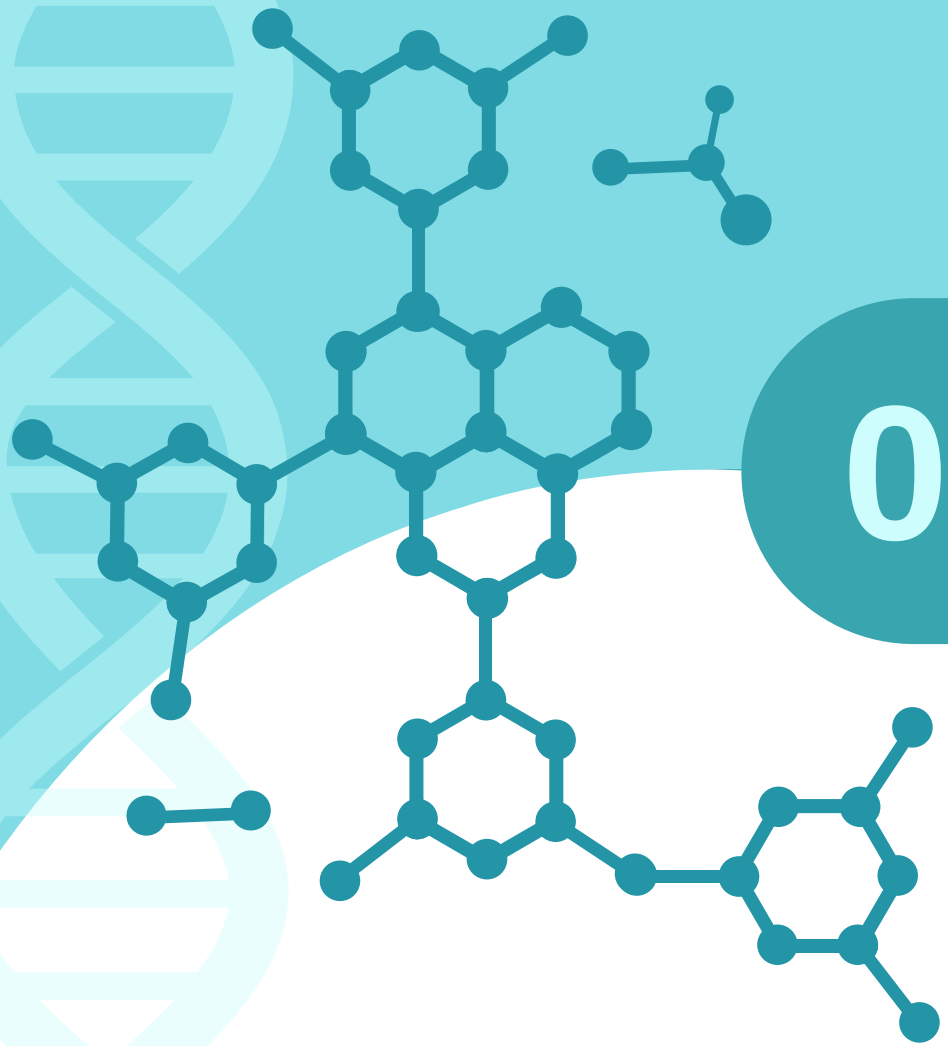
# Identification of genomic variants using the SILE Method

## Extension of the Research module & Focus on the Brugada Syndrome

# CONTENTS



# 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 identifing 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**

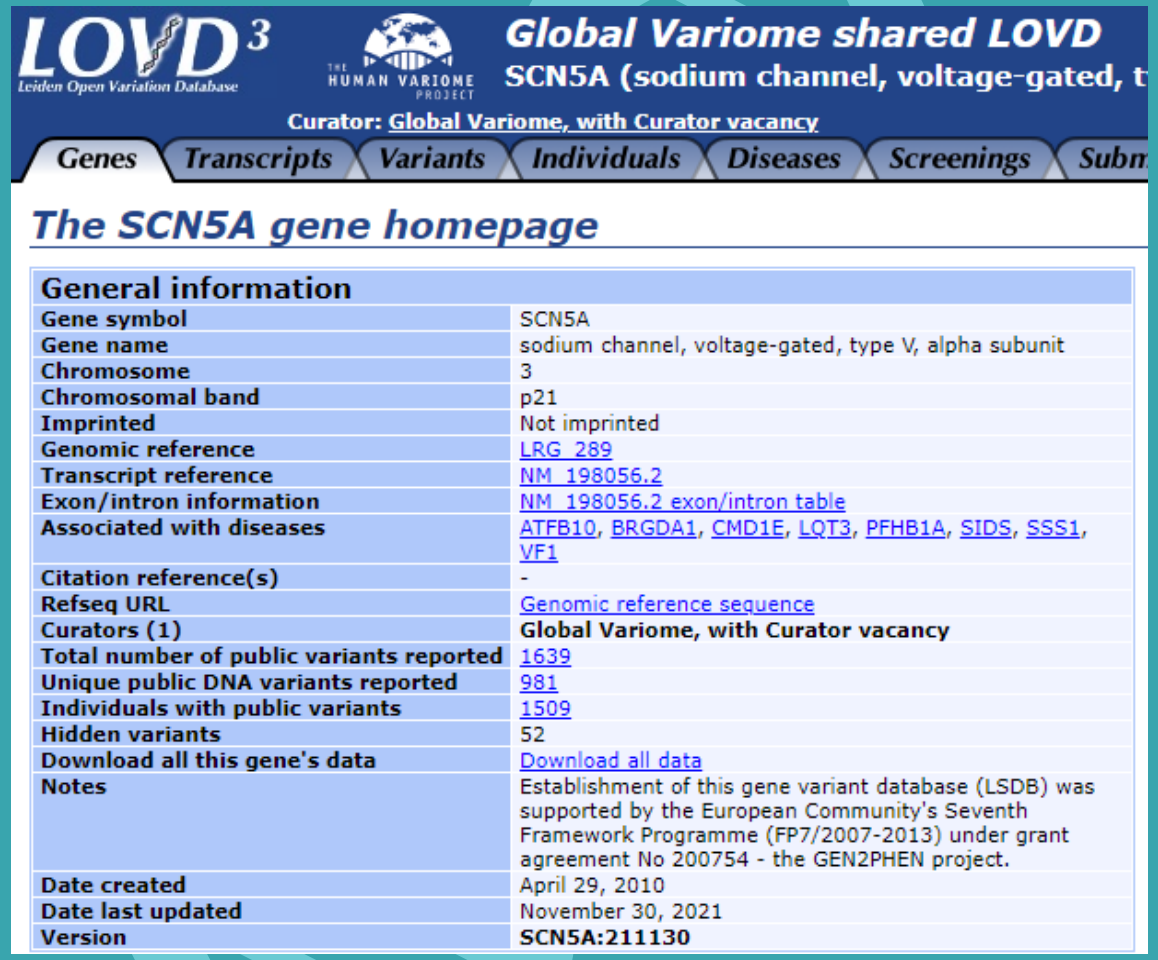
- **Filter** information gathered
- Discart non-relevant and duplicates
- Keep only variations that have sufficiently relevant evidence
- Manually **solve inconsistencies**

**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




**LOVD** (Leiden Open Variation Database)

**Open source** database containing information about genomic variations

More than 23,000 different genes

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

## 6 categories:

- **Genes**
- **Transcripts**
- **Variants**
- **Individuals**
- **Diseases**
- **Screenings**

# BRUGADA

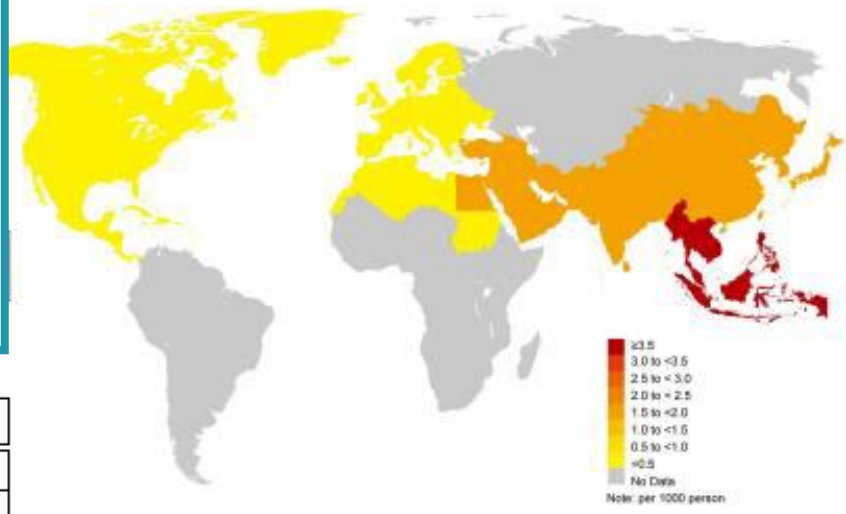
## DIAGNOSIS

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 Implantambel Cardioverterer-defibrillator (only treatment effective)

