IN THE NEWS

Genes to blame for drinking habits

How much you drink might be as much to do with your genes as your willpower, according to a new study.

People perceive tastes differently, and this is partly controlled by inherited factors. "Some of the differences in oral sensation are under genetic control, and these differences can explain some of the variability in what we like and ultimately choose to eat and drink", says Valerie Duffy at the Unversity of Connecticut (*CBS News*, 15 November 2004). As people who taste bitterness strongly are the least likely to enjoy alcohol, Duffy tested whether there is also a genetic basis for drinking habits.

Her group tested the reaction of 84 volunteers to the bitter chemical 6-n-propyl-thiouracil (PROP). They then looked at genetic variation among this group in the gene *TAS2R38*, which encodes a bitter-taste receptor. Two variants, PAV and AVI, were found among the study group, and the response to PROP corresponded to which combination of the two an individual carried. PAV/PAV individuals were the most sensitive to bitterness ("supertasters"), while those with two AVI variants were the least sensitive ("non-tasters").

Duffy also saw a similar correlation with the amount of alcohol that the volunteers reported drinking: "People who tasted the least bitterness from PROP or who were *TAS2R38* non-tasters consumed more alcohol than those who tasted the most bitterness from PROP or who were *TAS2R38* tasters" (*Daily Mail*, 15 November 2004).

Dennis Drayna, who discovered *TAS2R38*, believes this is an important step in understanding drinking problems: "It is well known that there are genetic influences on alcoholism, but it is a very difficult tangle of facts. That taste appears to be so clear a factor is very exciting" (*New Scientist*, 15 November 2004).

Louisa Flintoft

GENOMICS

Pecking away at evolution

In this era of increased genome sequencing, we have come to expect certain statistics from each new assembly: percent and make up of repeated sequences, G+C content, and so on. But how many groups are under the same pressure as the authors of three recent papers in *Nature*, from which everyone wants to know why their organism crossed the road?

Chickens are both the first agricultural animal to be sequenced and an important laboratory model system, contributing to Nobel prize-winning advances in immunology, developmental biology and cancer research. Chicken DT40 cells are used in laboratories around the world for homologous recombination of large sequences, and the well-studied chromatin-binding factor CTCF is among several proteins and genes that were originally identified in chicken. The current genome assembly for chicken is now reported by the International Chicken Genome Sequencing Consortium: it covers more than 95% of the bird's one billion euchromatic base pairs, including all 10 autosomal macrochromosomes, both the Z and W sex chromosomes, and two-thirds of the 28 microchromosomes. This assembly benefits from both whole-genome shotgun and some BAC-based sequencing, linking it to the physical map that is described by Wallis *et al.* in the same issue. The chicken genome is about three times smaller than that of the human, mainly owing to fewer repeated elements; this is the first vertebrate genome so far to show no active SINE elements in its recent history, resulting in the absence of one of the largest categories of interspersed elements known in vertebrate genomes.

For example, genetic research in chicken has focused on the breeding of more productive strains for meat and egg production and improvements in animal health and welfare — by reducing infectious disease and aggressive behaviours such as pecking their neighbours. Large commercial breeding programmes and several inbred lines have allowed geneticists to immediately apply the genomic information. These efforts will be greatly aided by the comparison — carried out by the International Chicken Polymorphism Map Consortium — of the red jungle fowl, the wild predecessor strain of which the genome was sequenced, with three domestic lines. By re-sequencing bits of each genome, the consortium has discovered over 2.8 million SNPs, which will be used to map traits that are both unique to chickens and are shared between some chicken and human diseases.

