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The genetic colinearity of rice and other cereals on the basis of genomic sequence analysis

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Small segments of rice genome sequence have been compared with that of the model plant *Arabidopsis thaliana* and with several closer relatives, including the cereals maize, rice, sorghum, barley and wheat. The rice genome is relatively stable relative to those of other grasses. Nevertheless, comparisons with other cereals have demonstrated that the DNA between cereal genes is highly variable and evolves rapidly. Genic regions have undergone many more small rearrangements than have been revealed by recombinational mapping studies. Tandem gene duplication/deletion is particularly common, but other types of deletions, inversions and translocations also occur. The many thousands of small genic rearrangements within the rice genome complicate but do not negate its use as a model for larger cereal genomes.

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Abbreviations

a1	*anthocyaninless1*
adh1	*alcohol dehydrogenase1*
LTR	long terminal repeat
sh2	*shrunken2*

Introduction

Compared to other grasses and cereal crops, rice has a small genome, a large research community, and exceptional agricultural importance. Rice researchers have developed a comprehensive array of physiological, molecular, genetic, and genomic tools that allow the precise characterization of rice genome organization and gene function. The landmark draft sequences of the *indica* and *japonica* rice genomes published in 2002 [1•,2•], along with the more complete draft sequence that is being rapidly developed by the International Rice Genome Sequencing Project ([3]; http://rgp.dna.affrc.go.jp), have provided a powerful new resource for studies in rice. The highly conserved gene order and gene content within the cereals indicate that rice research can greatly benefit other grass research programs.

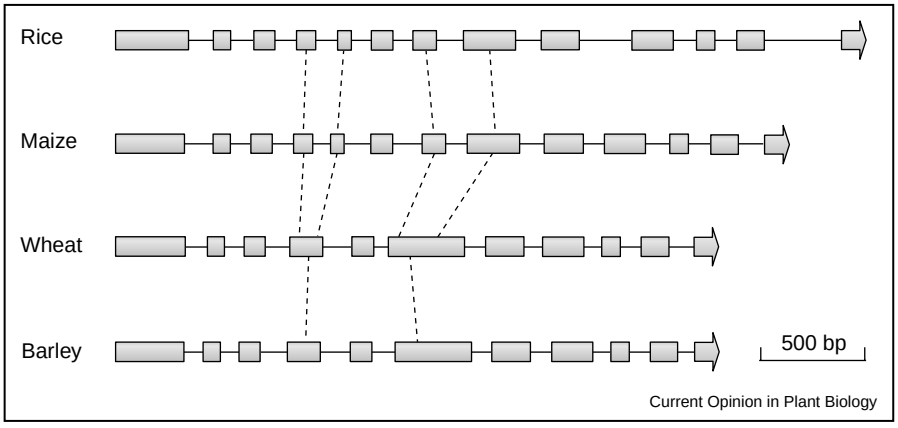
Initial studies of the organization of grass genomes indicated that individual rice chromosomes were highly colinear with those of maize, barley, wheat and other grass species [4–7]. These studies led to the prediction that grasses could be studied as a single syntenic genome [8,9]. Therefore, if the ortholog of a studied gene could be confirmed by comparative genetic maps, then knowledge acquired from one species could be compared to the results of similar experiments in another species. This unified grass genome model has had a substantial effect upon plant biology, but has not yet lived up to its potential [10]. There appear to be two major reasons for the relatively slow application of this approach. First, genomic sequence data are largely lacking for grass species other than rice. Second, the colinearity of gene order and content observed at the recombinational map level is often not observed at the level of local genome structure [11•,12•]. In this review, we describe recent advances in and the current state of genomic sequence comparison in the cereals, utilizing rice as the reference genome.

Conservation of gene structure in rice and other grasses

One of the standard and most powerful tools of molecular biology is the ability to efficiently compare the sequence of any gene with the sequences of all previously characterized genes. Comparative genetics has been facilitated by the development of massive databases, efficient query and comparison software, and ever-improving computers.

Many of the first genes to be sequenced in rice and other grasses were represented by abundant mRNAs (e.g. those encoding storage proteins, photosynthetic proteins and so on). Thus, members of the same gene families (e.g. paralogs), including those that mapped to the same genomic position and thus were derived by vertical descent from a common ancestral gene (i.e. orthologs), were often cloned and analyzed in multiple species. Comparisons of gene family members within and between species yielded the expected result, that is, that the genes were most highly conserved between the most closely related species. Moreover, sequence conservation was greatest in the protein-coding portions of the exons. Additional short sequences were also conserved outside of the coding exons, some of which were presumably parts of the regulatory regions (e.g. promoters) [13] whereas others were of unknown functional significance [14].

Figure 1



Intron number variation but exon content conservation in the *Waxy* genes of several cereal species. Boxes represent exons and lines represent introns, whereas the arrowheads indicate transcriptional orientation. Dotted lines connect two exons in rice and maize that have been fused by intron loss in the Triticeae lineage that gave rise to barley and wheat.

Most of the species whose gene sequences have been compared to those of rice shared a common ancestor with the *Oryzae* more than 50 million years ago. Little research has involved closer rice relatives. After a separation of more than 50 million years, coding exon sequences and intron/exon boundaries are highly conserved, but intron sequences, 5′-leader sequences and 3′-trailer sequences show little convincing homology across species [15,16]. One or more introns may be missing from an orthologous gene in some of the compared species. For instance, Figure 1 depicts comparisons of published sequences of the *Waxy* locus. These comparisons suggest that two different introns were lost from *Waxy* within the Triticeae lineage before the ancestors of barley and wheat diverged about 10–14 million years ago. These differences in intron presence/absence are usually precise removals that have little or no effect on the sequence of the encoded protein.

