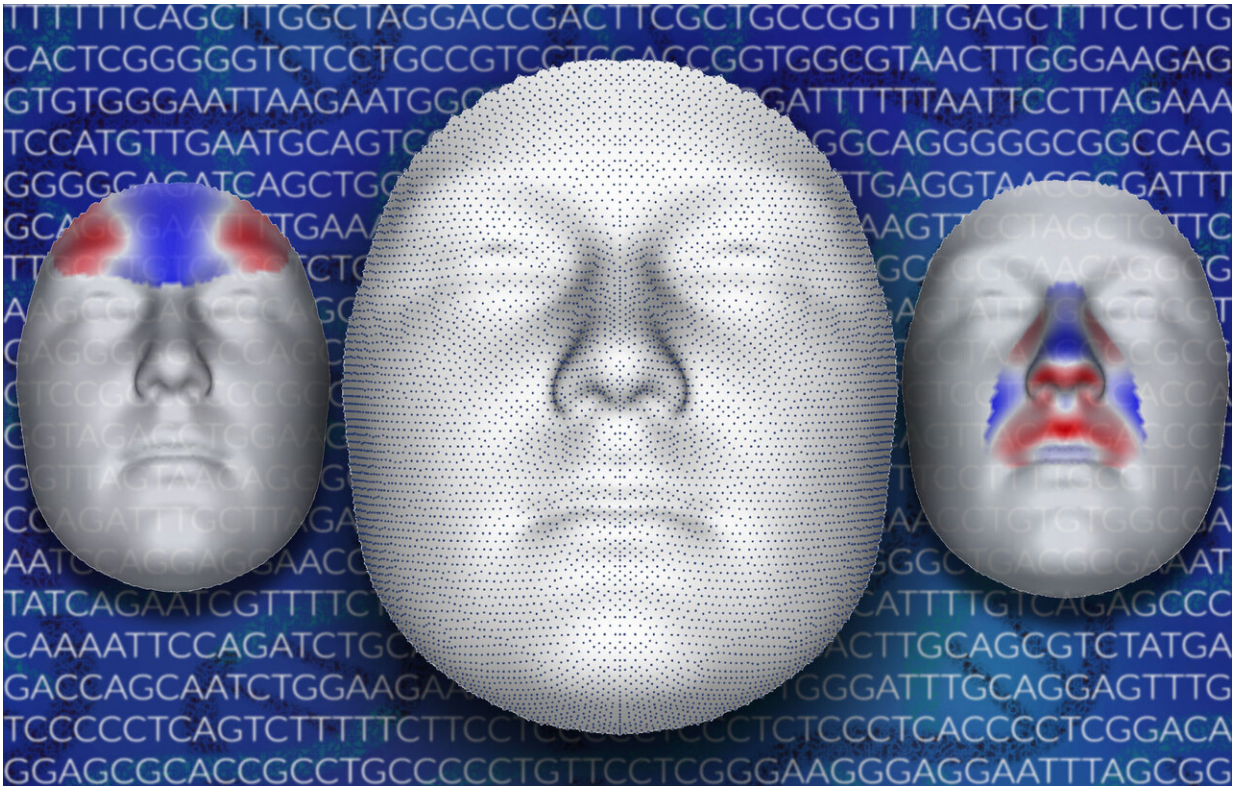
Genetics of human face begin to reveal underlying profile

December 7 2020



Using 3-D facial images with over 7,000 data points, researchers have identified changes in the DNA sequence of European individuals that contributes to variation in facial features. These findings help us better understand human variation and facial birth defects. Credit: Julie White, Penn State

The genetics behind the shape of the human face are difficult to

decipher, but now an international team of researchers has connected specific genetic signals with specific areas of the face. They not only can see the signals of normal facial features in the genome, but also hope their work can shed light on craniofacial malformations such as cleft lip and palate.

"The face tells the outside world about your identity, who you are related to, where your ancestors come from and even your health," said Julie White, graduate student in anthropology, Penn State. "But we only know a fraction of how faces are formed. The facial structure comes together in early development, and if it doesn't go right, you can get a cleft palate or other problem, but we don't fully know what controls those processes."

In many cases of facial dysmorphology there are limited numbers of subjects, making location and identification of errant genetics difficult. However, White believes that if researchers knew the genetic location for normal range lip formation, that location might be a site contributing to malformations of the lip.

Another area where understanding the genetics of normal facial structure can help is in understanding the evolution of the face.

"I personally don't do much work in this area, but Mark Shriver (professor of anthropology, Penn State) does and he asks, why do people look different?" said White. "What makes up the differences in various groups? Is it selection, genetic drift or something else?"

The researchers note that another possible use for their work is in forensics, but there is a long way to go until DNA facial reconstruction can be legal evidence.

The researchers used two data sets, one from the Avon Longitudinal

Study of Parents and Children in the U.K., containing 3,566 individuals and one from the U.S. containing 4,680 individuals. All subjects had highly detailed 3-D facial photographs and the researchers placed over 7,000 point locations on the images using a gridded mask that was digitally stretched and pulled to conform to the facial contours of each individual.

"Collaborations in jointly analyzing multiple datasets in combinations with better analysis techniques are key to push this research," said Peter Claes, associate professor of engineering science (ESAT-PSI) and human genetics, and head of the Laboratory for Imaging Genetics, who pioneered the 3-D analysis method.

Claes also divided the face into 63 segments using data-driven relationships to avoid pre-existing ideas of which facial areas were important and allowing the researchers to look at variation in small subsets of the face.

"We looked for connections between shared genetics and facial features, asking things like, do people with upturned noses share a genotype?" said White.

To give more power to the study, the researchers considered the U.S. data set and the U.K. data set separately and they varied the search, using each dataset in turn to find and then replicate genetic sites associated with facial features.

"We found an extensive set of locations in our DNA that play a role in the development of the human face," said Karlijne Indencleef, graduate student in biomedical sciences at KU Leuven, Belgium.

Eventually, looking at only genetic locations that had similar associations in both datasets, the researchers identified 203 genomic regions.

"If you look at what we found and look at previous literature, you see that there is overlap with our genes and genes that had previously been implicated in non-facial things such as limb development and organ and skeletal abnormalities," said White. "There are shared genetics. Things that are related to the face and related to another part of the body."

Some facial deformities are associated with other physical problems, so finding shared genetics was not surprising, according to the researchers. Many of the genes identified begin working in the early stages of embryonic development and the researchers are identifying their physical presentation in adults. However, according to the researchers, more work must be done to verify these associations.

"Our post-analyses provide us with additional evidence, for example the epigenetic analyses showed that the genetic regions we found get expressed in cells relevant for craniofacial development," said Indencleef. "We have tagged locations that can be interesting for wet labs to validate and further investigate their exact functions."

Of the 203 genetic locations identified as significant for facial structure, 89 had already been found from other studies, either using the same data or with independent data. They also found 61 locations that were already implicated as the source of facial malformations in humans or mice. 53 locations were completely new to this study.

The study is published in *Nature Genetics*.

More information: Insights into the genetic architecture of the human face, *Nature Genetics*, DOI: 10.1038/s41588-020-00741-7 , www.nature.com/articles/s41588-020-00741-7