Although the chicken genome sequence cannot resolve whether the chicken or the egg came first, it does contribute some fascinating insights. The analysis carried out by the International Chicken Genome Sequencing Consortium reveals that, although the chicken and human genomes have been evolving separately for around 310 million years, numerous blocks of highly conserved sequence between the two include regions that are far away from any known genes. There is also

AGEING

The price of a longer life

The discovery of genes that are involved in controlling lifespan has led to speculation that, with a little genetic tweaking, we could all live for decades beyond our designated years. But — as anyone who has ever been told they've won a lottery they didn't enter will tell you — if something seems too good to be true, then it probably is. In a recent study, Nicole Jenkins and colleagues looked at mutations that extend lifespan in *Caenorhabditis elegans* and revealed the biological cost that comes with increased longevity.

The insulin-like growth factor type-I (IGF-I) signalling pathway has a conserved role in regulating lifespan. It has been suggested that altering components of this pathway might be one way to increase longevity without suffering any adverse consequences, as mice that carry mutations in the gene that encodes the IGF-I receptor (*Igfr1*) show no noticeable defects in metabolism, fertility or reproduction. However, in these studies mutants are generally reared separately from animals of other genotypes, so they are not subject to the effects of natural selection that would apply in natural surroundings.

To take natural selection into account, Jenkins and colleagues studied the fate of a *C. elegans* line with mutations in the *Igfr1* orthologue, *daf-2*, that was cultured alongside wild-type worms. Similar to their mouse counterparts, *daf-2* mutants show normal growth and fertility when reared in isolation. By contrast, in mixed populations, the *daf-2* mutation became extinct in just four generations, indicating a strong effect on fitness.

This seems to be at least partly due to effects on fertility. *daf-2* mutants produced an average of 22.5 eggs in the same time that wild-type worms produced 50. Applying these numbers to a fitness model predicted that *daf-2* mutants would become extinct

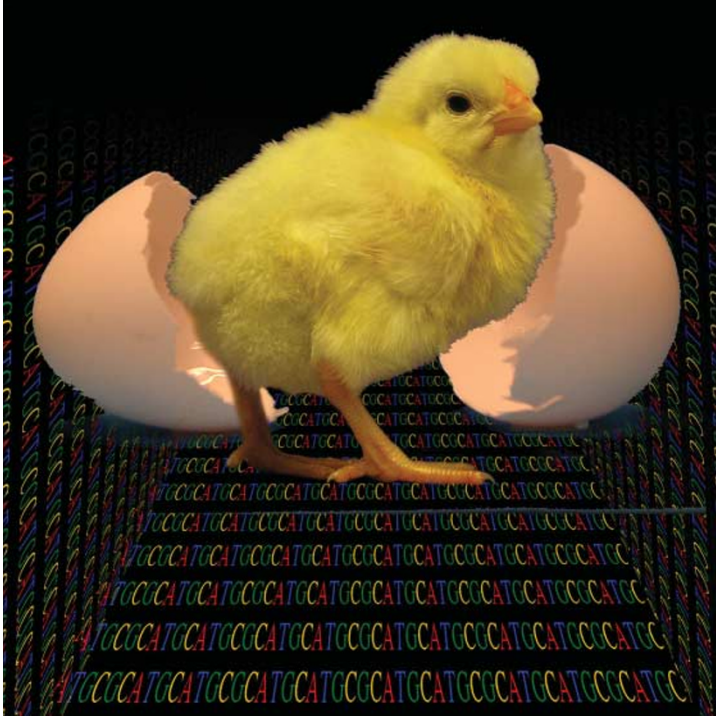

Image courtesy of Mary E. Delany, University of California, Davis. Graphic design courtesy of Washington University Medical Public Affairs.

at least one fact for you to share in the pub: the discovery of hundreds of olfactory-receptor genes contributes to a long-standing debate by indicating that chickens have at least the genetic capability for a well-developed sense of smell. Who says genomics can't be controversial?

