IN BRIEF

DNA REPAIR

Chromatin context affects DNA repair pathway

To determine whether the balance of double-stranded DNA break repair pathways is affected by chromatin context in K562 cells, Schep et al. used Cas9 to cut a reporter that produces pathway-specific detectable repair 'scars', along with a version of their previously published multiplexed reporter assay to conduct whole-genome probing at >1,000 genomic sites. The researchers found a strong bias towards non-homologous end joining in euchromatin and a moderate bias towards single-stranded template repair in heterochromatin. Microhomology-mediated end joining was favoured in specific types of heterochromatin, particularly H3K27me3-marked regions. Although this method cannot detect homologous recombination, which does not produce repair scars, this work shows that Cas9 editing efficiency is reduced specifically in heterochromatin featuring H3K9me2, lamina-associated domains and late replication.

ORIGINAL ARTICLE Schep, R. et al. Impact of chromatin context on Cas9-induced DNA double-strand break repair pathway balance. *Mol. Cell* https://doi.org/10.1016/j.molcel.2021.03.032 (2021)

TELOMERES

Alternative splicing regulates telomerase repression

Telomere length is a tightly regulated determinant of cellular lifespan that is reset during the blastocyst stage of embryogenesis and maintained in pluripotent cells. Penev et al. report that levels of human telomerase reverse transcriptase (hTERT), the enzyme responsible for building telomeres, are primarily controlled by an alternative splicing event regulated by the mRNA splicing cofactor SON (although transcriptional silencing also contributes to hTERT repression). The researchers showed that in differentiated cells, *TERT* mRNA transcripts lack exon 2 and are degraded, whereas in inner blastocyst cells, pluripotent cells and also in some cancer cells, *TERT* mRNA transcripts include exon 2 and are translated. Dysregulation of *TERT* alternative splicing is therefore implicated in some cancers and in disorders of telomere biology.

ORIGINAL ARTICLE Penev, A. et al. Alternative splicing is a developmental switch for hTERT expression. *Mol. Cell* https://doi.org/10.1016/j.molcel.2021.03.033 (2021)

GENOME STABILITY

Ribosomal protein genes as sensors of aneuploidy

In *Drosophila*, cell competition eliminates cells bearing inactivating mutations in ribosomal protein (Rp) genes from the imaginal disc. As Rp genes are distributed throughout the genome, aneuploidy also differentially alters Rp gene copy number. To determine whether aneuploid cells are eliminated by cell competition, Ji et al. used targeted recombination to generate chromosomal excisions resulting in segmental aneuploidy. Whereas aneuploid cells with either normal Rp gene dosages or inactivated cell competition pathways survived and contributed to adult tissue, those with altered Rp gene dosages were eliminated by cell competition, specifically via the RpS12–Xrp1 pathway. Interestingly, cells with segmental aneuploidy of *eIF2g* were also eliminated, implicating this transcription factor in cell competition. Overall, the researchers estimated that cell competition removed 58–86% of cells with damaged genomes, which could otherwise become neoplastic.

ORIGINAL ARTICLE Ji, Z. et al. Cell competition removes segmental aneuploid cells from *Drosophila* imaginal disc-derived tissues based on ribosomal protein gene dose. *eLife* **10**, e61172 (2021)

Journal Club

PLANT GENETICS

PURPLE TOMATOES, BLACK RICE AND FOOD SECURITY

Rice grains are a staple food source in many parts of the world. They are rich in diverse nutrients, including protein, unsaturated oil, minerals, vitamins, dietary fibre, flavonoids and polysaccharides, among others. These nutrients are present in the pericarp, seed coat, aleurone, germ and endosperm. Yet, for thousands of years, culinary tastes have preferred polished rice, which is more palatable but discards ~80% of the nutrients and beneficial components of the grain as bran.

In 2008, Butelli et al. published a paper in *Nature Biotechnology* reporting a transgenic purple tomato with greatly enhanced levels of anthocyanins. This study showed that the lifespan of cancer-susceptible *Trp53*$^{-/-}$ mice fed a diet supplemented with such tomatoes was extended by 28% relative to the average lifespan for this mouse strain. It has been proposed that the health benefits of anthocyanins are a direct effect of their function as antioxidants, and an indirect effect of their ability to activate endogenous antioxidant defence systems and signalling pathways.

> "black rice, in particular, is considered in Chinese legend to be a panacea for health and longevity"

As a rice researcher, I immediately considered the implications of this paper in relation to the role of rice in human nutrition and switched my research focus from generating high-yield rice plants to improving the nutritional value of rice grains.

Rice grains exist in many different colours, but black rice, in particular, is considered in Chinese legend to be a panacea for health and longevity. Indeed, numerous studies have shown that water-soluble extracts are protective against a wide range of non-communicable diseases, including cancers, cardiovascular diseases, diabetes mellitus and metabolic syndrome. Red rice and black rice obtain their colouring from proanthocyanins and anthocyanins in the pericarp and seed coat of the grain. Thus, consumption of whole-grain rice will be necessary to maximize its health benefits. Moreover, eating the whole grain would amount to a >30% increase in the edible portion relative to polished rice, thereby also enormously reducing the pressure on demand and contributing to food security. But, at the time, the available varieties of black rice were particularly unpalatable and difficult to cook as whole grains, presenting a major obstacle to their consumption.

Since then, advances in genomic research have made it feasible to breed black rice varieties with improved texture and flavour. In particular, my research group has found landrace varieties of black rice with good cooking quality and palatability, and we have applied genomic breeding technologies to increase their yield and their resistance to disease and insects. These improved rice lines have now been under field trials in multiple locations with promising results.

Thus, achievements in one system — in this case, purple tomatoes — can point to beneficial genetic improvements in another, black rice. Such approaches may hold the key to unlocking the huge unmined treasury of plant genomes for improving human nutrition.

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ORIGINAL ARTICLE Butelli, E. et al. Enrichment of tomato fruit with health-promoting anthocyanins by expression of select transcription factors. *Nat. Biotechnol.* **26**, 1301–1308 (2008)