

**Supplementary Table S1.** List of landmarks used in the 3D cephalometric analysis and anatomical definitions.

| Landmarks                 | Symbol  | Definition   |
|---------------------------|---------|--|
| Nasion                    | N       | Midpoint of the fronto-nasal suture  |
| Orbitale                  | Or      | Most antero-inferior point on the inferior orbital rim   |
| Supraorbitale             | SOr     | The most superior and anterior point of the superior orbital rim   |
| Frontozygomatic Suture    | FronZyg | Antero-lateral point on the fronto-zygomatic suture on the orbital rim   |
| Zygomatic Arch            | ZygArch | Most latero-inferior point on the lateral curve of the zygomatic arch  |
| Jugale                    | J       | Deepest midpoint of the jugal process of maxilla   |
| Nasal Cavity              | NasCav  | Point of junction of lateral wall of nose, nasal floor and nasal process of maxilla                                      |
| A Point                   | A       | Point of maximum concavity of the maxillary alveolar process in the midline  |
| Prosthion                 | Pr      | Most anterior point of the maxillary alveolar process in the midline.  |
| Anterior Nasal Spine      | ANS     | Most anterior mid-point of the anterior nasal spine of maxilla   |
| Posterior Nasal Spine     | PNS     | Most posterior mid-point of the posterior nasal spine of the palatine bone   |
| B Point                   | B       | Point of maximum concavity of the mandible alveolar process in the midline   |
| Infradentale              | Id      | Point of transition from the crown/tooth of the most prominent mandibular medial incisor to the alveolar projection.     |
| Pogonion                  | Pog     | Most anterior point on the symphysis of the mandible   |
| Gnathion                  | Gn      | Point on the chin between the Menton and Pogonion.   |
| Menton                    | Me      | Most inferior point of the mandibular symphysis  |
| Condylion                 | Co      | Most superior and posterior point on the condyle of the mandible   |
| Articulare                | Ar      | Most posterior point of the curvature of the head of the condyle   |
| Gonion                    | Go      | Highest point of the curvature of the mandibular angle formed by the junction of the ramus and the body of the mandible. |
| Antegonion                | Ag      | Highest point of the concavity of the lower border of the ramus where it joins the body of the mandible                  |
| Cribriform Plate          | Cr      | Most superior and mid-point of the crista galli  |
| Midpoint of Sella turcica | Sella   | Mid-point of the sella turcica   |
| Basion                    | Ba      | Midpoint of the anterior curvature of the foramen magnum   |
| Opisthion                 | Opi     | Midpoint of posterior curvature of the foramen magnum  |
| Porion                    | Po      | Most superior and mid-point of the external auditory meatus  |

|                          |         |   |
|--------------------------|---------|---|
| Internal Acoustic Meatus | AcM     | Most posterior lateral point on the posterior border of the internal acoustic meatus  |
| Foramen Ovale            | ForOval | Most antero-medial and superior point of the anterior border of the foramen ovale   |
| Anterior Cranial Fossa   | AntCF   | Most anterior superior point on the anterior border of the middle cranial fossa   |
| Glenoid Fossa            | G_Fos   | Most superior point of maximum curvature in the glenoid fossa   |
| Hypoglossal Canal        | Hypog   | Present on the foramen magnum. Most antero-medial point of the canal. Point should roughly lie on the axis bisecting the canal in anteromedial direction. |

**Supplementary Table S2.** Showing the cephalometric analysis value of the proband, the proband's mother and the proband's father. Norm: Anglo American.