**Asymptomatic:**
Individual risk assesment
Consider other risk factors (age, sex, external)

# GENOMICS CONCEPTS

**HUMAN GENOME:**
DNA and RNA

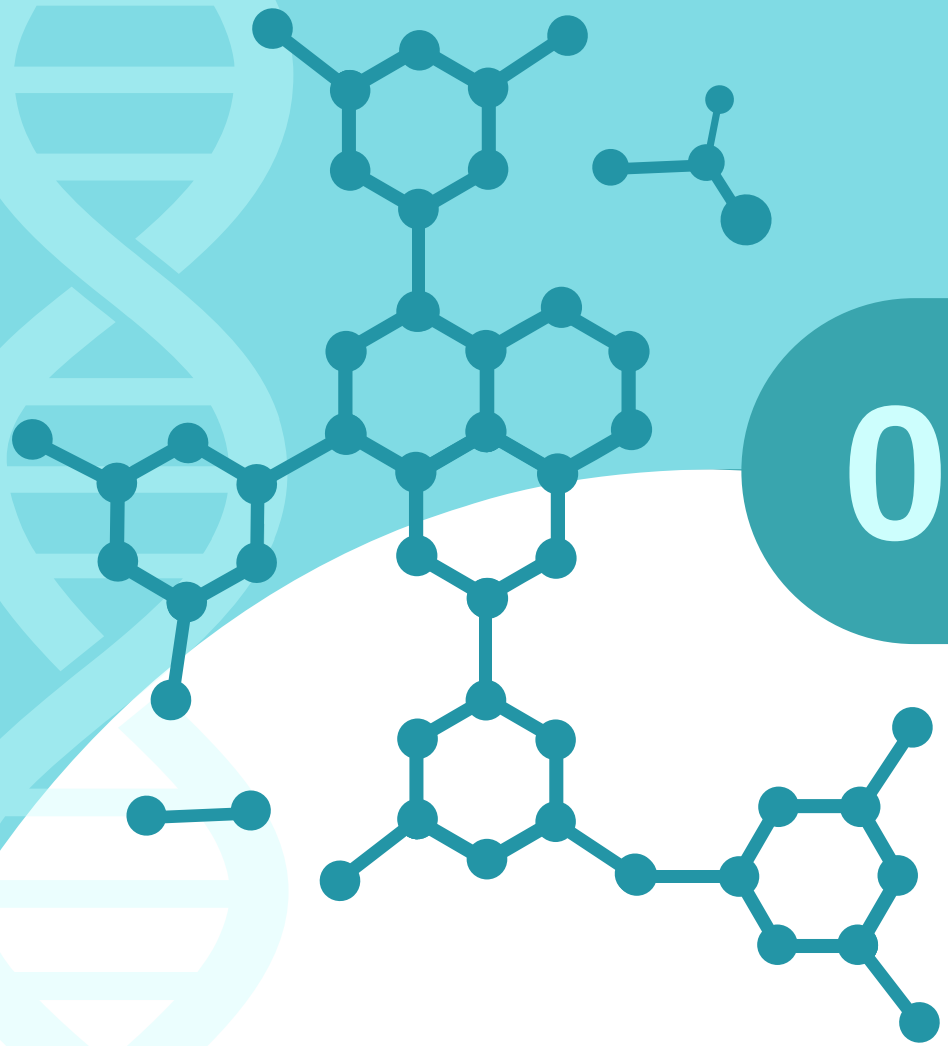
**CHROMOSOMES**

**GENES**

**VARIATIONS**

**PHENOTYPE**

**GENOTYPE**



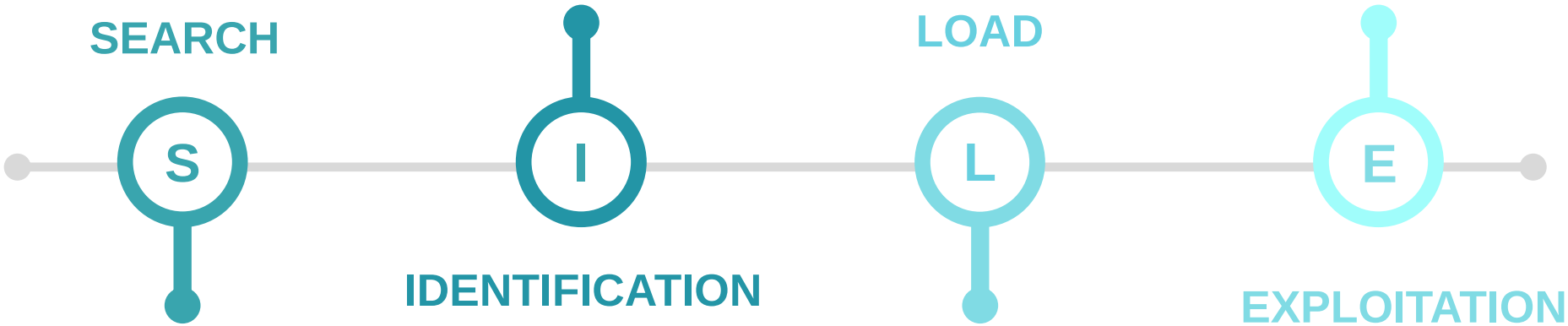
# 02 Methods

# 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 SILE

**Rselenium** library used for:

Transcripts, Individuals, Screenings

## 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 | |
| Notes | |
| Date created | |
| Date last updated | |
| Version | |

## 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? | |
| -?/. | - | 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.(?) | |

## All diseases associated with gene SCN5A

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

100 per page | Legend | How to query

| ID | Abbreviation | Name | OMIM ID | Inheritance |
|---|---|---|---|---|
| 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 |
| | | | 3829 | - |

## 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 ›

| 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) | - |

## All screenings for gene SCN5A

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

100 per page | Legend | How to query | « First | ‹ Prev | 1 2 3 4 5 6

| 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 SILE

## VARIANTS ON TRANSCRIPTS

### 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 | NCBI ID | NCBI Protein ID | Variants |
|---|---|---|---|---|---|
| 00001160 | 12 | transcript variant 18 | NM_000719.6 | NP_000710.5 | 355 |
| 00024102 | 12 | transcript variant 1 | NM_199460.2 | NP_955630.2 | 352 |

100 per page | How to query

## SCREENINGS TO VARIANTS

### All screenings for gene SCN5A

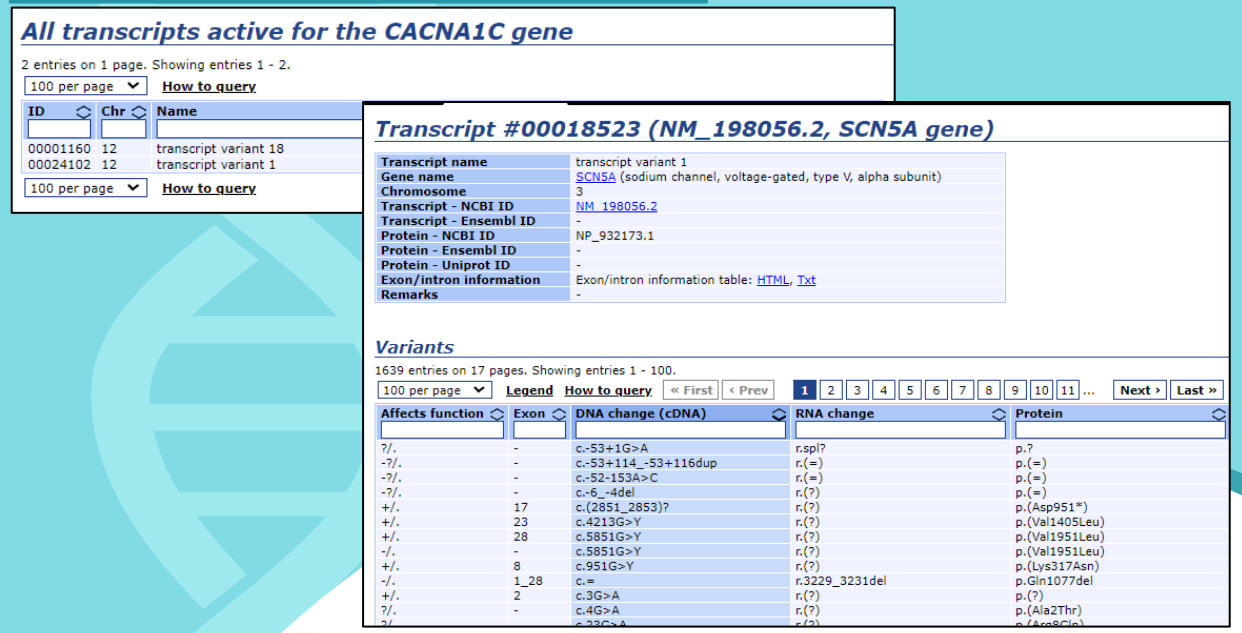
693 entries on 7 pages. Showing entries 1 - 100.

