32 °C. This is a much more useful activation temperature than that of many other technologies, although similar activation temperatures have been reported for other systems based on smart polymers[8].

The superior modulatory properties were achieved by paying close attention to the conditions used to synthesize the microgels. Li *et al.* developed conditions that allowed the generation of microgels that have an extremely uniform density of crosslinks between polymer chains, and a structure that allows the particles to swell greatly in water. The authors also fine-tuned the reactions to produce microgels that swell to a diameter of 1.4 micrometres at 25 °C. The resulting particles scatter very little light, and are highly transparent below temperatures of about 32 °C. Crucially, however, the microgels collapse and expel water at higher temperatures, whereupon they scatter light at wavelengths primarily dictated by their collapsed-state diameter and refractive index.

Smart windows need to scatter the near-infrared (NIR) wavelengths that are predominantly responsible for heating up spaces. The collapsed microgels in Li and colleagues' windows have a diameter of 546 nm and a refractive index of about 1.4 at NIR wavelengths — which means that they scatter NIR wavelengths effectively. They also scatter shorter wavelengths in the ultraviolet and visible regions of the spectrum, which means that the activated windows are opaque to the human eye. Most importantly, when Li and co-workers exposed a chamber fitted with a microgel-based smart window to a solar simulator (a device that produces radiation that approximates sunlight), they observed that the temperature increase in the chamber was significantly reduced compared with the increase obtained when a standard double-pane window was fitted.

Li *et al.* also showed that the windows could be activated and inactivated at least 1,000 times with no noticeable systematic loss in performance, and are also seemingly unaffected by freezing. As an added benefit, visible light scattered by the windows could, in principle, be used to illuminate a room, reducing the need for interior lighting and thereby saving even more energy. Finally, the cost of generating the microgels should not prohibit the commercialization of the technology. Taken together, these properties suggest that Li and colleagues' smart windows are suitable for real-world applications.

"The use of energy-efficient building materials could have a profound impact for society."

Nevertheless, there are some drawbacks to this technology. For example, the inability to darken the windows on demand means that they would be transparent at night when temperatures are cool, reducing privacy and, if used in bedrooms, potentially disrupting people's sleep cycles. These issues can, of course, be addressed by using curtains, but this would be inconvenient at best. Moreover, because the activated windows are opaque, users would be unable to see out of them. The bottom line is that this technology is one option out of many, and will not be the perfect solution for all situations.

In my view, smart windows should allow users to choose whether infrared and/or visible light enters a room. For example, windows could actively and continuously prevent NIR sunlight from entering a space when activated by a user, but still allow visible light to enter, so that the room could be warmed and illuminated. If windows could self-regulate their behaviour in a user-defined manner, then the technology would be perfect. Some emerging smart-window technologies can also generate energy while modulating sunlight[9], although much more development is needed to make them commercially viable. Finally, it should be noted that although energy-efficient windows can minimize the energy used by buildings, other energy-efficient building materials need to be developed in parallel. Together, they could have a tremendous impact on the world. ■

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GENOMICS

A chromosomal hub to tell odours apart

A study shows that a multi-chromosomal hub assembles in mouse olfactory neurons to ensure that only one odour-sensing receptor is expressed in each neuron — a feature essential to odour discrimination. SEE ARTICLE P.448

FRANÇOIS SPITZ

Mammals can discriminate between a vast number of volatile compounds — perhaps more than a trillion[1]. This extraordinary capacity is encoded by a repertoire of hundreds of olfactory-receptor genes, distributed in small groups that are present on almost all chromosomes[2]. To ensure that the response to individual odours is specific, each olfactory sensory neuron (OSN) expresses a single, randomly selected olfactory-receptor gene. On page 448, Monahan *et al.*[3] show that, in the nuclei of mouse OSNs, certain regions of multiple chromosomes assemble in a structure that controls the expression of the full repertoire of olfactory-receptor genes in the nose, while making sure that each cell expresses only one type of receptor. These exciting findings show that interchromosomal interactions can have a determinant role in regulating gene expression.

The expression of vertebrate genes is regulated by activating genomic elements called enhancers. Enhancers can be located far from the genes themselves[4], but they are typically present on the same chromosome as the gene they regulate (*cis* interactions). These regulatory interactions are mediated by transcription factors, assisted by other proteins, and require the participating proteins and DNA elements to be closely connected in the nucleus.

Molecular techniques, such as Hi-C (ref. 5), that capture the 3D folding of chromatin (DNA and associated proteins) have revealed that the interactions between genes and their enhancers occur in compact structures called topologically associating domains (TADs) that organize chromosomes into distinct *cis* neighbourhoods[6]. Hi-C analyses have also uncovered specific interactions between genes and genomic elements located much farther away from each other, in different TADs and even on different chromosomes (these are called *trans* interactions)[7,8]. These observations raised the possibility that *trans* interactions influence gene expression. However, because the frequency of *trans* interactions is so much lower than that of *cis* interactions, their functional relevance has remained debatable.

