HUMAN GENETICS

Individual genomes diversify

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The link between a person's genetic ancestry and the traits — including disease risk — that he or she exhibits remains elusive. Routine sequencing of the genomes of an African and an Asian individual offer a step forward.

The rapid progress in genetic screening assays and DNA sequencing techniques promises to increase our understanding of the complex relationship between the human genetic make-up (the genotype) and its associated traits (the phenotype). For example, using the composite human genome sequences[1–3], genome-wide association studies have identified regions that control specific traits through single nucleotide polymorphisms (SNPs) — the most common form of genetic variation. In this issue, Bentley *et al.*[4] (page 53) and Wang *et al.*[5] (page 60) detail the development and application of a high-throughput technology for sequencing DNA to decipher the genomes of two people, one of West African descent and the other of Han Chinese descent. This advance provides a technology that might eventually relate specific sequences and regions of DNA directly to human phenotypes.

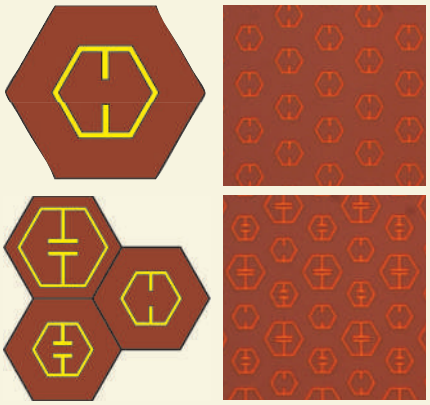
Although genome-wide association studies can establish a link between a genetic locus marked by adjacent SNPs and its associated phenotype, they do not automatically identify the implicated nucleotide's position, as they use only a fraction of human SNPs. Genome-wide association studies were used because of their relatively low cost compared with the technological challenge and high cost of sequencing genomes in large human populations. Sequencing the genomes of many individuals would overcome the problem of identifying which nucleotide(s) are implicated in a phenotype, as long as the procedure could be performed accurately and completely. From such data sets, DNA variants can be identified, and the frequency with which they occur in humans who carry a particular trait — such as a disease — can then be compared with their frequency in people who lack that trait. Thus, all genetic variants contributing to the trait can be identified, giving a more complete picture of the biology involved.

The genomes of the anonymous African and Asian individuals supplement the existing sequenced genomes of two people of European origin, Craig Venter[6] and James Watson[7]. Both teams involved in the latest work[4,5] used the Illumina GA sequencing instrument, in which sequencing is performed by synthesizing fluorescently detectable DNA molecules, using the DNA from the genome being sequenced as a template. In a single cycle, this platform can produce more than 40 million discrete 'reads' of 35 nucleotides from either end of a 200- or a 2,000-nucleotide DNA fragment. Compared with the instruments used to complete the initial human genome sequence[1–3], the Illumina GA generates three to four orders of magnitude more sequence per operation cycle. This instrument therefore joins the 454 Life Sciences sequencer[7] as yet another 'next generation' technology for sequencing individual human genomes.

How do the two new genome sequences allow a better understanding of human genetics? Both studies[4,5] confirm that it is possible to routinely sequence the genome of an individual to discover the wide spectrum of DNA variations that it harbours. Of course, this process is greatly facilitated by having a reference human genome against which to compare sequence data from the two individuals. This allows the identification of SNPs, as well as insertion/deletion polymorphisms and structural variations (Fig. 1, overleaf). Extensive validation of the SNPs detected shows that sequencing accuracy is high. A strength of this

OPTICS

Metamaterial Persian carpets



OSA

Metamaterials gained renown as a way of creating invisibility cloaks — devices that could make an object 'disappear' before one's eyes. Less well known is that they can also act as detectors for biological compounds. Writing in *Optics Express*, Bingham *et al.* describe two-dimensional metamaterials designed so that, when exposed to electromagnetic radiation, their resonant frequencies coincide with those of vitamin H (C. M. Bingham *et al. Optics Express* **16,** 18565–18575; 2008). The resonant frequencies of vitamin H occur in the terahertz range, and these results thus provide an example of biodetection in that frequency regime.

The properties of metamaterials lie in their structure rather than their chemical composition. One asset of these man-made materials is that they can be engineered to possess a precise response to electromagnetic radiation. Bingham and colleagues created metamaterials with designs that mimic several types of symmetry observed in nature, using both square and hexagonal tiles. Their tiles, the unit cells of metamaterial structures (shown on left of picture), consist of up to three different subunits. The overall structures (shown on right) look rather like a Persian carpet.

To maximize the electromagnetic response of a metamaterial, the unit cells must be tightly tessellated — that is, the gaps between tiles must be minimized. But why incorporate more than one subunit into a tile? The advantage is that the metamaterial preserves the different electromagnetic properties of each subunit: a material formed with three distinct subunits is resonant at three different frequencies. A triple-resonator metamaterial allows a biological compound to be identified more accurately because there are three frequency-match points of comparison.

With this in mind, the authors simulated metamaterial structures computationally to find the best materials for the job. They then made the best designs, shone terahertz radiation on them and recorded the electromagnetic response. As predicted, metamaterials with structures that combined three distinct subunits (such as that pictured on the lower right panel) resonated at three distinct frequencies, the individual frequencies of the different subunits.

As the authors had hoped, the simulated and experimental resonances of their metamaterials were a good match for those of vitamin H. This match could therefore form the basis of a biodetector. Bingham *et al.* have found that their multi-subunit tiling techniques can create multi-resonator metamaterials that can be used as biodetectors. But that is not all. Their metamaterials could potentially detect hazardous chemicals.

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