Population health science

An early look at birth cohort genetics in China

Nicholas John Timpson

Genetic sequencing data from more than 4,000 Chinese participants in the Born in Guangzhou Cohort Study provide insights into the population, and a snapshot of what is to come in future phases of the project. See p.565

The charting of genetic variation in populations is one of the standout achievements of human scientific endeavour and an area that has exploded since the early 2000s. Moving on from the first sequencing of the human genome, a combination of technology and ambitious sampling has changed the way people think about genetic variation, the nature of the relationship between genetic variants and measured characteristics (phenotypes) and the culture of trusting researchers to access our genomes. On page 565, Huang *et al.*[1] report on the first phase of the prospective and longitudinal Born in Guangzhou Cohort Study (BIGCS), which has been tracking a huge birth cohort in China since 2012 (ref. 2).

The authors describe findings from a large-scale genomic study containing whole-genome sequencing data from 4,053 Chinese participants — mainly mother–infant duos (Fig. 1), or mother–father–infant trios. The study provides insight into the population genetics of the sample, the parameters of the study itself and the data available within it, and is a precursor to expansion of the work, which could involve up to 50,000 participants.

The BIGCS joins a growing number of large-scale genetic data collections. Stemming from early investigations of populations and disease[3–5], genome-wide sequencing data sets now encompass population-level analyses, such as those in Estonia (https://genomics.ut.ee/en), Finland (www.finngen.fi/en), Iceland (www.decode.com) and elsewhere, and focused clinical applications, such as Genomics England (www.genomicsengland.co.uk). With these substantial collections, the move towards representative sampling of population-level genetic variation is becoming a reality. The work presented by Huang *et al.* charts another step of the journey towards a large and well-characterized cohort that includes genetic sequencing data.

The sample itself is fascinating, with the potential to reveal information about the population genetics and characteristics of people from southern China. More broadly, this study presents an opportunity to expand the field of human genetics beyond existing data sets. There is a worrying absence of diversity in genetic data catalogues — particularly with respect to humanity's shared ancestral genome[6]. However, even with the modest sample size of the first phase of the BIGCS genetics collection, Huang and colleagues have already started to address this lack of representation. They have identified new genetic variants, generated a panel of reference genomes specific to individuals of Chinese descent, and examined patterns of genetic variation alongside demographic and linguistic variation. The resulting dissection of genetic ancestry groups in the population and the connection to local dialects is reminiscent of work done in the 1990s, which looked at the interplay between biological, demographical and cultural factors in determining the genetic composition of populations[7].

The applications of this study of genetic variation are limited by the size of this phase of BIGCS data collection, but the authors do report a series of associations between genetic variants and biomedical traits that seem to be specific to people from East Asia, and might be informative in understanding the causes of disease. Arguably, the work — at least at this stage — is better focused on the task of describing the potential of this data set, which includes detailed phenotypic and physical characteristics, weight changes from early life, and molecular profiles, such as levels of cholesterol, at different ages. Taken together with a growing genetics collection, this record of biomedical traits should become a key resource as sample sizes increase.

We should also take a guarded interest in the applied genetic epidemiology used so far. This looks to explore the relationships between measures available in the cohort, such as the phenotypes of mothers (for example, height, blood glucose levels and lipid profile) and their children (for example, birth weight and length). Although one would almost expect to see genetic epidemiology[8] and its applications[9] in this type of work, the findings so far are of interest and will prompt follow-up studies that can confirm or challenge the suggested intergenerational effects in this specific population.

Probably the most important aspect of this contribution to the global collection of genetic

Figure 1 | A mother and her newborn infant in a maternity hospital in China.

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data is that it shows more evidence that data generation and sharing are broadening, and that there is a shift towards a culture of acceptance and openness as members of the public become more comfortable with sharing their genetic information. The collection and study of such data call for cultural sensitivity and a combination of ethical and scientific rigour, so it is encouraging to see progress in this area. We should also be excited about having a deeper understanding of populations, sociodemographic histories and fresh biological insights, as well as about the willingness of BIGCS participants to take part. Indeed, although ancestry, genetic association and applied research are illuminating, it is incumbent on the research community to remember the commitment of those who make this type of work possible.

