall **quality** of acquired data

FUTURE WORKS

Algorithm developed able to add biological data **not only** related to **Brugada**, that **overcomes** the **limitations** imposed by the database, allowing to search data starting from a selected **phenotype**

Platform in future will become more **user friendly**, in order to make it usable by professionals in field of Precision Medicine

Since biological data are **scattered** and **heterogeneous**, adding more **data sources** could help to perform a better analysis as the cost of more time for searching and standardizing data

Cyclical update in automated way of the data from the various data sources

Perform **researches** starting from a specific **Gene**

Follow further developments in the data currently available, especially **VUS**