conflict of interest with her team of helpers.

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Polyploidy: Doubling up for Evolutionary Success

How does having more than one genome give plant species an advantage when it comes to adaptive evolution? Recent molecular studies have shown that altered patterns of gene expression may offer polyploids a broader phenotypic range than that of their progenitors.

Matthew Hegarty and Simon Hiscock

Polyploidy, or the presence of multiple genomes within a single nucleus, is a widespread phenomenon in the plant world. It is estimated that nearly 70% of plant species have a polyploid history and many plants once thought to be diploid are now known to be ancient polyploids. The abundance of polyploids indicates that the possession of multiple genomes confers an evolutionary advantage, probably through increased fitness afforded by fixed heterozygosity and because of the greater pool of genes and alleles available for selection. Polyploids can arise in two ways: autopolyploidy occurs when a single individual undergoes a chromosome doubling event (for example, due to unreduced gamete formation); and allopolyploidy — an important mechanism of abrupt speciation in plants — results from hybridisation between two related species with differing chromosome complements [1].

An immediate question is what is the effect of polyploidy on gene expression? A number of recent studies (largely focussing on allopolyploidy) have addressed this question, including that just published in *Current Biology* by Liu and Adams [2] on allopolyploid cotton (*Gossypium hirsutum*), which shows for the first time that different parental gene copies can be preferentially switched off in response to external stimuli. In previous work, Adams and co-workers [3,4] noted that certain genes in cotton are expressed from different parental genomes in a tissue-specific manner (Figure 1). In their new study [2], using the *AdhA* gene, they show alterations to parental gene expression in a developmentally regulated manner and, crucially, that partitioning of parental gene expression can occur in response to abiotic stimuli. By partitioning ancestral expression patterns in different tissues or in response to environmental stresses, duplicated genes become subfunctionalised and thus undergo separate processes of genetic evolution. This enables the retention of duplicate gene copies. On a larger scale, the potential of this mechanism to allow the polyploid to survive environmental conditions that are unfavourable to the parents could facilitate the process of ecological speciation.

The work of Liu and Adams [2] has important implications for other phenomena seen in polyploids, all of which are potential mechanisms driving plant speciation and evolution. Subfunctionalisation may well be a factor in the emergence of transgressive characteristics, whereby the phenotype of a hybrid individual exceeds the range of either parent [5]. This has been demonstrated primarily in non-polyploid hybrid species, most notably hybrid sunflowers (*Helianthus* spp.) [5]. Three species of *Helianthus* from North America were found to be the result of hybridisation between the same two parental taxa, *H. annuus* and *H. petiolaris*. All three hybrid species grow in habitats too extreme for either parent to survive, due to transgressive segregation of phenotypic traits associated with parental quantitative trait loci (QTLs) fixed in opposite directions [5].

While transgressive phenotypes can be explained by inheritance of novel combinations of parental
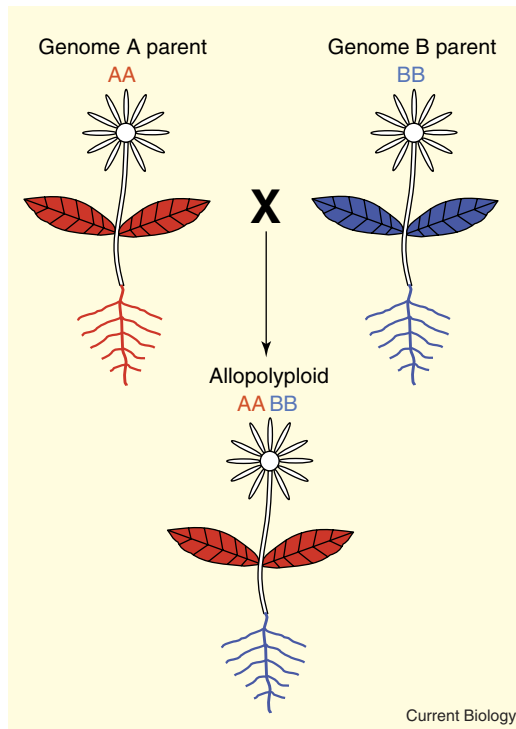
Figure 1. Differential expression of parental gene copies in allopolyploids.

Hybridisation, either involving unreduced gametes or later chromosome doubling, results in the formation of an allopolyploid individual. A gene expressed in both leaves and roots in the parental species shows expression partitioning in the allopolyploid hybrid, with the A genome copy expressed in leaves and the B genome copy in roots.

alleles, immediate changes to expression of different parental gene copies (homoeologues) could produce a similar effect if they allow the polyploid to "put the best foot forward" by pre-adapting it to a novel niche. Importantly, Liu and Adams [2] show that differential homeologous expression occurs in resynthesised *Gossypium* hybrids, suggesting that a new hybrid individual may indeed be immediately pre-adapted for survival in a different ecological niche, provided that these changes are stable. Indeed, work on synthetic allohexaploid *Senecio cambrensis* has demonstrated that polyploidisation can result in an immediate and stable change in levels of gene expression relative to its parental taxa *S. squalidus* and *S. vulgaris* and their intermediate triploid hybrid *S. x baxteri,* and some of these expression patterns are transgressive [6,7]. Similar non-additive changes to gene expression were observed in synthetic *Arabidopsis* allopolyploids [8], although in this case the authors concluded polyploidisation had little impact on expression compared to hybridisation. However, a similar study [7] on synthetic allohexaploid *Senecio cambrensis*, in which the

two processes of hybridization and polyploidization are separated temporally, suggests that polyploidy does indeed have a distinct, secondary effect on transcription.

