Genes and social habits

An international team including Trust-funded researchers from the University of Leicester has studied patterns of sex-specific inheritance, and discovered that societal structure leaves its mark on our genes.

Parts of the human genome are inherited only through one parent: mitochondrial DNA comes from the mother, while fathers always contribute a Y chromosome to their sons. Previous genetic studies in large populations suggest that, on average, mitochondrial DNA types are more geographically spread, and thus that women move around more.

The researchers developed a mathematical formula that relates differences in sex-specific and regular DNA to population size and migration. They sampled a number of populations in Central Asia, including Tajiks, Kazakhs, Karakalpaks, Kyrgyz and Turkmen. Traditionally, most of these groups consist of herders organised into paternal descent groups that choose brides outside of their own social group. The Tajiks, in contrast, place equal importance upon male and female lines, and marry within their own social group, often to cousins.

The authors found the signature of the two different social organisations in the genomes of the current members of each society. As expected, the women seemed to move around more among the herders, as they live in their husbands' villages, far from their birthplaces. But more surprisingly, the calculations suggest that there is a larger effective population of women compared with men in these populations – meaning that, within populations, men are more genetically related than expected, because of the importance of paternal descent in their social organisation.

Since humans aren't the only ones with complex social dynamics, the methods in this study may also be useful for studying the ecology of animal species.

Ségurel L et al. Sex-specific genetic structure and social organization in Central Asia: insights from a multi-locus study. PLoS Genet 2008;4(9):e1000200.

Kyrgyz people in front of a yurt. *Laure Ségurel*

Q&A

Michelle Teng, now at MedImmune, Inc. in Cambridge.

In studies of G-protein-coupled receptors (important targets of many human diseases) and their ligands, Dr Michelle Teng – then working at the Wellcome Trust Sanger Institute – and colleagues have developed assays using the nematode worm *Caenorhabditis elegans*. In 2006, they showed that worms expressing human receptors in their sensory neurons can 'taste' and deliberately avoid soluble forms of the receptor's ligand. Now, the team has developed a feeding assay that can be used to test variants of the ligand.

What's new for this paper?

We've taken advantage of the fact that *C. elegans* eat bacteria. We give the worms a strain of *E. coli* called OP50. It's like cat food to them – they'd rather be eating something else, but we use it as it stops them growing too fast. This time, we've expressed the ligand in the bacteria. As our earlier paper showed that worms can taste soluble ligand, we reasoned they should be able to taste it when expressed in *E. coli*.

How does this feeding assay work?

We give the worms a choice between bacteria that express the test ligand (MIP-1ß) and bacteria that express something that does not trigger an avoidance response. We found that the worms specifically avoid eating the bugs that express the ligand; they only eat it when other food sources run out.

What did you find?

We generated a library of genetic variants of the MIP-1ß peptide, in which we mutagenised nearly every amino acid residue. Each mutant was tested in the feeding assay, and we identified 13 residues involved in the activation of human chemokine receptor 5 (CCR5), the receptor responsible for HIV entry into cells which also binds its native agonist, MIP-1ß. Of these 13 residues, we found four that had not been described before, despite detailed mutagenesis work in the 1990s.

How could this assay be used in the future?

The beauty of this system is that you don't have to purify the mutated ligand, you just express it in bacteria – so it's a really fast method for structure–function studies. You get a narrowed-down list of residues that are important in the receptor–agonist interaction, which you can then test in more conventional assays.

The assay could, in the future, facilitate the discovery of agonists from libraries of bacteria expressing different ligands, so it has potential for drug screening. The proteins/peptides we (and others) have expressed in bacteria are functionally active, so we could apply this feeding assay system to other ligands and other transgenic worms. I certainly hope other groups will try out the system.

How has the Trust helped you?

The Trust funded my postdoctoral fellowship at the Sanger, and my PhD, through a Wellcome Trust Prize Studentship. The Trust support is especially helpful as it allows postdocs to pursue their ideas in an independent fashion. If I wasn't at the Sanger, I don't think I would have been given the opportunity to develop a wacky idea and then work on it for three or four years.

What do you do outside of the lab?

I'm an endorphin addict: I have a black belt in tae kwon do and do lots of yoga, running and climbing.

Teng MS et al. Control of feeding behavior in C. elegans by human G protein-coupled receptors permits screening for agonist-expressing bacteria. Proc Natl Acad Sci USA 2008;105(39):14826–31.