100 per page | Legend | How to query | « First | ‹ Prev

| Screening ID | Individual ID | Template | Technique |
|---|---|---|---|
| 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 SILE

## VARIANTS ON TRANSCRIPTS



### 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 |

100 per page | How to query

### 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 | - |

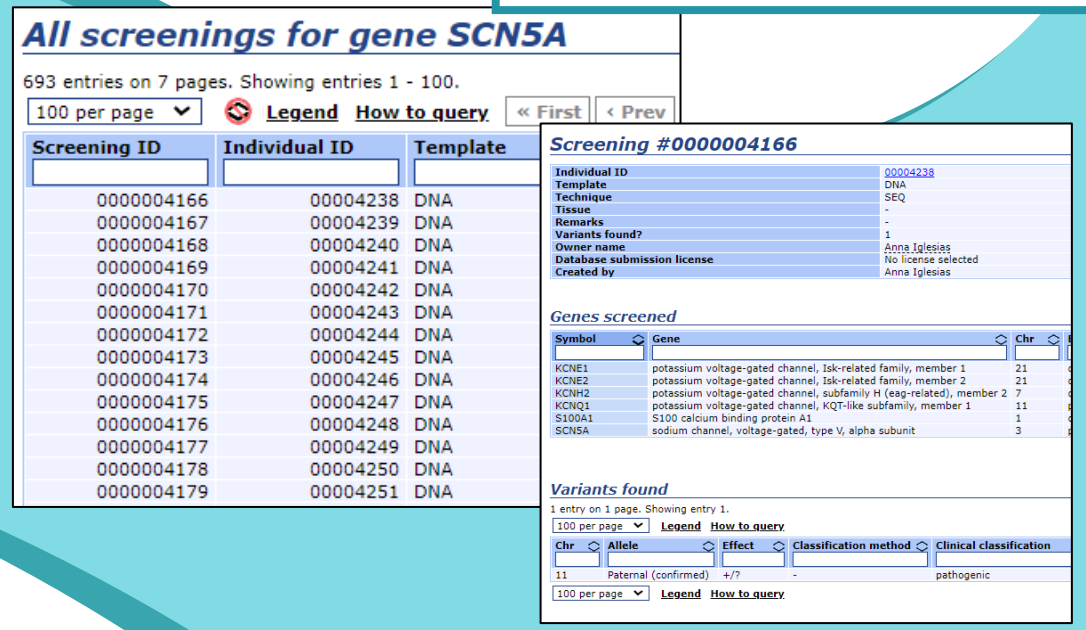
#### Variants

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) |
| -/. | - | c.5851G>Y | r.(?) | p.(Val1951Leu) |
| +/. | 8 | c.951G>Y | r.(?) | p.(Lys317Asn) |
| -/. | 1_28 | c.= | r.3229_3231del | p.Gln1077del |
| +/. | 2 | c.3G>A | r.(?) | p.(?) |
| ?/. | - | c.4G>A | r.(?) | p.(Ala2Thr) |
| ?/. | - | c.23G>A | r.(?) | p.(Arg8Gln) |

## SCREENINGS TO VARIANTS



### 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 |

100 per page | Legend | How to query

# EXTENSION SILE

## VARIANTS ON TRANSCRIPTS

### 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 |

100 per page | How to query

### 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*) | 17 |
| 6 | 0000164872 | 00018523 | c.4213G>Y | r.(?) | p.(Val1405Leu) | 23 |
| 7 | 0000165023 | 00018523 | c.5851G>Y | r.(?) | p.(Val1951Leu) | 28 |
| 8 | 0000470179 | 00018523 | c.5851G>Y | r.(?) | p.(Val1951Leu) | - |
| 9 | 0000164705 | 00018523 | c.951G>Y | r.(?) | p.(Lys317Asn) | 8 |
| 10 | 0000242392 | 00018523 | c.= | r.3229_3231del | p.Gln1077del | 1_28 |
| 11 | 0000164641 | 00018523 | c.3G>A | r.(?) | p.(?) | 2 |
| 12 | 0000519571 | 00018523 | c.4G>A | r.(?) | p.(Ala2Thr) | - |
| 13 | 0000519570 | 00018523 | c.23G>A | r.(?) | p.(Arg8Gln) | - |

## SCREENINGS TO VARIANTS

### 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

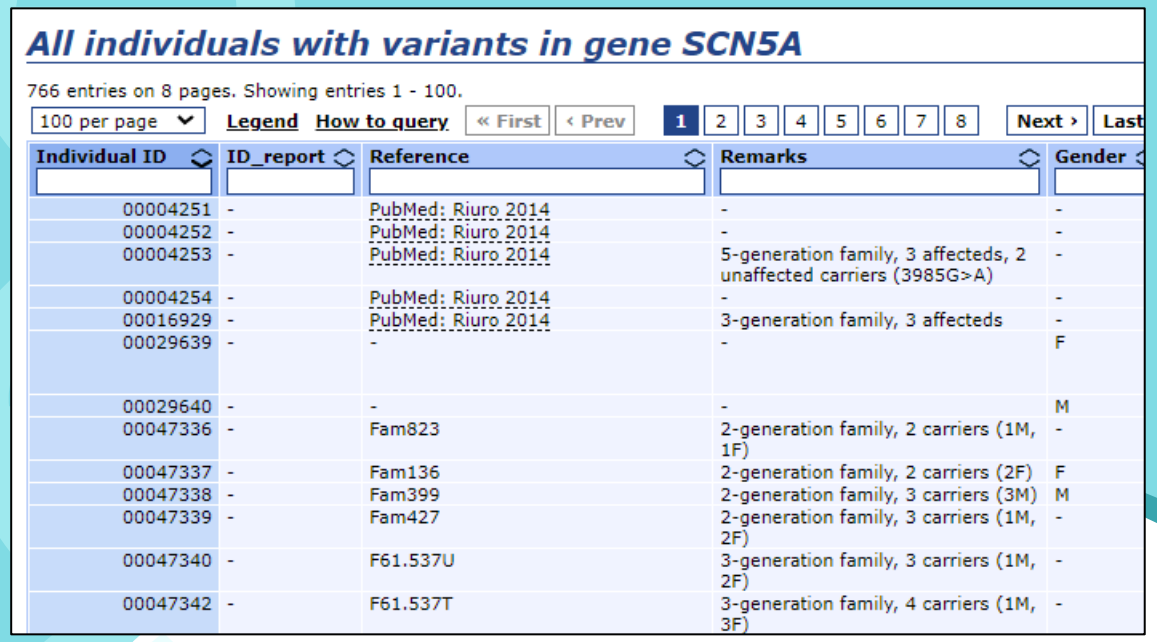
| Chr | Allele | Effect | Classification method | Clinical classification |
|---|---|---|---|---|
| 11 | Paternal (confirmed) | +/? | - | pathogenic |

100 per page | Legend | How to query

| | screeningid | variantid |
|---|---|---|
| 1 | 0000309522 | 0000684387 |
| 2 | 0000309541 | 0000684406 |
| 3 | 0000309542 | 0000684407 |
| 4 | 0000309542 | 0000684431 |
| 5 | 0000309807 | 0000684680 |
| 6 | 0000309807 | 0000684710 |
| 7 | 0000310440 | 0000685351 |
| 8 | 0000310441 | 0000685352 |
| 9 | 0000329184 | 0000713307 |

# EXTENSION SILE

## INDIVIDUALS TO DISEASES



*All individuals with variants in gene SCN5A*

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

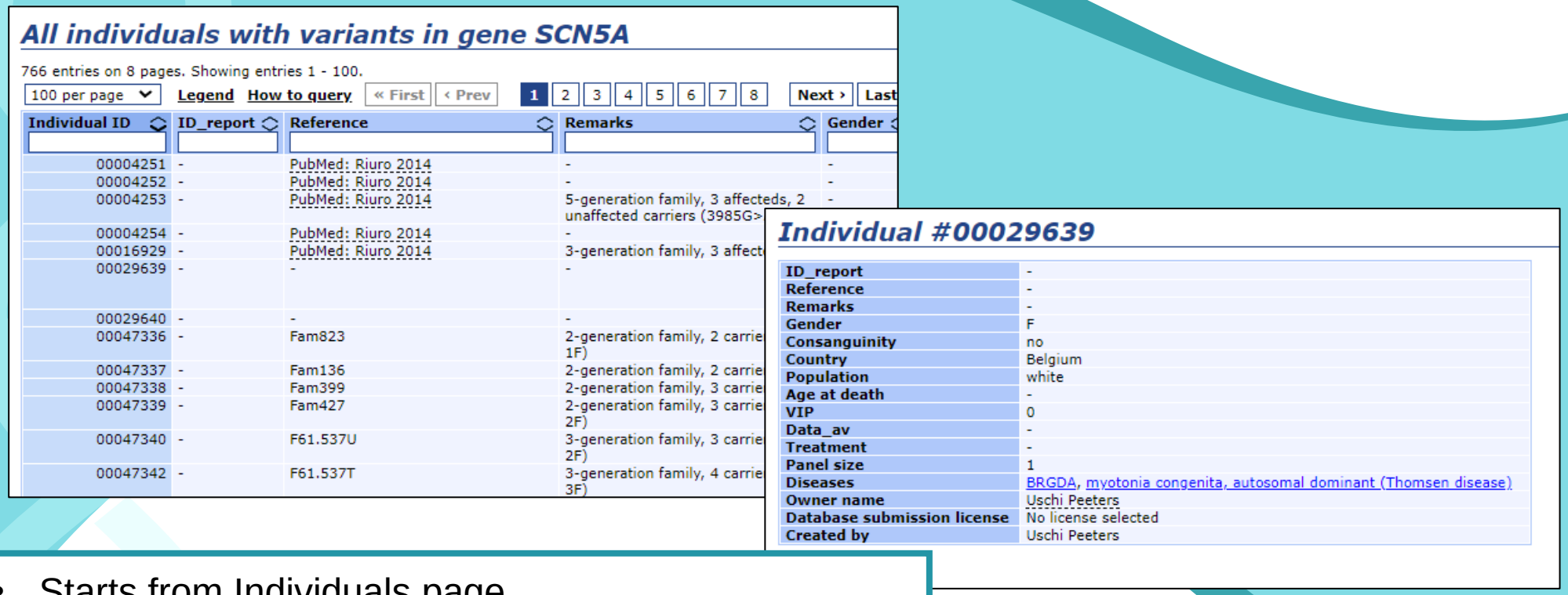
100 per page | Legend | How to query | « First | ‹ Prev | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | Next › | Last

| 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>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) | - |