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From the archive

River monitoring needed to address pollution, and the case for having a minister for science in government.

100 years ago

The difficulty in deciding a status of pollution ... is well illustrated by ... the lack of critical and co-ordinated information regarding ... conditions in fresh-water streams, rivers, and in estuaries. The absence of this kind of information must render much work on the conditions in polluted waters inconclusive or even futile. The present letter is therefore written to demonstrate ... the necessity for organised continuous work on the biological, physical, and chemical conditions in streams, rivers, and estuaries, *whether polluted or not*.
From *Nature* 16 February 1924

150 years ago

We are glad to see that the *Times* has at last opened its pages to the question of the propriety of appointing a responsible Minister, whose duty it shall be to look after the interests of Science and of scientific research and education, and take charge of the scientific institutions of the country ... The whole question could not be better stated than in Colonel Strange's letter which ... runs as follows: ... "[S]cientific research must be made a national business ... [T]he point at which Science, in most of its leading branches, has now arrived and the problems presented for solution are such as to need for their adequate treatment, permanent well-equipped establishments with competent staffs ... [W]e are being rapidly outstripped by nations who, though they encourage private exertion, are wise enough not to rely on it, but to establish a system free from the caprice, the incompleteness, the liability to interruption and cessation incident to all individual labour in whatever field ... [T]here must be a Minister for Science ... Let this be done, and we should cease to witness the farce of consulting the Chancellor of the Exchequer about observing eclipses of the sun, the Prime Minister about scientific Arctic expeditions, and the Treasury about tidal reductions."
From *Nature* 12 February 1874

Materials science

Layered ferroelectric materials make waves

Berit H. Goodge

By combining materials-synthesis techniques, researchers have come up with a way of building layered structures that display intriguing wave-like patterns of electric polarization, and could be useful for next-generation electronics. **See p.529**

A household refrigerator magnet has an inherent polarity, a characteristic it shares with other magnets of its kind, known as ferromagnets. Ferroelectric materials are also polarized — electrically rather than magnetically — with positive and negative charges instead of north and south poles. This polarity can be flipped by strong electric fields, a property that makes ferroelectrics attractive materials for computing, memory and sensing devices, especially if they can be manipulated at the nanometre scale. It also allows complex patterns of ferroelectric polarization to be generated through careful materials design and synthesis[1]. On page 529, Sánchez-Santolino *et al.*[2] describe a technique that combines strategies from several areas of materials research to generate and stabilize ferroelectric patterns.

A simple model of electric polarization holds that a charged ion that is offset from the charge centre of its neighbours will shift the distribution of electric charge to create a local polarization (Fig. 1a). Ferroelectricity is therefore closely tied to the arrangement of atoms in the bulk of a material, to the surfaces and interfaces that the atoms form, and to how these geometrical features impart mechanical stress, all of which affect the interactions between atoms.

Careful engineering of these 'boundary conditions' — by growing structures with several layers, for example — has proved to be a powerful way of generating ferroelectric textures such as waves, vortices and other twisting configurations[3–5]. Now, Sánchez-Santolino and colleagues have added a 'twist' to this approach by stacking two existing layers so that they are rotated relative to each other.

When a layer that is a single atom or a few atoms thick is placed on top of another such layer and rotated by a small angle, the overlap between the two crystal lattices creates a third distinct pattern. This pattern is termed a moiré lattice — named after a French method of fabric pressing — and the periodicity of this lattice is considerably larger than those of the original layers (Fig. 1b). The interactions between the two layers can impart entirely new properties to the overall twisted structure, and this 'twist and stack' approach has therefore garnered immense interest in physics and materials research[6].

Moiré structures are typically fabricated by peeling apart larger crystals of each material to isolate a thin layer, which can then be stamped