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## Supplemental Information

# Identification of Mutations in *SLC24A4*, Encoding a Potassium-Dependent Sodium/Calcium Exchanger, as a Cause of Amelogenesis Imperfecta

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### Supplemental Inventory

### Supplemental Figures and Tables

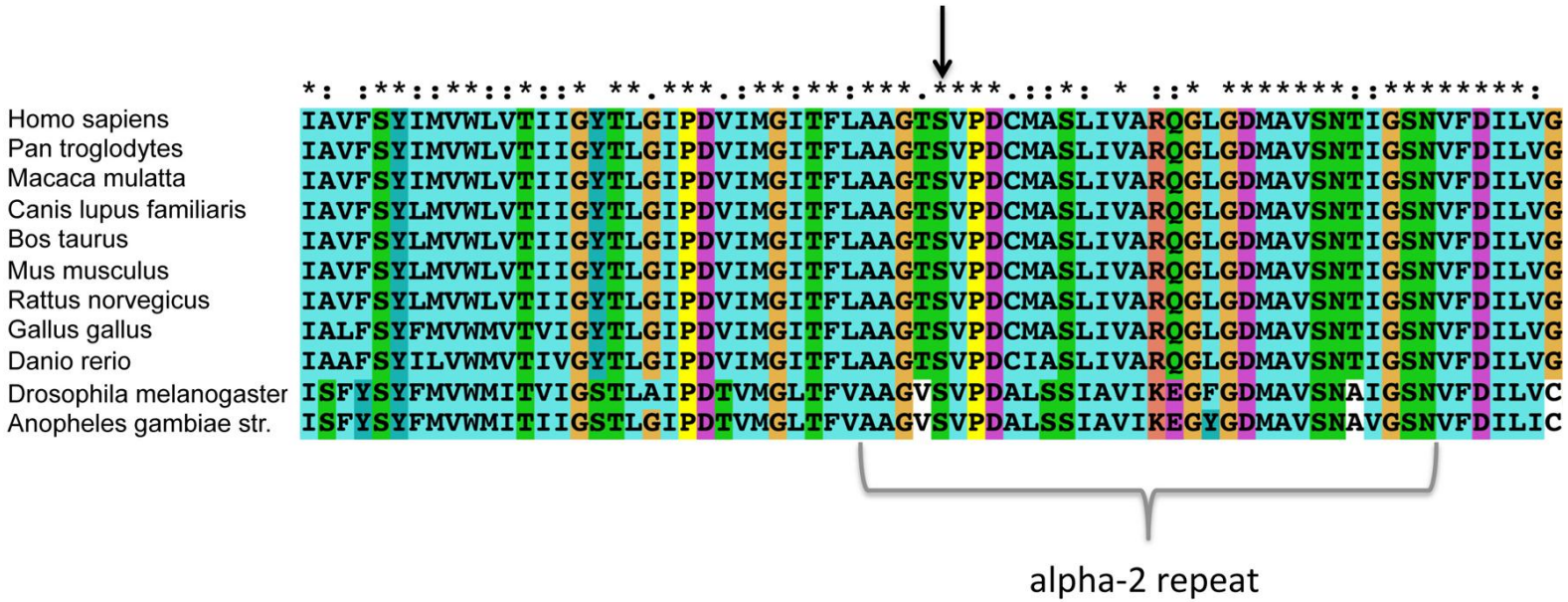


**Figure S1. ClustalX Alignment of SLC24A4 Orthologs**

The serine residue mutated in AI-131 is marked with an arrow. The conserved alpha-2 repeat is marked with a bracket. The following RefSeq protein sequences were used: NP_705932.2, XP_522932.2, XP_001093162.2, XP_849226.1, NP_001180017.1, NP_742164.1, NP_001101521.1, XP_001235438.1, NP_001017770.1, NP_649459.3 and XP_313818.3.