- 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

# 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 dominant (Thomsen disease) |
| 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

# 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 |

| | 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 |

- 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

# EXTENSION SILE

**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 |

- 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

**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 | Inheritan |
|---|---|---|---|---|
| 0000034680 | asymptomatic Brugada syndrome | - | - | Familial |

- 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

## 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

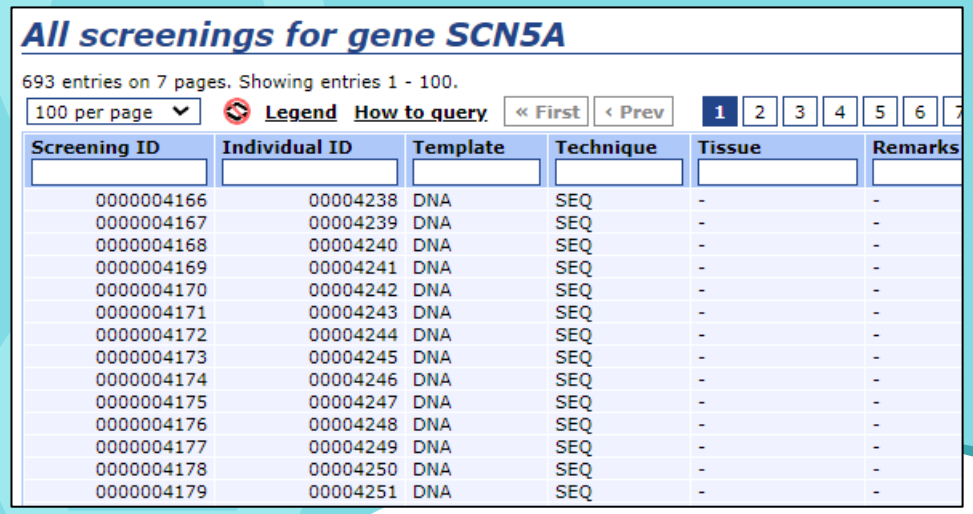
| Phenotype ID | Phenotype details | Diagnosis/Initial | Diagnosis/Definite | Inheritan |
|---|---|---|---|---|
| 0000034680 | asymptomatic Brugada syndrome | - | - | Familial |

| | id | diseaseid | individualid | Phenotype/Inheritance | Phenotype/Age | Phenotype/Additional | Phenotyp |
|---|---|---|---|---|---|---|---|
| 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.

100 per page | Legend | How to query | « First | ‹ Prev | 1 | 2 | 3 | 4 | 5 | 6 | 7

| 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 | - | - |

- 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

## SCREENINGS TO GENES

### All screenings for gene SCN5A

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

100 per page | Legend | How to query | « First | ‹ Prev | 1 | 2 | 3 | 4 | 5 | 6 | 7

| 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 | q22.1-q22.2 | |
| KCNE2 | potassium voltage-gated channel, Isk-related family, member 2 | 21 | q22.1 | |
| KCNH2 | potassium voltage-gated channel, subfamily H (eag-related), member 2 | 7 | q36.1 | |
| KCNQ1 | potassium voltage-gated channel, KQT-like subfamily, member 1 | 11 | p15.5 | |
| S100A1 | S100 calcium binding protein A1 | 1 | q21 | |
| SCN5A | sodium channel, voltage-gated, type V, alpha subunit | 3 | p21 | |

- 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

## SCREENINGS TO GENES

### All screenings for gene SCN5A

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

100 per page | Legend | How to query | « First | ‹ Prev | 1 | 2 | 3 | 4 | 5 | 6 | 7

| 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

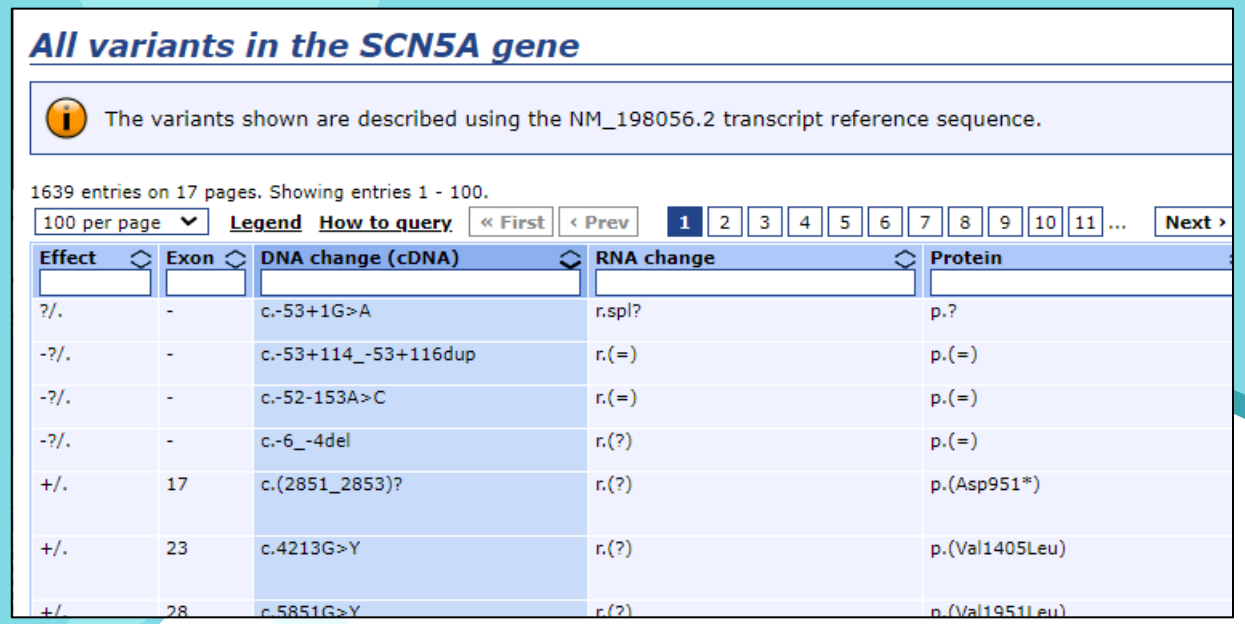
| Symbol | Gene | Chr | Band | Transc |
|---|---|---|---|---|
| KCNE1 | potassium voltage-gated channel, Isk-related family, member 1 | 21 | | |
| KCNE2 | potassium voltage-gated channel, Isk-related family, member 2 | 21 | | |
| KCNH2 | potassium voltage-gated channel, subfamily H (eag-related), member 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 | 11 | ... | Next ›

| 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) |

- 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 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) |

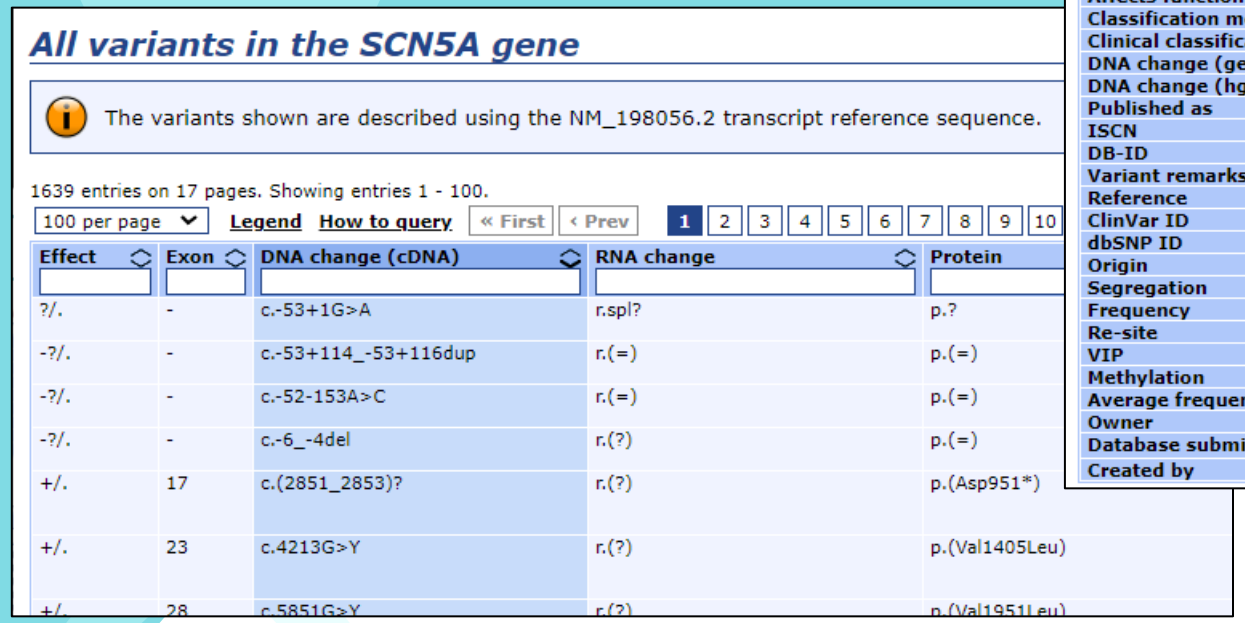
### *Variant #0000519573 (NC_000003.11:g.38691021C>T, SCN5A(NM_198056.2):c.-53+1G>A)*

| | |
|---|---|
| **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 v.2.1.1)** | Variant not found in online data sets |
| **Owner** | VKGL-NL_Nijmegen |
| **Database submission license** | (cc) BY-NC-SA |
| **Created by** | VKGL-NL_Nijmegen |