What then are the mechanisms by which these rapid and reproducible changes to gene expression arise in newly formed polyploids? Current understanding of transcriptional and post-transcriptional control of gene expression in plants suggests a number of possibilities. In the case of allopolyploids, the hybrid origin of the polyploid means that genetic loci may now be under the control of a novel combination of regulatory factors [9]. This has been demonstrated as a mechanism for novel patterns of gene expression in *Drosophila* hybrids [10] and so could play a role in any hybrid system. Many, though not all, hybrid plants are also known to undergo extensive chromosomal rearrangement within a few generations of formation [11]. This could lead to different parental regulatory elements being brought from *cis* to *trans* relative to the genes they control. Gene dosage effects may also play a role in altering gene expression in polyploids,

particularly in the case of regulatory networks, which are generally dosage-dependent [9].

Epigenetic modification of gene expression is another mechanism by which polyploids may differ from their progenitors. Histone acetylation, DNA methylation and microRNA activity are all well-known, interrelated processes by which plants can modulate gene expression. Of these, histone acetylation and DNA methylation have been shown to be associated with changes to gene expression in allopolyploids, while microRNA activity can currently only be inferred. Changes to flowering time in synthetic *Arabidopsis* allotetraploid lines were found to be caused by *trans*-activation of the *FLC* allele from *A. thaliana* by the *FRI* allele from *A. arenosa* via acetylation and methylation of histone H3, resulting in a late-flowering phenotype [12]. Large-scale changes to DNA methylation have been frequently linked to polyploidy, as demonstrated in *Arabidopsis* [13], *Spartina* [14] and *Brassica* [15]. Histone acetylation and DNA methylation are known to be dynamic, reversible processes which can be triggered in response to a number of internal and external signals [16,17] and are both linked to the phenomenon of nucleolar dominance — the silencing of one parental set of ribosomal RNA genes irrespective of maternal or paternal status — which is commonly associated with hybridisation and polyploidy [18]. It is important to note, however, that neither large-scale genome rearrangement nor DNA methylation have yet been observed in the synthetic *Gossypium* allopolyploids studied by Liu and Adams [19]. Nevertheless, this does not rule out the possibility that small numbers of particular genes are silenced — such as those involved in regulatory networks — leading to a larger 'knock-on' effect.

A further key question is do these large-scale changes to gene expression observed in polyploids have any impact at the phenotypic level? Anyone who has attempted to create an antisense plant will know that it is possible to remove

upwards of 80% of the messenger RNA for a particular gene and still get a 'normal' plant, because mRNA levels are not always proportional to the amount of protein actually produced (or required). The possibility exists, therefore, that the alterations in gene expression observed in polyploids are compensated for at the translational level. Logic, however, suggests that this is probably not the case, because of the phenotypic success of most polyploids compared to their progenitors, and recent evidence from proteomic studies supports this assumption. In a study of synthetic *Brassica* allopolyploids, Albertin *et al.* [20] discovered a large number of proteins displaying non-additive changes to expression when compared to the parental taxa (305 in stem, 200 in root). They then undertook an *in silico* gene expression analysis to determine whether these proteins were restricted to a particular grouping, such as cellular function and/or localisation, and found that, as with genes identified in transcriptional expression studies, this was not the case. Similarly, Albertin *et al.* [20] found that different proteins within the same complex could have their expression altered in opposing directions — again, as observed in transcriptional studies.

Recent studies therefore suggest that the process of polyploidisation, whether incorporating a hybridisation event or not, has a large-scale impact on gene expression in the new individual, thereby providing raw material upon which selection can act. Small wonder, then, that polyploid species are so numerous — in evolutionary terms, it would seem that two genomes are indeed better than one.

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Human Genetics: The Hidden Text of Genome-wide Associations

Genome-wide association studies are finally leading geneticists straight to the genetic susceptibility factors for complex diseases. Several challenges lie ahead, including translation of the findings into practical public health outcomes, and integrating genetic analysis with broader biological understanding.

Greg Gibson[1] **and David B. Goldstein**[2]

Human genetics is in the midst of a revolution. Testing for association between hundreds of thousands of polymorphisms in several thousand unrelated cases and controls allows the genome to be scanned in an unbiased manner for the major susceptibility variants for complex diseases. Up until eighteen months ago only a handful of gene variants had been securely associated with any common diseases and the majority of published claims of association were at best unsubstantiated, but