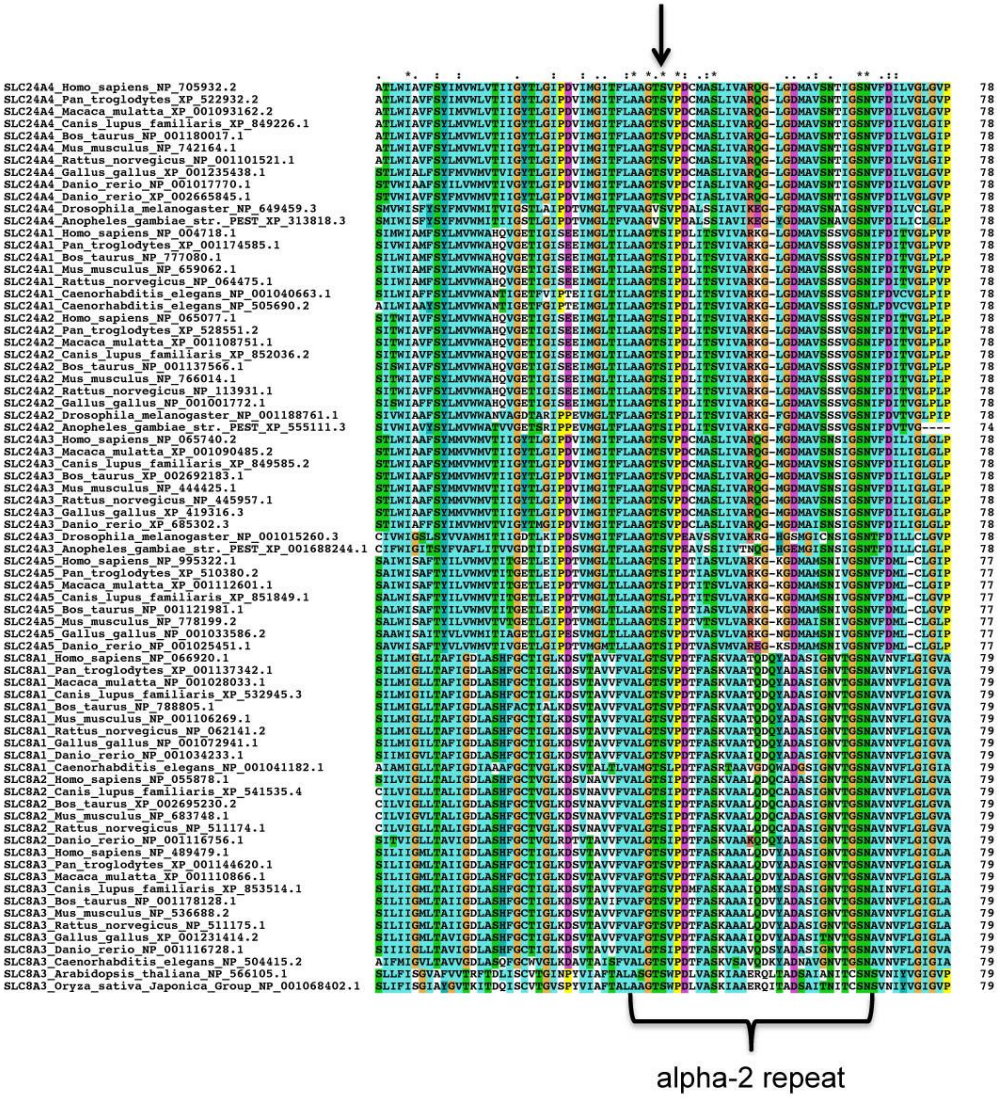


**Figure S2. ClustalX Alignment of Vertebrate Sodium/Calcium Exchangers**

Full-length members of the SLC24 and SLC8 solute carrier families were identified using homologene (www.ncbi.nlm.nih.gov/homologene/). SLC24A6 family members were not included in this alignment due to evidence that these proteins comprise a divergent branch of the calcium/cation antiporter gene superfamily[28,29]. Each sequence is labelled with the corresponding symbol for the Human ortholog, the species and the RefSeq protein identifier. The serine residue of SLC24A4 mutated in AI-131 (Ser499) is marked with an arrow and the alpha-2 repeat marked with a bracket.

| Region | Length (Mb) | RefSeq Coding Exons in Region | Variants Passing Filters | …and not in dbSNP129 or MAF < 1% | …or 10 Ethnically Matched In-House Exomes | …and Functional |
|---|---|---|---|---|---|---|
| chr6:163023850-168394923 (rs7756486;rs3752611) | 5.37 | 187 (28 Kb) | 296 | 39 | 26 | 0 |
| chr14:90556897-96655642 (rs12880982;rs12436690) | 6.10 | 544 (100 Kb) | 535 | 65 | 49 | 2 |
| chr16:71591014-73454749 (rs7200212;rs12447968) | 1.86 | 179 (41 Kb) | 141 | 15 | 6 | 0 |
| chr17:55361975-57267940 (rs2531899;rs12602103) | 1.90 | 268 (45 Kb) | 161 | 21 | 18 | 1 |
| chr17:59852249-60558723 (rs4078306;rs414341) | 0.71 | 116 (19 Kb) | 30 | 4 | 3 | 0 |
| **Total** | 15.95 | 1294 (232 Kb) | 1163 | 144 | 102 | 3 |

**Table S1. Summary of Variants AI-112 Candidate Disease Regions and Variants Discovered by Exome Sequencing**

The total variants identified in each region are shown. "Functional" variants are defined as coding non-synonymous variants, exonic insertions or deletions, or variants at splice consensus sites.

| Exon | Forward | Reverse |
|---|---|---|
| 3 | ctcggccactgattgcac | aaggaggggaaaacatctcg |
| 4 | cagggctgttgctgacatag | tggctgtaaccacccacata |
| 5 | gaactctcagaagtcaagtgaggt | agatctcagacacgccacg |
| 6 | ctggtttggggtgtggtg | ctcggtgtgacagtctttgc |
| 7 | ttggctgtagagcgtccagt | tgaggctcagagctgacaaa |
| 8 | aaaggggacactgaggaag | gctaccccaacctcttgtca |
| 9 | gtggcctggagttaggaggt | agtgccaggggcagagat |
| 10 | gagcagctcagaaatggacc | aacgattcagggaacccaac |
| 11 | cacttctggacccctcattc | ttctccctgctgtcacaaaa |
| 12 | agggatggggtgtgatcc | tctcttagggcacctgtggt |
| 13 | tcacaaggtgaggggaagtc | atcaatggcaccaggaagag |
| 14 | tccccagggttgttgttcta | acagattcgcctcctaagca |
| 15 | ctagagtcacatcggtggca | gtggttagccttgaacccag |
| 16 | tgtttcctacgcttacagtgtctc | aagtcaggcagggacgag |
| 17 | ttccaaggaatggcactgat | tagagcctctggctggaact |
| 18 | gctgggatttctggatgga | gtaagtgacgaggcggaatc |
| 19 | tgaggatcagactgcagcac | gcctatgcaggagagacctg |

**Table S2. SLC24A4 Primer Pairs**

Primer sequences used to amplify and sequence coding exons of *SLC24A4* (RefSeq transcripts NM_153646.3, NM_153647.3 and NM_153648.3).