- 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 SILE

## VARIANTS ON GENOME



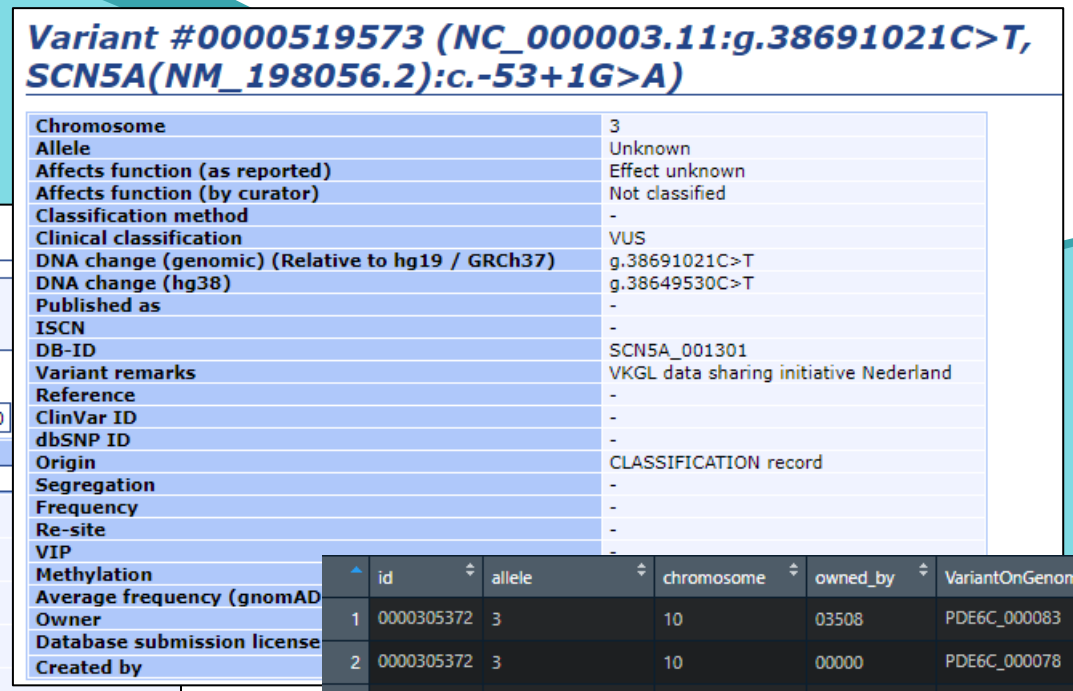
### All variants in the SCN5A gene

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 SILE

## 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 | Associ |
|---|---|---|---|---|---|---|---|---|
| 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 | - |
| 03264 | BRGDA6 | Brugada syndrome, type 6 (BRGDA-6) | 613119 | - | 0 | 0 | KCNE3 | - |
| 03265 | BRGDA7 | Brugada syndrome, type 7 (BRGDA-7) | 613120 | AD | 0 | 0 | SCN3B | - |
| 03267 | BRGDA8 | Brugada syndrome, type 8 (BRGDA-8) | 613123 | - | 0 | 0 | HCN4 | - |
| 04540 | BRGDA9 | Brugada syndrome, type 9 (BRGDA-9) | 616399 | AD | 0 | 0 | KCND3 | - |

100 per page | Legend | How to query

- Starts from the Disease page related to the Disease choosen
- 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 SILE

## 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 | Associ |
|---|---|---|---|---|---|---|---|---|
| 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: Allegue 2015, Journal: Allegue 2015 | - | F | - | Belgium |
| 00028977 | - | PubMed: Allegue 2015, Journal: Allegue 2015 | - | M | - | United States |
| 00028978 | - | PubMed: Allegue 2015, Journal: Allegue 2015 | - | M | - | United States |
| 00028979 | - | PubMed: Allegue 2015, Journal: Allegue 2015 | - | | | |
| 00028980 | - | PubMed: Allegue 2015, Journal: | | | | |

- Starts from the Disease page related to the Disease choosen
- 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 SILE

# 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 | Associ |
|---|---|---|---|---|---|---|---|---|
| 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: Allegue 2015, Journal: Allegue 2015 | - | F | - | Belgium |
| 00028977 | - | PubMed: Allegue 2015, Journal: Allegue 2015 | - | M | - | United States |
| 00028978 | - | PubMed: Allegue 2015, Journal: Allegue 2015 | - | M | - | United States |
| 00028979 | - | PubMed: Allegue 2015, Journal: Allegue 2015 | - | | | |
| 00028980 | - | PubMed: Allegue 2015, Journal: | | | | |

## 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) (h |
|---|---|---|---|---|---|
| 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 choosen
- 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 SILE

## 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 |

## OTHER GENES

- 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

# EXTENSION SILE

## 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 | - |
| 00028989 | - | PubMed: Allegue 2015, Journal: Allegue 2015 | - |
| 00028997 | - | PubMed: Allegue 2015, Journal: Allegue 2015 | - |
| 00064708 | - | - | - |
| 00143766 | - | - | - |
| 00143767 | - | - | - |
| 00180902 | 8 | - | - |

## OTHER GENES

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# EXTENSION SILE

## 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) (hg |
|---|---|---|---|---|---|
| 11 | Unknown | ?/. | - | VUS | g.123504959C>G |
| 11 | Unknown | ?/. | - | VUS | g.123524411G>A |
| 19 | Unknown | ?/. | - | VUS | g.35521779G>T |
| 19 | Unknown | ?/. | - | VUS | g.35524824T>C |

## OTHER GENES

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- Merges Individuals and Variants tables
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# EXTENSION SILE

## 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) (hg |
|---|---|---|---|---|---|
| 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 |

- 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
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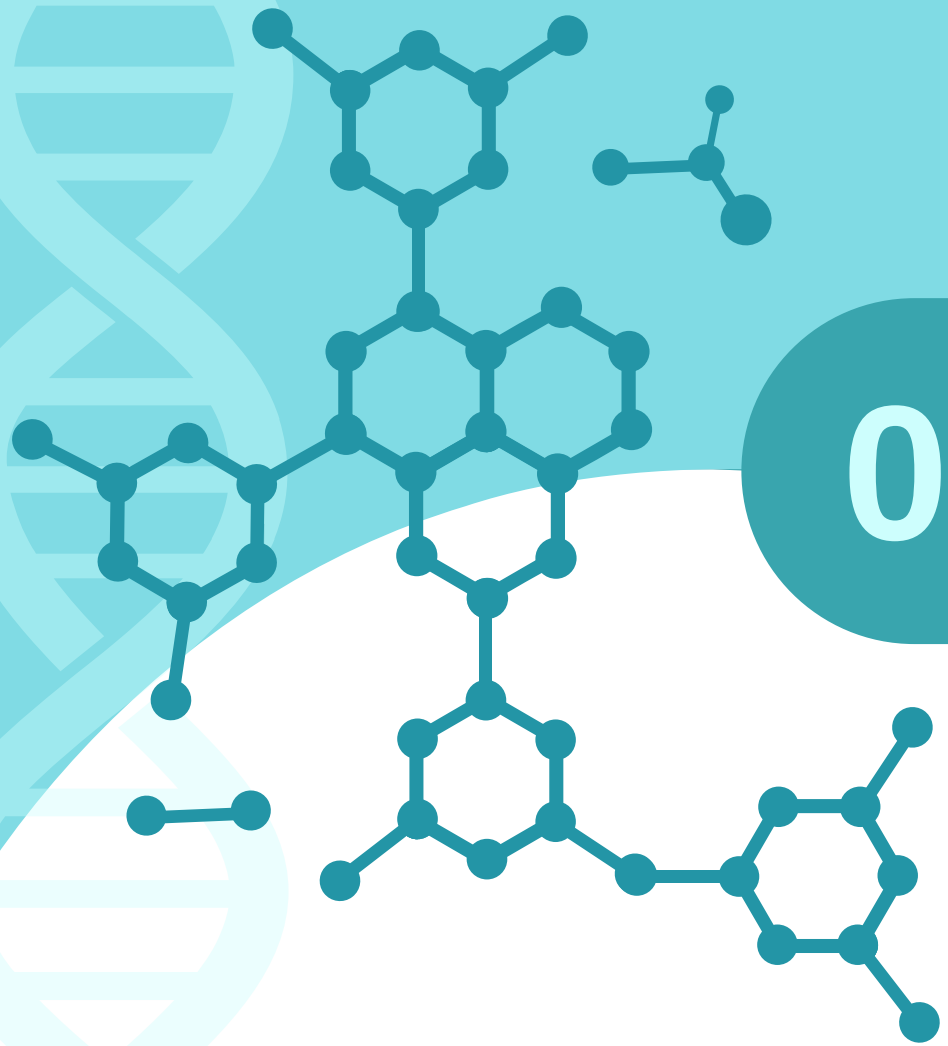
- Merges Individuals and Variants tables
- Filter the obtained table by the column ‘‘Disease’’ by taking only the related ones

