IN BRIEF

RNA INTERFERENCE

RNA interference-mediated suppression and replacement of human rhodopsin *in vivo*.

O'Reilly, M. *et al. Am. J. Hum. Genet.* **81**, 127–135 (2007)

Mutational heterogeneity presents a challenge to the therapeutic correction of genetic disease. In mice carrying a dominant mutation in the rhodopsin gene, which is mutated in retinitis pigmentosa, the authors suppressed wild-type and mutant rhodopsin expression by RNAi. The simultaneous expression of a replacement rhodopsin gene that was refractory to RNAi owing to a modified codon composition resulted in the expression of functional rhodopsin. The same therapeutic molecules could be used to correct a range of rhodopsin mutations.

DEVELOPMENT

Transcription factor modularity in a gene-centered *C. elegans* core neuronal protein–DNA interaction network.

Vermeirssen, V. *et al. Genome Res.* 22 May 2007 (doi:10.1101/gr.6148107)

This study describes the mapping of a core network of transcription factors and their target genes in *C. elegans* sensory neurons, providing insights into how the architectures of such networks relate to their functions. The network consists of two distinct modules: one contains transcription factors that are involved in reproduction and target genes that are expressed in both neurons and other tissues, whereas the other is enriched for transcription factors with targets that are mainly expressed in neurons.

EPIGENETICS

DNA damage, homology-directed repair and DNA methylation.

Cuozzo, C. *et al. PLoS Genet.* 22 May 2007 (doi:10.1371/journal.pgen0030110.eor)

This work provides a link between DNA repair and DNA methylation. The authors showed that, in mouse and human cells, DNA double-strand breaks are repaired through homology-directed repair and half of the repaired molecules are marked by *de novo* DNA methylation. This occurs independently of the methylation status of the template DNA, and can silence the repaired gene. This mechanism can alter the overall expression of genetic information; therefore, if expressing the repaired gene is harmful, cells that inherit the silenced repaired gene have selective advantages.

TECHNOLOGY

Genome-wide mapping of *in vivo* protein–DNA interactions.

Johnson, D. S., Mortazavi, A., Myers, R. M. & Wold, B. *Science* 31 May 2007 (doi:10.1126/science.1141319)

A new method, ChIPSeq, involving chromatin immunoprecipitation and ultra-high-throughput DNA sequencing allows high-resolution genome-wide mapping of protein–DNA interactions. ChIPSeq has several advantages over methods that couple ChIP to microarray analysis: for example, it can be performed on any sequenced genome and single-copy sites that might be under-represented in microarrays are accessible. Through ChIPSeq, the authors identified 1,946 binding sites for the neuron-restrictive silencer factor (NSFR) and several previously unknown NSFR targets.

SOCIOGENETICS

Cheating gets you nowhere

Cooperative behaviour is susceptible to cheats — individuals who reap the benefits of collective behaviour but do not contribute their fair share will do better than altruists. It has been assumed that cooperation persists despite this because individuals tend to interact with their relatives, and reducing the fitness of relatives by cheating indirectly reduces an individual's own fitness; however, this has been difficult to demonstrate. Research on the social amoeba *Dictyostelium discoideum* has now shown experimentally that cheats do not prosper because of the high levels of relatedness in natural populations.

When food is scarce, solitary *D. discoideum* cells aggregate into a fruiting body that distributes spores. However, only 75% of the aggregating cells become spores — the other 25% form the body's stalk and altruistically die. Mutants that are less likely to contribute to the stalk are at a selective advantage, and one such mutant is *fbxA*$^-$.

The authors showed that *fbxA*$^-$ cells had a fitness advantage when introduced into a wild-type population at any frequency, but also that the spore production of the whole fruiting body declined sharply with an increase in *fbxA*$^-$ frequency. From this data they showed that, in fruiting bodies in which more than 25% of the cells were cheats, *fbxA*$^-$ cells are less fit than wild-type cells are in the absence of cheats. This means that if cells are more likely to make fruiting bodies with their relatives — in other words, if the level of relatedness in the population is high — different fruiting bodies will have different fitnesses depending on whether they contain a clone of cheats. Cheats will be selected against because the bodies in which they participate will do less well than predominantly wild-type ones.

So, what are the levels of relatedness in natural populations? The authors showed that most fruiting bodies consisted of just one clone. The average relatedness within fruiting bodies was more than 0.86, which from their experiments above is sufficient to put the cheats at a disadvantage. As expected, therefore, they did not find any *fbxA*$^-$ cheats in the natural populations that they studied, despite the huge selective advantage of such mutants in low-relatedness populations.

It remains unclear why relatedness is so high in *D. discoideum* populations, higher even than in eusocial insects, but it does explain how cooperative behaviour can be maintained. This has been difficult to show in other multicellular species, for which relatedness is easily measured but in which no cheater mutations are available for study.

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ORIGINAL RESEARCH PAPER
Gilbert, O. M. *et al.* High relatedness maintains multicellular cooperation in a social amoeba by controlling cheater mutants. *Proc. Natl Acad. Sci. USA* **104**, 8913–8917 (2007)
FURTHER READING Robinson, G. E., Grozinger, C. M. & Whitfield, C. W. Sociogenomics: social life in molecular terms. *Nature Rev. Genet.* **6**, 257–270 (2005)