Supplementary Material

# Supplementary Figures and Tables

## Supplementary Figures

# Mapa Descripción generada automáticamente

**Supplementary Figure 1:** Global distribution of AI cases. In the red circle, the countries with the highest frequency of described cases are highlighted; in the following order: Turkey (56), United States (30), France (24), Pakistan (19), Korea (16), China (15) and United Kingdom (14). The blue circles represent the rest of the countries in the world where AI cases have been found with a range of 1 to 9. (https://www.mapamundiparaimprimir.com/wp-content/uploads/2018/07/mapa-mundi-politico-con-nombres.jpg)

## Supplementary Tables

**Supplementary Table 1:** Genes that participate in isolated and syndromic AI, inheritance patterns and associated type and subtype of AI.

|  |  |  |
| --- | --- | --- |
| **GENE NAME** | **INHERITANCE** | **TYPE/SUBTYPE OF AI** |
| ***ACP4***, Acid Phosphatase 4 | AR | Hypoplastic AI |
| *AMBN*, Ameloblastin | AR/AD | Hypoplastic AI |
| *AMELX*, Amelogenin | X-LD | Hypoplastic/hypomaturation AI |
| ***AMTN****,* Amelotin | AD | Hypomineralized AI |
| *COL17A1*,Type I collagen alpha 1 chain | AD | Hypoplastic AI Hypoplastic/hypomaturation AI |
| *ENAM*,Enamelin | AD/AR | Localized Hypoplastic AI  Generalized Hypoplastic AI |
| *FAM83H*, Family with sequence similarity 83, member H | AD | Hypocalcified AI |
| *GPR68*, G-protein coupled receptor | AR | Hypomaturation AI |
| *ITGB6*, Integrin beta 6 chain | AR | Hypoplastic AI |
| *KLK4*, Peptidase 4 related with Kallikrein | AR | Hypomaturation AI |
| *LAMA3*, Laminin alpha 3 chain | AD | Hypoplastic AI |
| *LAMB3*, Laminin beta 3 chain | AD | Hypoplastic AI |
| ***MMP20***, Metalloprotease 20 | AR | Hypomaturation AI  Hypoplastic/hypomaturation |
| ***ODAPH***, Odontogenesis Associated Phosphoprotein | AR | Hypomineralized AI  Hypomineralized/hypoplastic AI |
| ***RELT***, Receptor Expressed in Lymphoid Tissues | AR | Hypoplastic AI  Hypomineralized AI |
| ***SLC24A4***, Solute carrier family 24, member A4 | AR | Hypomaturation AI |
| ***SP6***, Factor de especificidad 6 | AD | Hypoplastic AI |
| **GENE /SYNDROME OR PATHOLOGY** | **INHERITANCE** | **TYPE/SUBTYPE OF AI** |
| *CLDN16*, Claudina 16  Familial hypomagnesemia with hypercalciuria and nephrocalcinosis | AR | Hypoplastic AI |
| *CLDN19,* Claudina 19  Familial hypomagnesemia with hypercalciuria and nephrocalcinosis | AR | Hypoplastic AI  Hypomaturation AI |
| *CNNM4*, Ancient conserved domain protein 4  Jalili Syndrome | AR | Hypoplastic AI  Hypomaturation AI  Hypomaturation/hypoplastic AI |
| *DLX3,* Distal Less 3  Tricho Dento Osseous Syndrome. | AD | Hypoplastic AI  Hypoplastic/hypomaturation AI |
| *FAM20A,* Family with sequence similarity 20, member A  Enamel renal gingival Syndrome | AR | Hypoplastic AI |
| *LTBP3*, Latent growth factor binding protein 3  AI with Brachyolmia | AR | Hypoplastic AI |
| *SLC10A7*, Solute transporter of family 10, member A7  AI with eskeletal dysplasia. | AR | Hypomineralized AI |
| *STIM1*, Stromal interaction molecule 1  Syndromic AI | AR | Hypomaturation AI |
| *TP63*, Tumoral protein 63  Ectodermal dysplasia | AD | Hypoplastic/hypomaturation AI |
| *WDR72*, Protein 72 with repeats WD  AI with Distal renal tubular acidosis (dRTA). | AR | Hypomaturation AI  Hypoplastic/hypomineralized AI |

**Supplementary Table 2:** Countries with the highest number and percentage of mutations in the five continents.

|  |  |  |
| --- | --- | --- |
| **COUNTRY** | **Nº MUTATIONS** | **%** |
| Turkey | 56 | 18,4 |
| Estados Unidos | 30 | 9,9 |
| France | 24 | 7,9 |
| Pakistan | 19 | 6,3 |
| Korea | 16 | 5,3 |
| China | 15 | 4,9 |
| United Kingdom | 14 | 4,6 |
| Thailand | 9 | 3,0 |
| Costa Rica | 6 | 2 |
| Brazil | 6 | 2 |
| Morocco | 3 | 1 |
| Australia | 2 | 0,66 |
| **TOTAL** | **200** | **65,9** |

**Supplementary Table 3:** Number and percentage of mutations by continent.

|  |  |  |
| --- | --- | --- |
| **CONTINENT** | **Nº MUTATIONS** | **%** |
| ASIA | 153 | 50,3 |
| EUROPE | 61 | 20,1 |
| NORTH AMERICA | 31 | 10,2 |
| CENTRAL AMERICA | 11 | 3,6 |
| SOUTH AMERICA | 8 | 2,6 |
| AFRICA\* | 9 | 3,0 |
| OCEANIA | 2 | 0,7 |
| N. D.\*\* | 29 | 9,5 |
| **TOTAL** | **304** | **100,0** |

\* Una ethnicity is african.

\*\* To 29 ethnicities, marked as N. D., no continent could be assigned to them.

**Supplementary Table 4:** Summary that relates the categorization of the AI genes with their specificity. Genes marked in bold and blue color show association with cancer.

|  |  |  |  |
| --- | --- | --- | --- |
| SPECIFICITY | % SPECIFICITY (RANK) | GENE | GENE CATEGORY |
| Totally specific | 100 | *ACP4*  *AMTN*  *MMP20*  *ODAPH*  *RELT*  *SLC24A4*  *SP6* | CATEGORY 1  Genes with causal mutations of isolated or non-syndromic AI. |
| Very specific | 97-92 | *AMELX*  *ENAM*  *FAM83H* | CATEGORY 3  Genes with causal mutations of isolated AI and mutations responsible for other pathologies/conditions. |
| Medium specific | 83-50 | ***GPR68***  *AMBN*  *ITGB6* | CATEGORY **3** |
| *WDR72* | CATEGORY **5**  Gene with causal mutations of isolated AI, AI associated with syndromes and other pathologies/conditions. |
| Few specific | 40-3 | *COL17A1*  ***KLK4*** *LAMA3*  ***LAMB3*** | CATEGORY **3** |
| Non-specific | 0 | *CNNM4*  *DLX3*  *FAM20A* | CATEGORY **2**  Genes with causal mutations of syndromic AI. |
| *CLDN16*  *CLDN19*  *LTBP3*  *SLC10A7*  ***STIM1***  ***TP63*** | CATEGORY **4**  Genes with causal mutations of syndromic AI and mutations responsible for other pathologies/conditions. |