CORRESPONDENCE

The Use of Forensic DNA Phenotyping in Predicting Appearance and Biogeographic Ancestry

by Prof. Dr. rer. nat. Peter M. Schneider, Prof. Dr. phil. Barbara Prainsack, Prof. Dr. rer. nat. Manfred Kayser in issue 51–52/2019

Biogeographic Ancestry Cannot Be Unequivocally Determined

Of course it would be desirable to live in a society in which the biogeographic ancestry matters so little that it would be useless for the purpose of criminalistic searches—but that is utopian. Criminology and criminalistics are based on the fact that human beings vary and look different from one another. If, for example, searchers in the USA want to know whether a wanted person is “black” or “white” (1), one can hardly reproach them—they cannot be better than the society in which they are searching.

The authors claim that the biogeographic ancestry they studied “solely concerns the geographical region(s) from which a person’s biological ancestors originated” and understandably differentiate this from terms such as ethnicity or race (2). In doing so they pretend to circumvent the classic problem of any definition of subgroups of humanity—namely, the differentiation of these groups on the basis of certain common traits. Geographical regions could, however, be defined without looking at people, so they hypothesize. The problem remains, however, that humans and peoples do not remain stuck in certain places.

Who, then, should be included in a geographically defined group? In two instances, the authors limit this to the “autochthonous” population, literally referring to the population “sprung from the soil it inhabits”.

But after how many generations of settledness does someone count as autochthonous?

If the aim is to achieve geographical allocation by DNA, the crucial question is how the comparison group is defined. Was a person with darker skin tone excluded from a European group, even though their ancestors had lived in Europe for three generations? And if so, based on which criteria? It is important to disclose these criteria. An objective and unprejudiced classification by geography is simply not possible (3).

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Conflict of interest statement

The author declares that no conflict of interest exists.

In Reply:

The correspondent questions the development of reference data for DNA-based biogeographic ancestry analysis. Unfortunately, we were not able in our article (1) to explain this topic in detail owing to reasons of space constraints.

Different genome-wide studies of various human population samples worldwide, and their specific statistical data analyses, have shown that based on such data, individuals form groups that can be distinguished from one another on the basis of the individual’s genomic data similarities or lack thereof (for example [2]).

The biogeographic ancestry or the appearance phenotypes of the studied individuals did not play any part in these genomic groupings. Retrospective inspection of the geographical origin of the studied individuals demonstrated that these genomic similarity groups corresponded to the continental regions of biogeographic ancestry of the studied individuals. This can be ex-

plained by the fact—among others—that families often live in one continental region over many generations, and tend to mix with people within their own continental region, rather than with people from distant continental regions.

Such population genetic studies form the foundation of genomic control analyses, which are undertaken when developing reference data sets for the biogeographic ancestry analysis. These are based on hundreds of thousands of genome-wide distributed DNA markers (single nucleotide polymorphisms, SNPs) and specific statistical analysis methods, which allow continental assignment and the finding of possible genetic-geographical admixture. In the result of these genomic control analyses, only data from those samples are finally used as reference data for biogeographic ancestry analysis that show the expected genomic similarity with other samples from the same continental region of origin. Samples that in such

genomic control analyses showed none or only a very limited genomic similarity with other samples from the same continental region of origin—for example, because of genetic ancestors from different continental regions—are not included in the reference data set for the biogeographic ancestry analysis.

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Conflict of interest statement

Prof. Kayser is a co-inventor of patent no. EP2195448A1 ("Method to predict iris color") but receives no license fees or royalties from this. He has appeared as an invited speaker at scientific meetings, with reimbursement of meeting participation fees and of travel and accommodation expenses by Thermo Fisher Scientific, Promega, and the Wenner-Gren Foundation. He is commissioned to provide medicolegal expert reports on DNA trace analysis for the investigative authorities in multiple countries. Prof. Kayser served until April 2018 as member of the Scientific Advisory Board of Identitas Inc., without receiving honoraria or other payments for this activity.

CLINICAL SNAPSHOT

Bilateral Corneal Changes in a Patient With Monoclonal Gammopathy

Slit-lamp photograph of the anterior segment of the eye under 25x magnification.

A 74-year-old man consulted us because of bilateral corneal opacification and mild subjective visual loss. Examination revealed bilateral, multiple, diffuse and also nummular stromal and pre-Desemet opacifications of the cornea (*Figure*). There was no prior history or family history of eye disease. The patient did, however, have a known monoclonal gammopathy of unclear significance, which was presumably the cause of his clinically evident paraproteinemic keratopathy.

We initially recommended no treatment, because the visual acuity was still 1.0. The potential therapeutic approaches would have included phototherapeutic keratectomy (PTK) and lamellar or perforating keratoplasty.

The clinical manifestations of paraproteinemic keratopathy, in which the observable changes are due to immunoglobulin deposition, are highly varied. The differential diagnosis includes dystrophic, infectious, and inflammatory processes of the cornea, as well as other metabolic diseases with potential corneal involvement. The frequency of keratopathy among patients with paraproteinemia is currently unclear. Plasma-cell disease should be ruled out in any patient with bilateral variable corneal opacifications of uncertain origin. Conversely, the possibility of corneal involvement should be considered in any patient with a known monoclonal gammopathy.

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