As the authors say, “conceptually, [PSI⁺] presents a new framework for phenotypic plasticity”. The [PSI⁺]-based mechanism means that organisms need not ‘wait’ for suitable mutations to occur when the environment changes; instead, they can draw on already existing, hitherto silent, genetic variation. Taken together with the authors’ previous findings that heat-shock proteins can also reveal hidden genetic variation, Lindquist and colleagues prompt us to re-examine protein folding mechanisms, for they could be unexpectedly important in translating genotypes into phenotypes.

Magdalena Skipper

References and links

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CHROMOSOME BIOLOGY

Global architecture

Models of how DNA is packaged into chromosomes in a series of compaction steps have been around for many years. But, with the exception of specific loci such as that of β -globin, we had little knowledge of how higher orders of chromatin might affect gene distribution and expression, until now. A recent paper from Wendy Bickmore and colleagues provides a global, genome-wide analysis of the chromatin-fibre structure and its effects on the genome itself, including its expression and perhaps its evolution.

The authors’ goal was to map compact and open chromatin-fibre structures onto the whole human genome. To achieve this, they digested the chromatin with micrococcal nuclease into fragments of 10–30 Kb, on average, which were then separated by sucrose-gradient sedimentation. Their distribution in the genome was analysed by hybridization to metaphase chromosomes using fluorescence *in situ* hybridization and, to obtain a greater resolution and to link to the DNA sequence itself, to genomic microarrays.

This set of experiments, conceptually simple but performed on a massive scale, allowed Bickmore and colleagues to reveal some interesting, and at times surprising, facts about genomic architecture and its effects. They found that some, but not all, human satellite repeats are in compact chromatin fibres and that gene-poor euchromatin is packed in chromatin fibres with similar levels of compaction to heterochromatin, indicating that there might not be a simple structural distinction between euchromatin and heterochromatin, at least at the chromatin-fibre level. As expected, the most gene-rich chromosomes, such as 16, 17, 19 and 22, are highly enriched in open chromatin. But, interestingly, using genomic

microarrays to take a closer look — and in one case, a chromosome-22q-specific array — the authors discovered that the transitions between open and closed chromatin structures along a chromosome are sharp rather than gradual, suggesting that there are distinct boundaries.

Although, in general, open chromatin fibres tend to replicate early, high-resolution analysis on chromosome 22q indicates that there is no direct functional link between replication and this level of chromatin organization. Neither is there a simple relationship between gene expression and chromatin-fibre state. As open chromatin is seen where there is no transcription, transcription cannot itself serve to open up the chromatin fibres. Because the authors see enrichment of open chromatin fibres in gene-rich domains, and not just where transcription is active, they propose that open chromatin fibres might create an environment that facilitates transcription, which could account for the clustering of widely expressed genes in these regions.

In addition, the authors make an interesting cytological observation — that domains of open chromatin fibres are physically decondensed in the nucleus and lie outside chromosome territories.

So, Bickmore and co-workers have given us the first chromatin-fibre structure map of the human genome. Having already extracted a wealth of information from it, they suggest that it could serve as a “...framework on which to overlay other epigenetic information”. They hint at the end of their discussion that their next goal might be to extend this analysis to different cell types and species.

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WEB SITE

Bickmore’s laboratory:
<http://www.hgu.mrc.ac.uk/Research/Bickmore/>