## OTHER GENES

BRGDA

BRGDA

SUD
BRGDA
BRGDA
SUD



# 03 Validation of the Solutions

# BRGDA & BRGDA1

**BRGDA**:

From 120 individuals, 420 variations data

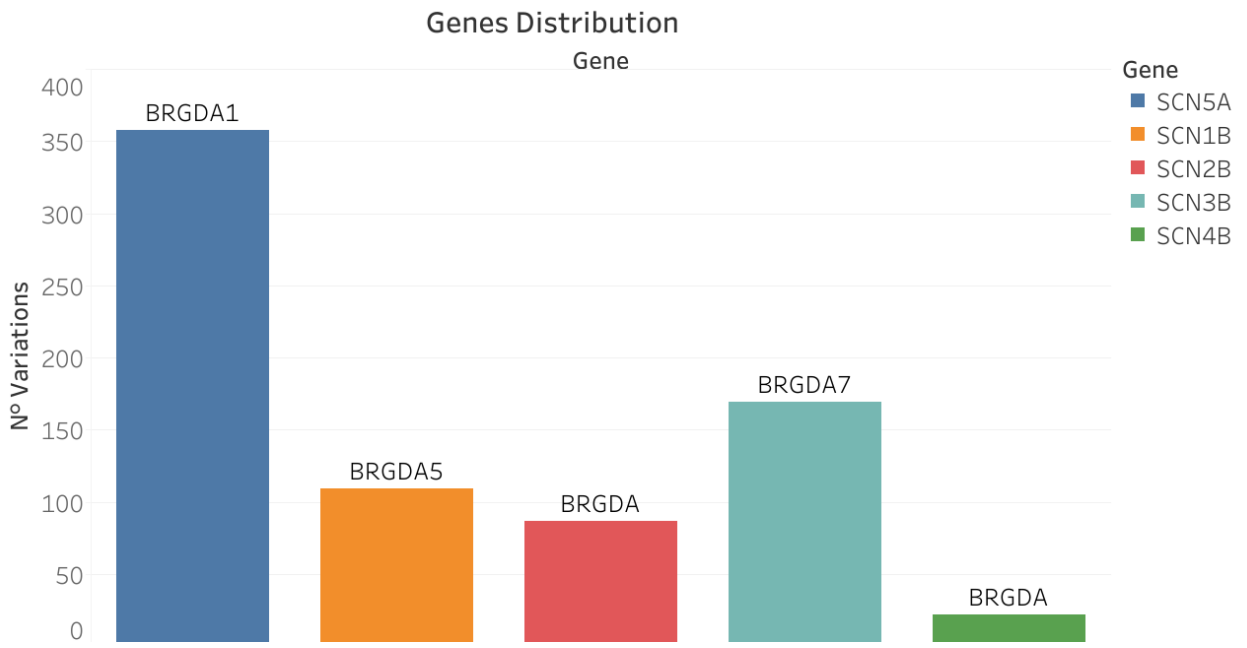
Study of *Peeters* on 74 unrelated individuals

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

**BRGDA 1**:

From 364 individuals, 366 variations data

## Genes Distribution



# BRGDA & BRGDA1

**BRGDA**:

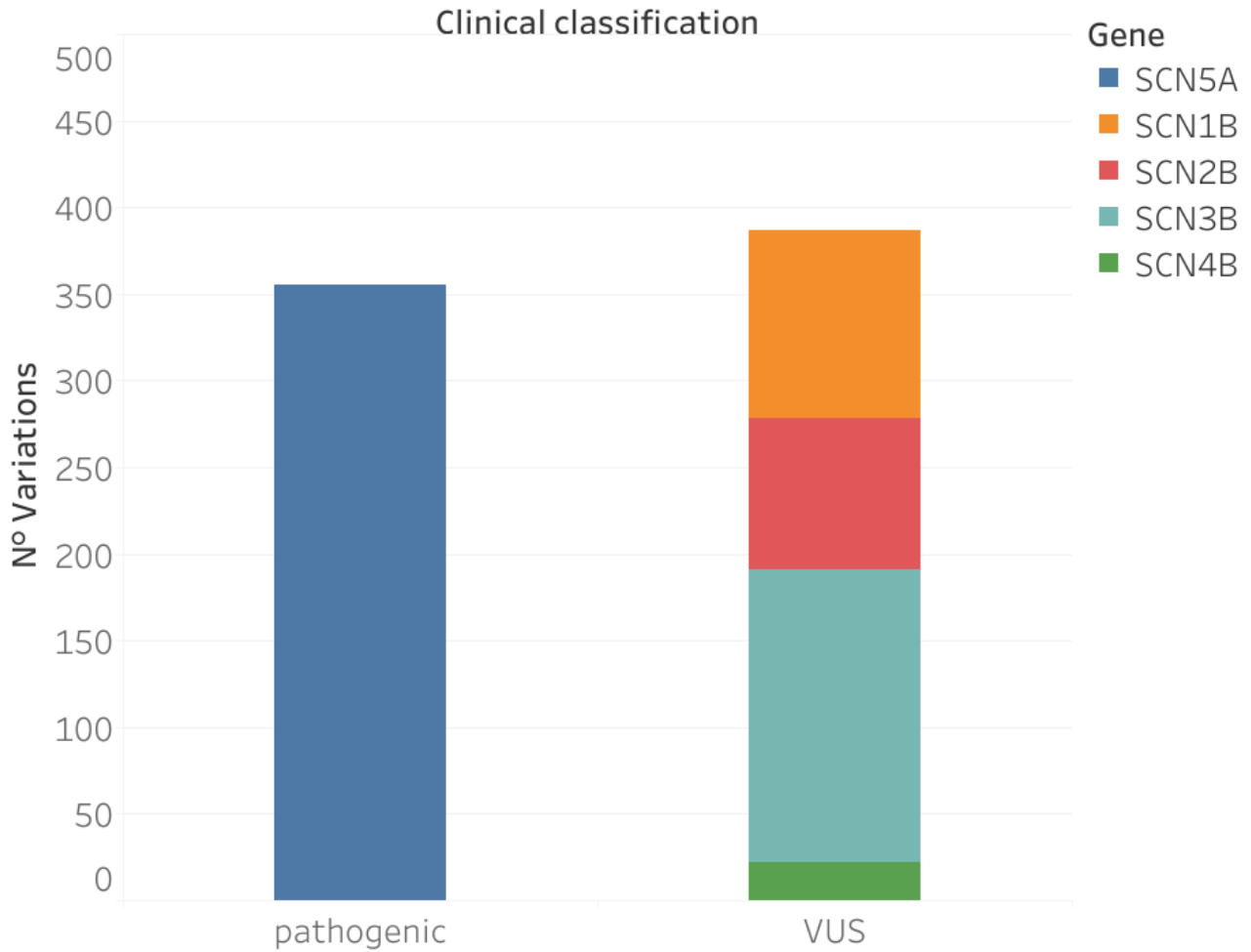
Totality of observations classified as "**VUS**"

(Variant of Uncertain Significance)

**BRGDA 1**:

Totality of observations classified as "**pathogenic**"