Olfactory-receptor genes were reported to form interchromosomal clusters more than a

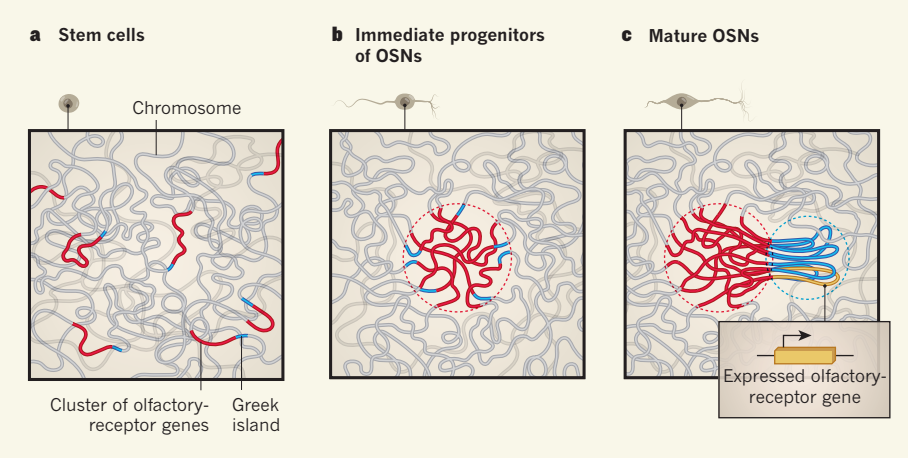

Figure 1 | Role of interchromosomal interactions in the expression of olfactory-receptor genes. Mammals rely on hundreds of olfactory-receptor genes to identify odours. These genes are grouped in clusters that are present on most chromosomes. Most clusters are associated with a regulatory region called a Greek island. **a**, **b**, Monahan *et al.*[3] show that, in stem cells (**a**), the clusters of olfactory-receptor genes are dispersed, but that in the immediate progenitors of olfactory sensory neurons (OSNs) (**b**), these clusters and their Greek islands form an aggregate (red dotted circle) in which gene expression is repressed. **c**, They further show that, in mature OSNs, the recruitment of the LHX2–LDB1 protein complex (not shown) by Greek islands leads to the formation of a distinct interchromosomal hub (blue dotted circle), where the Greek islands collectively activate and maintain the expression of a single olfactory-receptor gene per cell. (Adapted from Extended Data Fig. 10 of ref. 3.)

decade ago[9]. But the role of these clusters was unclear because deletion of potential *trans* enhancers affected only the expression of olfactory genes on the same chromosome[10]. Recently, researchers from the same group as Monahan *et al.* identified 63 potential olfactory-receptor-gene enhancers — which they named Greek islands — distributed across 16 of the 20 chromosomes of mice[11,12]. In the current paper, Monahan and colleagues provide a comprehensive and functional high-resolution analysis of the 3D organization of olfactory-receptor-gene clusters and Greek islands during the differentiation of mouse OSNs.

The authors used Hi-C to analyse the structural conformation of chromosomes in mature OSNs, the immediate progenitors of OSNs and the stem cells that give rise to these neurons. They observed interactions between olfactory-receptor-gene clusters from different chromosomes in OSNs and their immediate progenitors, but these interactions were nearly absent in stem cells (Fig. 1). The interactions involved the entire gene clusters, and probably correspond to the aggregation of olfactory-receptor genes in an area of dense chromatin (heterochromatin) that has been seen using microscopy[13]. This type of chromatin is associated with repressed gene expression, and probably helps to prevent the expression of more than one olfactory-receptor gene in each OSN.

Monahan and colleagues also report the presence of strong and focal reciprocal *cis* and *trans* interactions between Greek islands in mature OSNs. They go on to show, using cells from transgenic mice, that the Greek-island hub includes the active olfactory-receptor gene expressed in these particular OSNs, but not the other, silenced olfactory-receptor genes. They propose that the aggregation of olfactory-receptor genes in a 'compartment' of heterochromatin brings the Greek islands from different chromosomes together, and that this proximity favours their subsequent assembly into an active Greek-island hub that is separated from the repressive environment of the olfactory-receptor-gene aggregate. Deletion of the gene that encodes the protein LHX2, a transcription factor bound to Greek islands, or of the gene that encodes LDB1, a co-factor of LHX2, strongly reduced interactions between Greek islands and led to the loss of olfactory-receptor-gene expression. The authors conclude that these factors are key actors in the formation of the interchromosomal structure they identified.

Remarkably, Greek islands seem to act primarily as structural organizers throughout this biological process, folding chromosomes into specific repressive and activating structures, and guiding olfactory genes to these structures. Indeed, they might work as textbook enhancers that activate the transcriptional machinery at the start sites of gene transcription only in the final step of selection and activation of olfactory-receptor genes, by keeping the selected olfactory-receptor gene robustly expressed.

But why would olfactory-receptor genes require such a large number of elements to regulate their expression, whereas most other genes need only a few? One possibility is that the transition of olfactory-receptor genes from a repressed, heterochromatic state to an active state requires many LHX2 binding sites to ensure that enough chromatin-remodelling proteins, which are necessary for this transition, are recruited. Alternatively, the use of 'weak' enhancers that only function as activators collectively might limit the possibility that more than one olfactory-receptor gene is expressed in a cell, and also avoid favouring the expression of olfactory-receptor genes close to 'strong' enhancers. The principle underlying this mechanism would be similar to the use of transcription-factor binding sites that have low or modest affinity at enhancers to achieve specificity of gene expression[14].

Monahan and colleagues' findings emphasize the diversity of ways in which genomic elements can influence gene expression, and call attention to the limits and biases of the current assays used to identify and characterize such elements. They further highlight the role of 3D chromatin assemblies in gene regulation. The discovered *trans*-chromosomal hub might be similar to a TAD in the way it creates a local activating neighbourhood, but it is assembled by a distinct mechanism.

It remains unclear whether interchromosomal interactions similar to those displayed by olfactory-receptor genes in OSNs occur frequently between other genomic regions in other cell types, although *trans* interactions have been reported in a few other cases of stochastic regulation of gene expression[15,16]. Interchromosomal interactions might therefore be primarily a mechanism for generating diversity in a population of otherwise indistinguishable cells. Because their characteristic signatures are masked by cell-population averages, these cases are difficult to identify. The development and improvement of techniques for analysing gene expression and chromatin conformation in single cells might, in the near future, reveal new examples of 3D genomic structures and functional *trans*-regulatory interactions. ■

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