|  | Proband |        |           | Mother |        |           | Father |        |           |
|--|---------|--------|-----------|--------|--------|-----------|--------|--------|-----------|
| Cranial Base Measurements                      |         |        |           |        |        |           |        |        |           |
| Anterior Cranial Base(SN) (mm)                 | Value   | St.Dev | Dev. Norm | Value  | St.Dev | Dev. Norm | Value  | St.Dev | Dev. Norm |
|  | 64.9    | 3.0    | -1.9*     | 64.9   | 3.0    | -3.5*     | 71.6   | 3.0    | -1.9*     |
| Posterior Cranial Base(S-Ar) (mm)              | 29.1    | 4.0    | -0.3      | 31.0   | 4.0    | -1.0*     | 34     | 4.0    | -0.7      |
| Saddle/Sella Angle (SN-Ar)(°)                  | 118.1   | 5.0    | -1.2*     | 119.2  | 5.0    | -1.0*     | 123.1  | 5.0    | -0.2      |
|  |         |        |           |        |        |           |        |        |           |
| Sagittal maxillary measurement                 |         |        |           |        |        |           |        |        |           |
| SNA (°)  | 81.4    | 3.5    | -0.2      | 84.1   | 3.5    | 0.6       | 81.5   | 3.5    | -0.1      |
| N-A (HP)(mm)                                   | -1.5    | 3.7    | -0.4      | -1.4   | 3.7    | 0.2       | -1.4   | 3.7    | -0.4      |
| Midface Length (Co-A) (mm)                     | 74.7    | 4.0    | -2.9*     | 77.8   | 4.0    | -3.9*     | 84.5   | 4.0    | -2.9*     |
| Mx Unit Length (Co-ANS)                        | 77.2    | 5.0    | -1.6*     | 80     | 5.0    | -2.0*     | 87.7   | 5.0    | -0.5*     |
|  |         |        |           |        |        |           |        |        |           |
| Sagittal mandibular measurement                |         |        |           |        |        |           |        |        |           |
| SNB (°)  | 80.7    | 3.4    | -0.1      | 80.1   | 3.4    | -0.2      | 81.2   | 3.4    | -0.1      |
| N-Pg (HP)(mm)                                  | -1.1    | 8.5    | 0.4       | -8.6   | 5.1    | -0.4      | 4.4    | 8.5    | 1.0       |
| Md Unit Length (Co-Pog)                        | 93.2    | 8.0    | -1.5*     | 100.0  | 8.0    | -1.6*     | 112.4  | 8.0    | -0.1      |
|  |         |        |           |        |        |           |        |        |           |
| Sagittal jaw relationship                      |         |        |           |        |        |           |        |        |           |
| ANB (°)  | 0.7     | 1.5    | -0.6      | 3.9    | 1.6    | 1.5*      | 0.3    | 1.5    | -0.9      |
| Wits Appraisal (mm)                            | 0.3     | 1.0    | 1.3*      | 1.2    | 1.0    | 2.2*      | 2.0    | 1.0    | 3.0       |
|  |         |        |           |        |        |           |        |        |           |
| Vertical maxillary and mandibular measurements |         |        |           |        |        |           |        |        |           |
| MP-SN (°)                                      | 24.3    | 6.0    | -1.4*     | 33.9   | 6.0    | 0.2       | 26.9   | 6.0    | -1.4*     |
| Occ Plane to SN (°)                            | 9.7     | 2.5    | -1.9*     | 13.2   | 2.5    | -0.3      | 14.4   | 2.5    | -3.5*     |
| FMA (MP-FH) (°)                                | 16.7    | 4.5    | -2.1*     | 23.1   | 4.5    | -0.2      | 15.1   | 4.5    | -2.0*     |
| Y-Axis (SGn-SN) (°)                            | 59.6    | 5.5    | -1.4*     | 66.2   | 5.5    | -0.2      | 60.0   | 5.5    | -1.1*     |
| Lower Face Hight (ANS-Me) (mm)                 | 51.2    | 4.5    | -2.0*     | 61.3   | 4.5    | -0.8      | 48.3   | 4.5    | -0.0      |
| LFH/TFH (ANS-Me:N-Me) (%)                      | 56.5    | 3.0    | 0.5       | 56.7   | 3.0    | 0.6       | 55.0   | 3.0    | -0.1      |