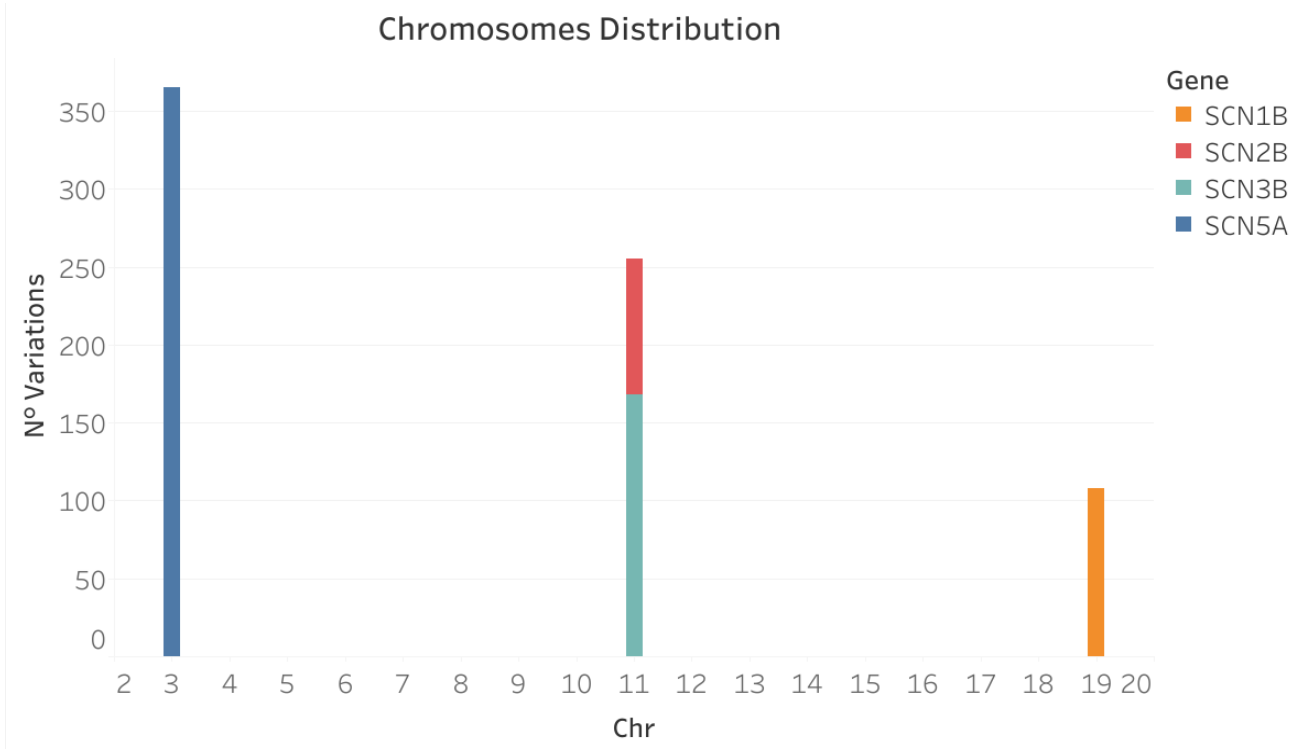
## Clinical Classification



# 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



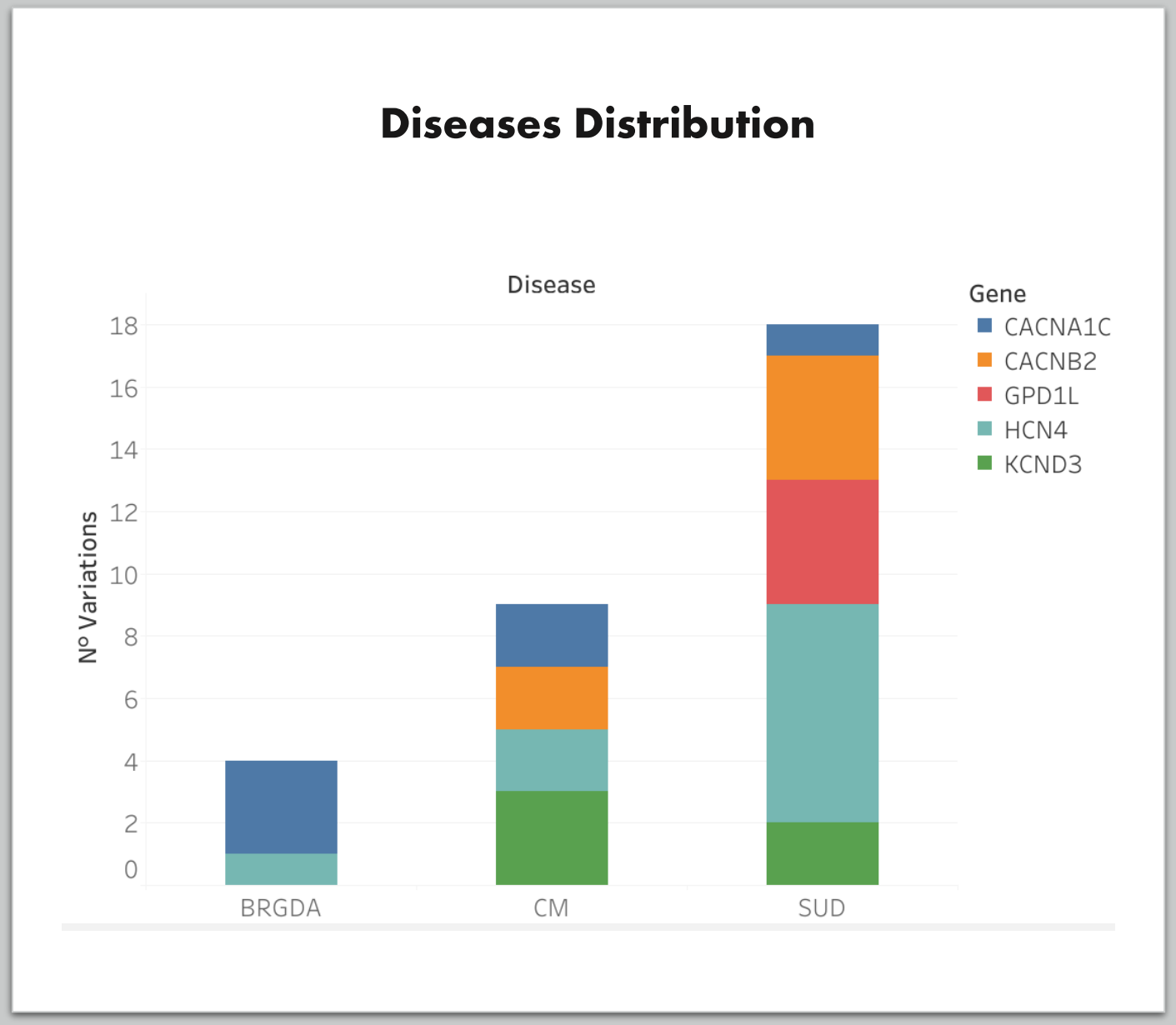
# OTHER GENES

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



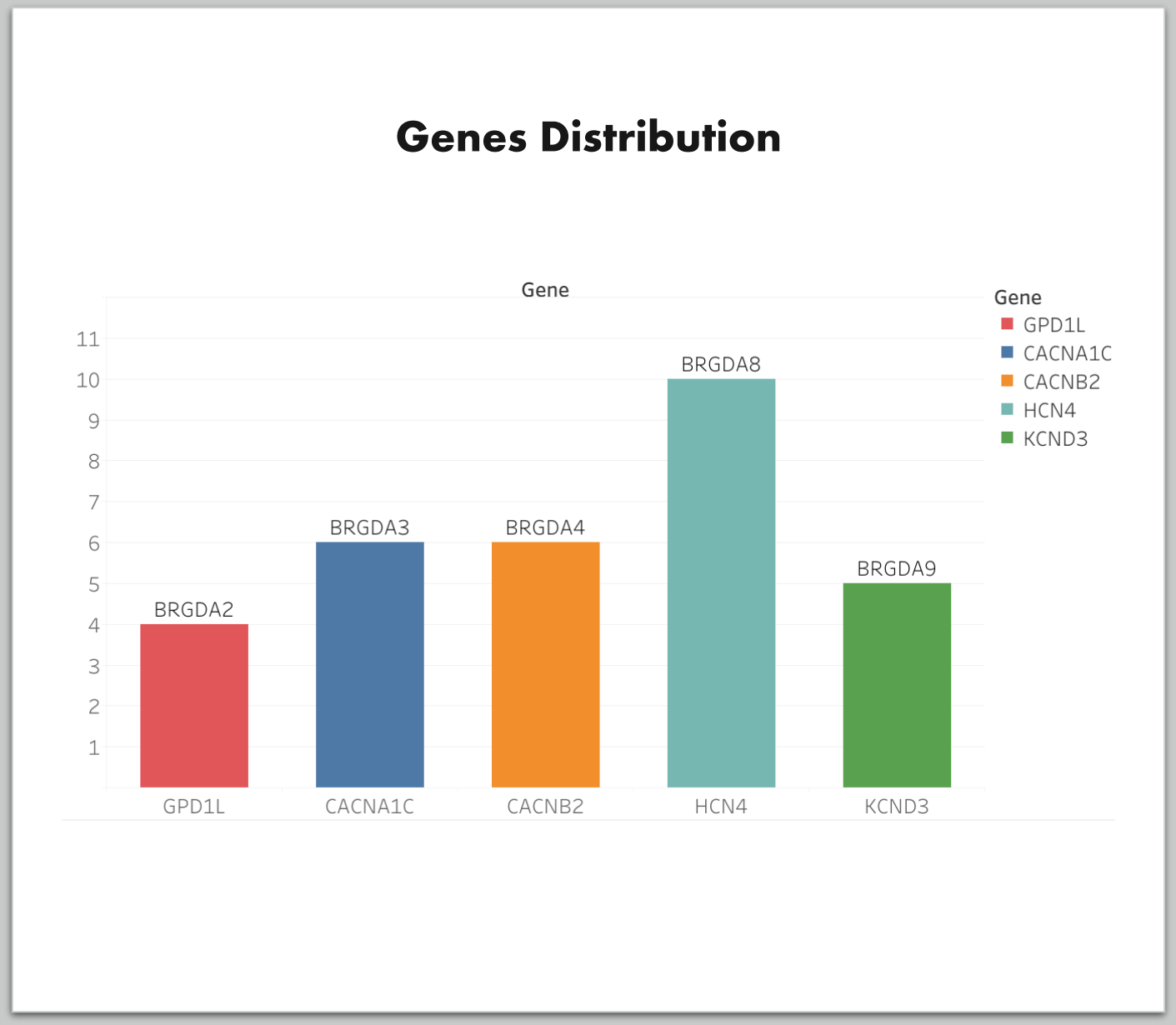
# OTHER GENES

**Variations** in:

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

Typically **associated** with:

