(((SCN1A) OR (SCN2A) OR (SCN3A) OR (SCN4A) OR (SCN5A) OR (SCN8A) OR (SCN9A) OR (SCN10A) OR (SCN11A)) AND ((gain-of-function) OR (loss-of-function)) OR ((GOF) OR (LOF)) AND ((electrophysiology) OR (patch clamp) OR (voltage clamp))) AND (("2021/04/28"[Date - Publication] : "2022/07/13"[Date - Publication]))

\*i.e. indexed in PubMed at this date

Start date: 28 April 2021

55 results, acc. 13/JUL/2022 2.17pm

Incl. criteria: Missense variant in Nav with experimental evidence of functional effect and clear net LOF or GOF

Removed variants from analysis that were present in the training data set.

15 studies

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Gene | Variant | Effect | Reference | Key phenotype | Brunklaus rule (SCN Viewer) | Pred fuNCion | Pred SCION-MTL | Phenotype terms for SCION-MTMKL | Pred SCION-MTMKL | Winner |
| *SCN2A* | Q1531K | GOF | 35637276 | See Table | NA | LOF 0.71 | GOF 0.81 | ORPHA:306 | GOF 0.52 | SCION |
| *SCN2A* | L1563V | GOF | 35637276 | See Table | NA | LOF 0.76 | GOF 0.76 | ORPHA:306 | GOF 0.48 | SCION |
| *SCN2A* | E1321K | GOF | 35637276 | See Table | NA | GOF 0.82 | GOF 0.59 | ORPHA:306 | GOF 0.48 |  |
| *SCN2A* | V1325I | GOF | 35637276 | See Table | NA | GOF 0.90 | GOF 0.63 | ORPHA:306, HP:0200134 | GOF 0.46 |  |
| *SCN2A* | D195G | LOF | 35637276 | See Table | NA | LOF 0.73 | LOF 0.55 | OMIM:619373 | LOF 0.86 |  |
| *SCN2A* | R853Q | LOF | 35637276 | See Table | NA | LOF 0.84 | LOF 0.64 | OMIM:619373  ORPHA:2382 | LOF 0.89 |  |
| *SCN5A* | V281A | LOF | 34628415 | BrS | NA | LOF 0.60 | LOF 0.85 | ORPHA:130 | LOF 0.89 |  |
| *SCN5A* | L1582P | LOF | 34628415 | BrS | NA | LOF 0.81 | LOF 0.69 | ORPHA:130 | LOF 0.79 |  |
| *SCN5A* | F543L | LOF | 34628415 | BrS | NA | GOF 0.52 | GOF 0.53 | ORPHA:130 | LOF 0.73 | SCION |
| *SCN5A* | K1419E | LOF | 34628415 | BrS | NA | LOF 0.60 | LOF 0.88 | ORPHA:130 | LOF 0.87 |  |
| *SCN5A* | L1412F | LOF | 34649698 | ERS | NA | LOF 0.66 | LOF 0.80 | HP:0031546 | LOF 0.66 |  |
| *SCN5A* | G452C | LOF | 34649698 | ERS | NA | LOF 0.68 | LOF 0.75 | HP:0031546 | LOF 0.62 |  |
| *SCN1A* | A1783V | LOF | 34776868 | DS | SCN9A p.A1746G: GOF  SCN2A p.A1773T: LOF | GOF 0.69 | LOF 0.83 | ORPHA:33069 | LOF 0.88 | SCION |
| *SCN5A* | R893C | LOF | 35305865 | BrS | **SCN1A p.R946C: LOF**  SCN1A p.R946H: LOF  **SCN2A p.R937C: LOF**  SCN2A p.R937H: LOF | LOF 0.75 | LOF 0.81 | ORPHA:130 | LOF 0.87 |  |
| *SCN5A* | L846R | LOF | 35305865 | BrS | NA | GOF 0.51 | LOF 0.73 | ORPHA:130 | LOF 0.78 | SCION |
| *SCN5A* | G897E | LOF | 35305865 | BrS | NA | LOF 0.65 | LOF 0.90 | ORPHA:130 | LOF 0.83 |  |
| *SCN5A* | R878H | LOF | 35305865 | BrS | NA | LOF 0.78 | LOF 0.90 | ORPHA:130 | LOF 0.86 |  |
| *SCN5A* | G1743E | LOF | 35305865 | BrS | SCN5A p.G1743R: LOF | LOF 0.79 | LOF 0.87 | ORPHA:130 | LOF 0.81 |  |
| *SCN4A* | R1463H | GOF | 33670307 | PMC | NA | GOF 0.73 | GOF 0.56 | OMIM:168300 | LOF 0.60 | (!) |
| *SCN5A* | G1481V | GOF | 33778442 | LQT3 | SCN4A p.G1306E: GOF  SCN8A p.G1745R: GOF | GOF 0.79 | LOF 0.71 | OMIM:603830 | GOF 0.80 |  |
| *SCN5A* | Q1491H | GOF | 33778442 | LQT3 | NA | GOF 0.66 | LOF 0.70 | OMIM:603830 | GOF 0.82 |  |
| *SCN5A* | V1667D | LOF | 33946750 | BrS | NA | GOF 0.53 | LOF 0.55 | ORPHA:130 | LOF 0.72 | SCION |
| *SCN2A* | V911A | GOF | 34093402 | ESES, DEE | NA | LOF 0.60 | GOF 0.65 | HP:0031491, HP:0200134 | GOF 0.55 | SCION |
| *SCN2A* | K1933M | GOF | 34093402 | ESES, DEE | NA | LOF 0.60 | GOF 0.79 | HP:0031491, HP:0200134 | GOF 0.52 | SCION |
| *SCN2A* | S863F | LOF | 34093402 | BFIS, ESES | NA | LOF 0.59 | LOF 0.74 | HP:0031491, ORPHA:306 | LOF 0.84 |  |
| *SCN5A* | R104W | LOF | 34122134 | BrS | SCN4A p.R104H: LOF  SCN5A p.R104Q: LOF | LOF 0.82 | LOF 0.83 | ORPHA:130 | LOF 0.89 |  |
| *SCN5A* | P1310L | LOF | 34204499 | BrS | NA | GOF 0.86 | LOF 0.83 | ORPHA:130 | LOF 0.86 | SCION |
| *SCN9A* | E44Q | GOF | 34222704 | Paroxysmal pain | NA | LOF 0.67 | GOF 0.78 | HP:0012531 | GOF 0.81 | SCION |
| *SCN2A* | R853Q | LOF | 34287911 | DEE | SCN4A p.R672G: LOF  SCN4A p.R672H: LOF  SCN5A p.R811H: LOF | LOF 0.79 | LOF 0.61 | HP:0200134 | LOF 0.71 |  |
| *SCN5A* | G1712S | LOF | 34348284 | BrS | **SCN10A p.G1662S: GOF** | LOF 0.72 | LOF 0.88 | ORPHA:130 | LOF 0.84 |  |