| <b>Dentoalveolar Measurements</b>  |       |     |              |       |     |              |       |     |              |
|------------------------------------|-------|-----|--------------|-------|-----|--------------|-------|-----|--------------|
| U1-SN (°)                          | 108.1 | 5.5 | <b>1.1*</b>  | 104.3 | 5.5 | 0.3          | 118.8 | 5.5 | <b>2.9*</b>  |
| U-Incisor Protrusion (U1-APo) (mm) | 4.4   | 2.2 | -0.7         | 5.3   | 2.2 | -0.3         | 2.1   | 2.2 | <b>-1.8*</b> |
| U1-NA (°)                          | 26.8  | 5.7 | 0.7          | 20.6  | 5.7 | -0.4         | 37.3  | 5.7 | <b>2.6*</b>  |
| U1-NA (mm)                         | 5.2   | 2.7 | 0.3          | 2.6   | 2.7 | -0.6         | 4.8   | 2.7 | 0.2          |
| L1-MP(LADH) (mm)                   | 31.3  | 3.0 | <b>-2.9*</b> | 36.7  | 2.0 | <b>-1.6*</b> | 39.2  | 3.0 | <b>-2.3*</b> |
| L1 Protrusion (L1-APo) (mm)        | -0.8  | 1.7 | <b>-2.0*</b> | 1.1   | 1.7 | <b>-1.0*</b> | -0.2  | 1.7 | <b>-1.7*</b> |
| L1-NB (°)                          | 13.8  | 6.0 | <b>-1.9*</b> | 21.8  | 6.0 | -0.6         | 22.5  | 6.0 | -0.5         |
| L1-NB (mm)                         | 0.6   | 4.0 | <b>-1.9*</b> | 3.6   | 1.8 | -0.2         | 2.4   | 1.8 | -0.9*        |
| Interincisal Angle (U1-L1) (°)     | 138.8 | 6.0 | <b>1.5*</b>  | 133.7 | 6.0 | 0.6          | 119.9 | 6.0 | 1.7          |
| <b>Soft Tissue Measurements</b>    |       |     |              |       |     |              |       |     |              |
| Upper Lip to E-Plane (mm)          | -5.8  | 2.0 | <b>-2.2*</b> | -9.0  | 2.0 | <b>-1.5*</b> | -10.6 | 2.0 | <b>-1.3*</b> |
| Lower Lip to E-Plane               | -2.8  | 2.0 | 0.4          | -5.5  | 2.0 | <b>-1.7*</b> | -7.4  | 2.0 | <b>-2.7*</b> |
| Nasolabial Angle (Col-Sn-UL) (°)   | 104.3 | 8.0 | 0.3          | 127.0 | 8.0 | <b>3.1*</b>  | 111.8 | 8.0 | <b>1.2*</b>  |
| Chin Angle (Ig-Pg-MP) (°)          | 70.5  | 5.0 | 0.1          | 69.9  | 5.0 | 0.0          | 60.5  | 5.0 | <b>1.9*</b>  |

**Abbreviations:** \*  $p < 0.05$

**Supplementary Table S3.** Mean values and number of standard deviations of the normal values for the general population of the angles SNA, SNB and ANB, which were used for the classification of the dentoskeletal malocclusions for the normative control groups.

|   | <b>Groups</b> | <b>SNA</b> | <b>SNB</b> | <b>ANB</b> |
|---|---------------|------------|------------|------------|
| <b>Mean values</b>  | Class I       | 83.10317   | 79.73317   | 3.37       |
|   | Class II      | 82.685     | 77.035     | 5.65       |
|   | Class III     | 79.72636   | 82.46591   | -2.73955   |
| <b>No. of Standard Deviations<br/>from the Norm Value</b> | Class I       | 3.926698   | 3.929718   | 1.126383   |
|   | Class II      | 3.762325   | 3.450656   | 2.103371   |
|   | Class III     | 4.734917   | 5.663599   | 2.249172   |

**Supplementary Table S4.** Primer and target for mutation sequencing

|                            | <b>Target</b>                     | <b>Forward/Reverse primer (5'-3')</b>  |
|----------------------------|-----------------------------------|--|
| <b>Mutation sequencing</b> | <i>FGFR3</i> (c.749C>G),<br>191bp | CGGCAGTGGCGGTGGTGGTGA<br>GACCCAAATCCTCACGCAACC<br>GenBank Accession #NG_012632.1 |

**Supplementary Table S5.** Antibodies used for immunofluorescence

| <b>Protein</b>                              | <b>Antibody</b>                    | <b>Catalog #</b> | <b>Supplier</b>                        |
|---|------------------------------------|------------------|--|
| Primary Antibody Anti-NANOG                 | Anti-Human; Rabbit polyclonal IgG  | RCAB004P-F       | Reprocell (distributed by CosmoBioUSA) |
| Primary Antibody Anti-OCT3/4                | Anti-Human; Mouse monoclonal IgG2b | SC-5279          | Santa Cruz                             |
| DAPI  | Anti-Human                         | Ab228549         | abcam                                  |
| Secondary antibody Alexa Fluor 488          | Goat anti-rabbit IgG               | A-11008          | Invitrogen                             |
| Secondary antibody Alexa Fluor 594          | Goat anti-mouse IgG                | A-11005          | Invitrogen                             |
| Alexa Fluor® 488-conjugated Isotype Control | Anti-Human; Rabbit polyclonal IgG  | IC1051G          | R&D Systems                            |
| Alexa Fluor® 594-conjugated Isotype Control | Anti-Human; mouse monoclonal IgG   | IC0041T          | R&D Systems                            |