BRGDA2
BRGDA3
BRGDA4
BRGDA8
BRGDA9

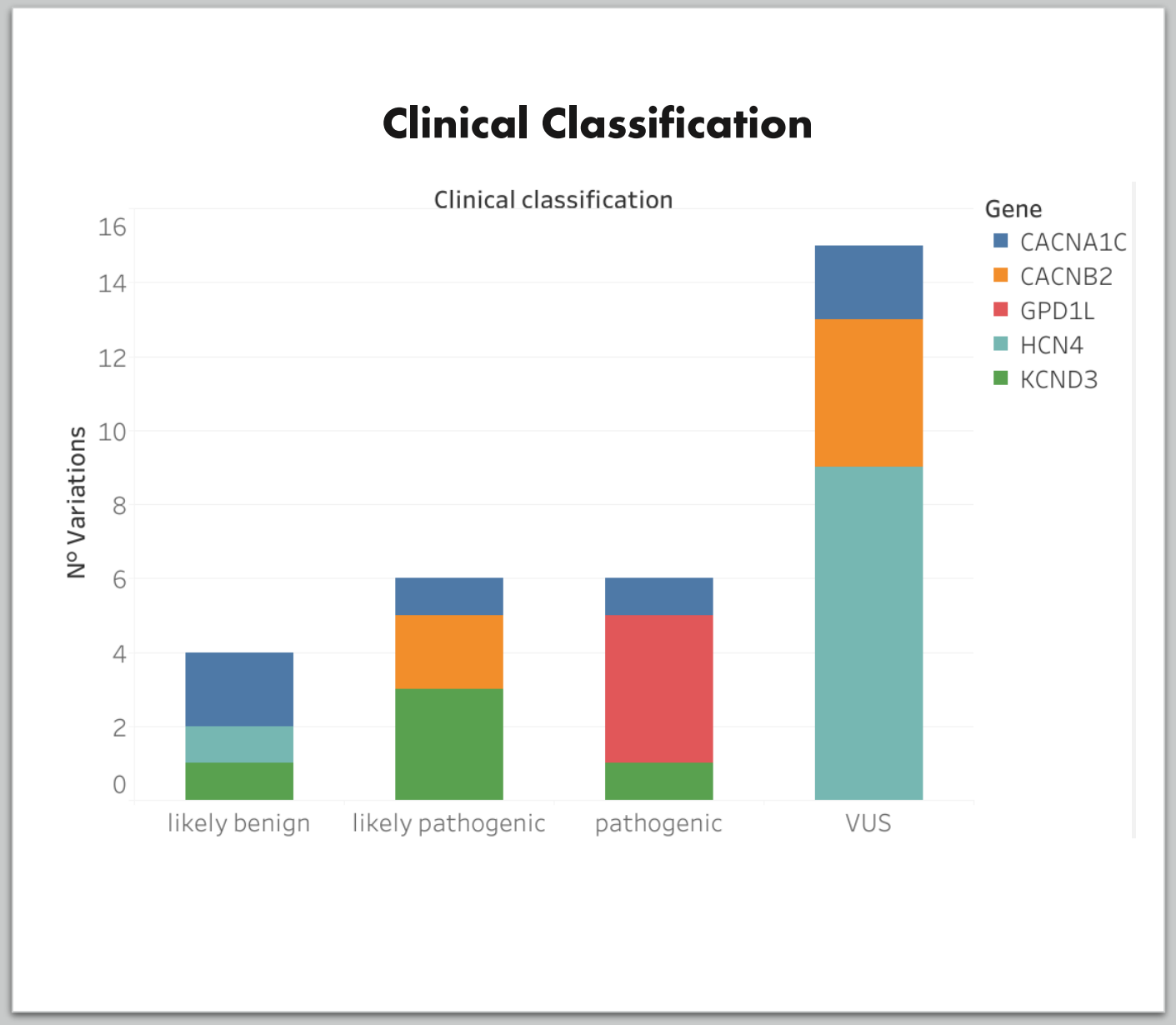


# OTHER GENES

**15** variations labeled as “VUS”

**GPD1L** labeled as “pathogenic” in all observations

**KCND3** in the majority “likely pathogenic”



# OTHER GENES

**GPD1L**, mutation in **chromosome 3** (Brs2)

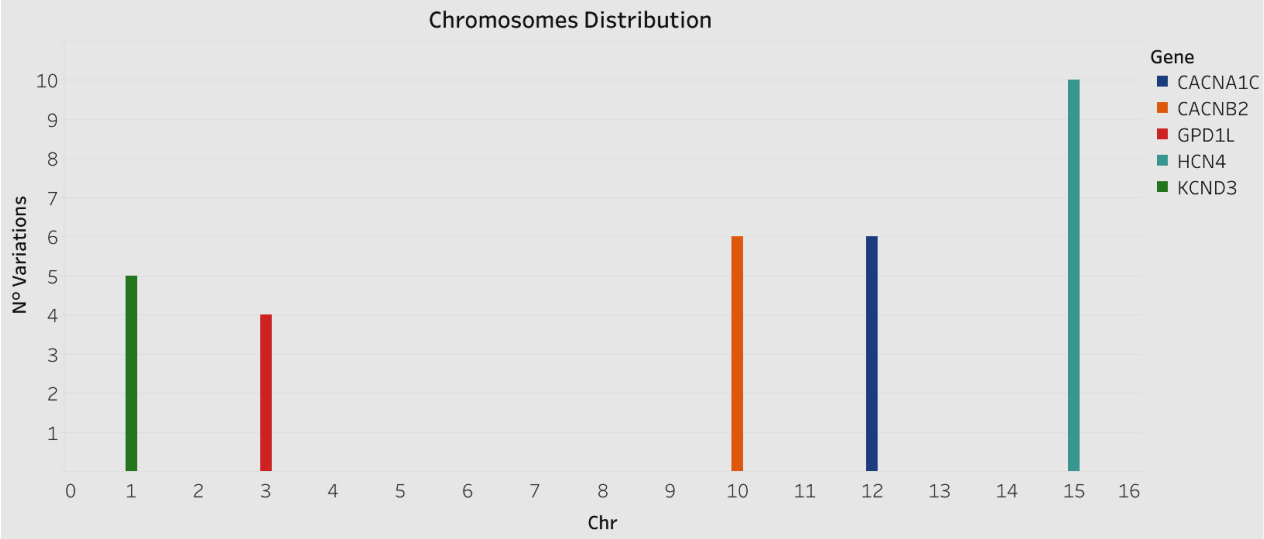
**CACNA1C**, mutation in **chromosome 12** (BrS3)

**CACNB2**, mutation in **chromosome 1** (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 U (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

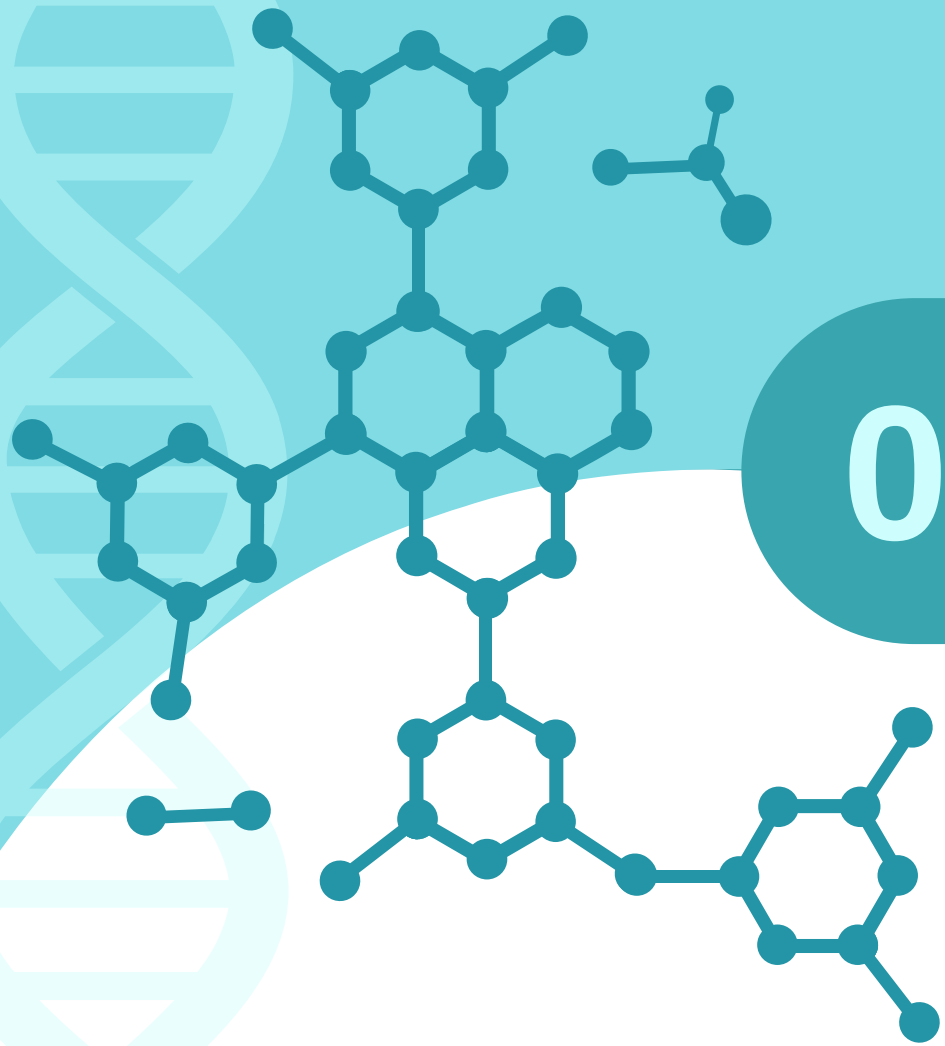
**Screenings** page, even in normal navigation, takes more time than others to load

**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** Syndome

# 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 keeped 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**