Chris Gunter, Senior Editor, Nature

References and links

ORIGINAL RESEARCH PAPERS International Genome Sequencing Consortium. Sequence and comparative analysis of the chicken genome provide unique perspectives on vertebrate evolution. *Nature* **432**, 695–716 (2004) | International Chicken Polymorphism Map Consortium. A genetic variation map for chicken with 2.8 million single nucleotide polymorphisms. *Nature* **432**, 717–722 (2004) | Wallis J. W. *et al.* A physical map of the chicken genome. *Nature* **432**, 761–764 (2004)

FURTHER READING Schmutz, J. & Grimwood, J. Fowl sequence. *Nature* **432**, 679–680 (2004)

WEB SITES

AvianNET: http://www.chicken-genome.org

Chicken variation database: http://chicken.genomics.org.cn/index.jsp

within seven generations. So, although other fitness effects might also contribute to the even shorter time to extinction seen in the experiments, decreased fertility seems to have an important role.

This fits in with evolutionary models which suggest that increased longevity is selected against owing to adverse effects on reproductive fitness earlier in life. Given the conserved nature of the IGF-I pathway, it seems likely that this will apply to other species as well, reinforcing the need to learn more about the factors that determine lifespan before we can even consider manipulating our own.

Louisa Flintoft

References and links

ORIGINAL RESEARCH PAPERS
Jenkins, N. L., McColl, G. & Lithgow, G. J. Fitness cost of extended lifespan in *Caenorhabditis elegans*. *Proc. R. Soc. Lond. B* 24 November 2004 (doi:10.1098/rspb.2004.2897)

WEB SITE
Gordon Lithgow's Laboratory: http://www.buckinstitute.org/lithgow/

IN BRIEF

RNA SILENCING

A link between mRNA turnover and RNA interference in *Arabidopsis*.

Gazzani, S. *et al. Science* **306**, 1046–1048 (2004)

MicroRNA binding sites in *Arabidopsis* class III HD-ZIP mRNAs are required for methylation of the template chromosome.

Bao, N. *et al. Dev. Cell* **7**, 653–662 (2004)

These papers provide new insights into RNA-mediated silencing. RNA-dependent RNA polymerase (RdRP) promotes RNA interference in several species, but its substrate is unknown. Gazzani *et al.* showed that mutation of the *Arabidopsis thaliana XRN4* exonuclease gene promotes RdRP-dependent silencing of a transgene. Plants that lack both RdRP and XRN4 accumulate decapped transgene mRNA, implicating uncapped transcripts as RdRP substrates. Bao *et al.* investigated the regulation of the *A. thaliana PHB* and *PHV* leaf-patterning genes. Both genes are heavily methylated in wild-type plants, but this is reduced by mutation of microRNA binding sites that are present in *PHB* and *PHV* mRNAs, but not in the corresponding genomic sequences. MicroRNAs therefore seem to regulate expression of these genes by interacting with their transcripts to produce epigenetic changes at the genomic level.

EPIGENETICS

DNA methylation profiling of the human major histocompatibility complex: a pilot study for the human epigenome project.

Rakyan, V. K. *et al. PLoS Biol.* **2**, e405 (2004)

DNA methylation has a crucial function in vertebrate development, gene regulation and disease. The Human Epigenome Project (http://www.epigenome.org) aims to identify and catalogue the pattern of cytosine methylation across the human genome. As a prelude to this large-scale project, Rakyan and colleagues have analysed the DNA-methylation profile of the human major histocompatibility complex. The project, which involved the development of high-throughput analysis methods, revealed that most regions of the 90 genes studied were either hypo- or hypermethylated.

TECHNOLOGY

A reverse genetic, nontransgenic approach to wheat crop improvement by TILLING.

Slade, A. J. *et al. Nature Biotechnol.* 5 December 2004 (doi:10.1038/nbt1043)

Modifying the wheat genome is an attractive goal for agriculture and industry, but the size of this large, polyploid genome makes the application of transgenic methods particularly challenging. Ann Slade and colleagues have now applied a reverse genetic, non-transgenic method called TILLING to isolate 246 alleles of a gene (*GBSSI*) that is involved in starch biosynthesis, showing that this method can be used effectively for crop improvement. Plants with null alleles of *GBSSI* produce highly branched starches that have unique and commercially valuable properties.