3D Analysis of Normal Facial Variation: Data Repository and Genetics

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Co-Investigators: Heike, Cunningham, Hecht

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FaceBase Annual Meeting: May 1-3, 2013
Goal 1: To construct a web-based normative repository of 3D facial measurements and images

1a) Ascertain 3500 European Caucasian individuals – age 3 to 40 – from multiple sites: Pittsburgh, Seattle, and Houston (and Iowa!)
1b) Acquire 3D facial surface images, basic demographic descriptors and saliva samples from each participant
1c) Extract quantitative data from 3D surface images including landmarks and linear measurements
1d) Deposit clean data (including images and measures) into a web-based repository accessible through FaceBase.org (3D Facial Norms)

Goal 2: To investigate the genetic basis of variation in facial shape

2a) Submit saliva samples for genotyping (proposed year 5)
2b) Perform morphometric analyses on 3D data set to derive shape variation descriptors
2c) Identify genetic variants associated with normal facial shape variation
2d) Submit genotype data and results to FaceBase.org
Progress over the Past Year

Overall Recruitment Effort

![Bar graph showing recruitment effort over the past three years.](image)

- 2010-11: 342
- 2011-12: 1296
- 2012-13: 1988

3D Facial Norms Repository

**Recruitment Target:**
3500 healthy unrelated individuals age 3-40

Site Recruitment Figures

- **Pitt:** 600
- **Seattle:** 645
- **Houston:** 685
- **Iowa:** 58
Progress over the Past Year

**Phenotypic Data Collection**
- 1259 in process
- 729 uploaded to Hub

**Saliva Kits**
- 1598 DNA extracted
- 390 in process

- Demographics
- 3D Facial Surfaces
- Landmark Coordinates and Measurements
3D Facial Norms Web-Interface

3D Facial Norms Database

3D DATABASE SEARCH
Explore the 3D Norms Database through a customizable search interface. This is the main portal for querying and downloading individual-level phenotype and genotype data based on user-defined parameters. Phenotypic data include 3D facial landmark coordinates, anthropometric facial measurements, demographic descriptors, and 3D facial surface models.

SUMMARY STATISTICS
View normative age- and sex-based averages for selected craniofacial measurements and 3D facial surface models.

TOOLS
A collection of practical web applications for the clinical and research community.

TECHNICAL NOTES
Detailed background information on all aspects of the 3D Facial Norms Project.

DATA ANALYSIS
A compendium of results from past analyses based on the 3D Facial Norms dataset.

ABSTRACT PAGE
Using the 3D Norms Data

Analyses of human craniofacial variation and growth patterns

Normative control data for craniofacial comparisons

Development of novel image analysis methods

Genomic studies of craniofacial traits
Sexual Dimorphism in facial shape across the lifespan

Juveniles 3-10 (n = 119)

Adults 18-40 (n = 722)
Relationship between facial shape and digit ratio in males
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Assessment of craniofacial dysmorphology in Cutis Laxa
Using Z-Score Calculator Tool to compare upper facial height

<table>
<thead>
<tr>
<th>MEASUREMENT</th>
<th>VALUE</th>
<th>Z-SCORE</th>
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</thead>
<tbody>
<tr>
<td>Lower Facial Depth Left</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphological Facial Height</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper Facial Height</td>
<td>92.10</td>
<td>2.02</td>
</tr>
</tbody>
</table>

The Z-score represents the number of standard deviations from the mean.
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Automated landmarking of facial surfaces

Step 1: Initial Identification of facial landmarks using geometric method

Step 2: Deformable registration – improves fit and adds additional landmarks

Compared to manual landmark placement

<table>
<thead>
<tr>
<th>Point Name</th>
<th>Geometric Method Average Distance(mm)</th>
<th>Deformable Method Average Distance(mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasion</td>
<td>2.92±1.62</td>
<td>2.92±1.62</td>
</tr>
<tr>
<td>Pronasale</td>
<td>1.29±0.68</td>
<td>1.59±0.81</td>
</tr>
<tr>
<td>Subnasale</td>
<td>2.35±2.16</td>
<td>2.45±0.80</td>
</tr>
<tr>
<td>Alare(R)</td>
<td>3.24±2.61</td>
<td>1.78±1.15</td>
</tr>
<tr>
<td>Alare(L)</td>
<td>3.14±2.41</td>
<td>3.07±1.15</td>
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<tr>
<td>Labiale Superius</td>
<td>2.77±1.15</td>
<td>2.77±1.15</td>
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<tr>
<td>Stomion</td>
<td>1.49±0.90</td>
<td>1.49±0.90</td>
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<tr>
<td>Labiale Inferius</td>
<td>2.27±1.41</td>
<td>2.27±1.41</td>
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<tr>
<td>Sublabiale</td>
<td>3.17±1.87</td>
<td>3.17±1.87</td>
</tr>
<tr>
<td>Subalar(R)</td>
<td>2.36±1.06</td>
<td>2.36±1.06</td>
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<tr>
<td>Subalar(L)</td>
<td>1.59±0.93</td>
<td>1.59±0.93</td>
</tr>
<tr>
<td>Crista Philtri(R)</td>
<td>2.31±0.27</td>
<td>2.31±0.27</td>
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<tr>
<td>Crista Philtri(L)</td>
<td>1.99±1.03</td>
<td>1.99±1.03</td>
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<tr>
<td>Cheilion(R)</td>
<td>3.14±2.41</td>
<td>3.08±2.14</td>
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<tr>
<td>Cheilion(L)</td>
<td>2.80±2.38</td>
<td>3.08±1.64</td>
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<tr>
<td>Gnathion</td>
<td>5.31±3.34</td>
<td>5.31±3.34</td>
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<tr>
<td>Endocanthon(R)</td>
<td>4.78±1.45</td>
<td>2.39±1.09</td>
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<tr>
<td>Endocanthon(L)</td>
<td>4.58±1.70</td>
<td>2.78±1.50</td>
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<tr>
<td>Exocanthon(R)</td>
<td>3.15±2.21</td>
<td>3.34±1.63</td>
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<tr>
<td>Exocanthon(L)</td>
<td>2.72±1.86</td>
<td>3.68±1.91</td>
</tr>
</tbody>
</table>
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Genotyping Strategy

- CIDR application planned for summer
- Goal is to have 2200-2500 samples in hand at the time of application
- Key factor in thinking about genotyping: **what is most useful for the FaceBase user community**
  - A genome-wide panel probably makes most sense for FaceBase users
    - Illumina Core Panel (300k SNPs) + Exome, or...
    - OmniExpress Panel (750k SNPs) + Exome, or...
    - Omni 2.5 Panel (2.5mil SNPs) + Exome
  - Additional custom panel for testing relevant SNPs from recent analyses
  - Replication and extension dataset
  - Meta-analysis/mega-analysis dataset
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