Colinearity of adjacent genes in the cereals

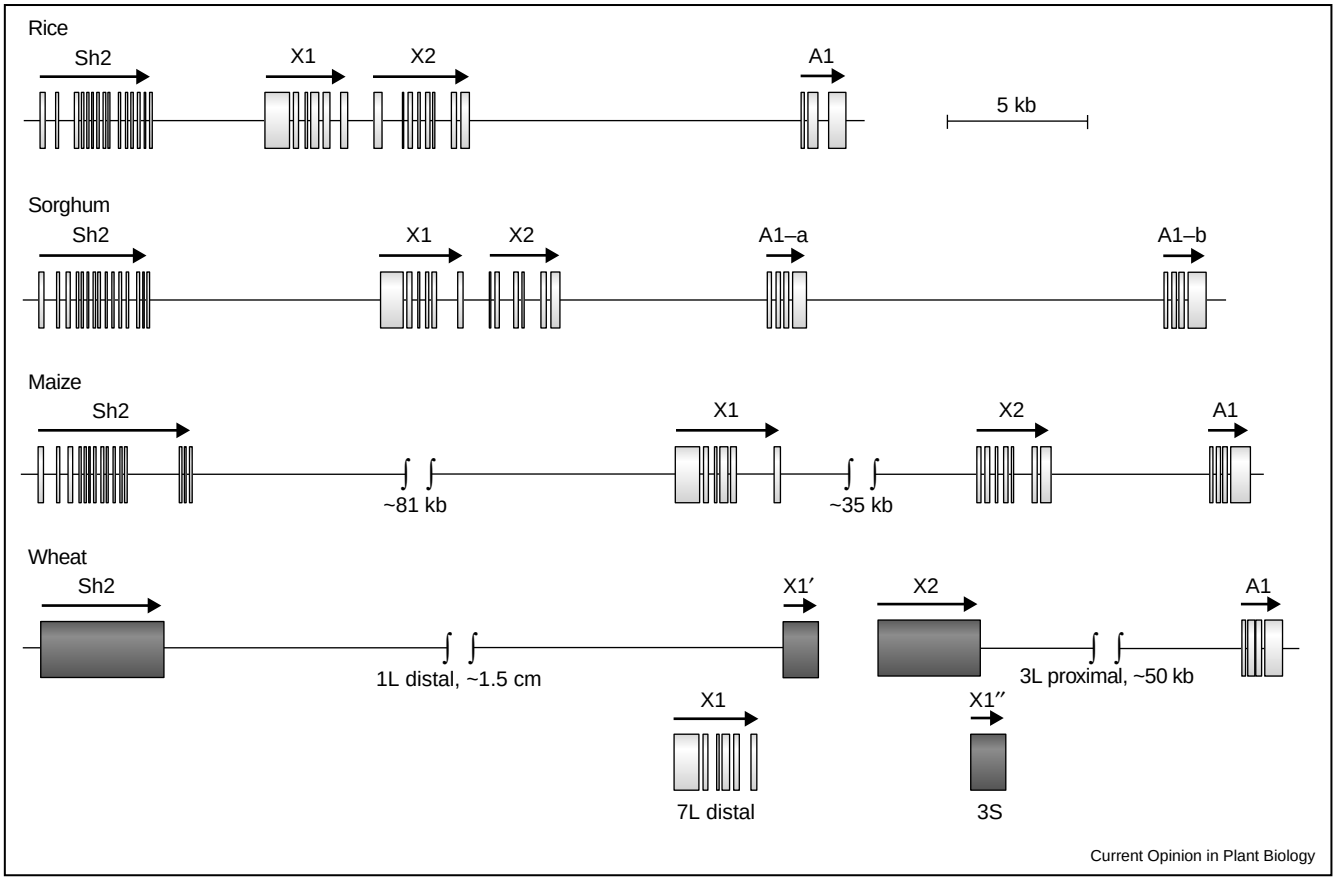
Despite the large and ever-expanding tracts of completed rice genome sequence, few studies have compared long stretches of rice genomic sequence to orthologous regions from other grass species. This data deficiency is caused, at least in part, by a shortage of substantial segments of contiguous genome sequences from other grasses. In addition, the very short contiguous sequences that are the primary product of analyses of the early draft rice genome [1•,2•] do not usually allow characterizations of multigene segments.

The first comparative study of local gene content and order in the grasses revealed that several genes are conserved in order and orientation in the *shrunken2* (*sh2*)/*anthocyaninless1* (*a1*)-homologous regions of maize, sorghum and rice [15,17]. Interestingly, the *sh2* and *a1* homologs are not closely linked in *Arabidopsis* [18], indicating that the *Arabidopsis* genome is highly rearranged relative to the genomes of rice and other grasses. Some colinearity exists between the rice and *Arabidopsis* genomes, but it is associated with many differences in gene presence/absence [19–23]. The simplest explanation for this is that most of these rearrangements occurred in the lineage that gave rise to *Arabidopsis* [24,25].

Segmental sequence comparisons between rice and other cereals

Figure 2 depicts the *sh2*/*a1*-homologous regions of maize, rice, sorghum, and wheat. The first detailed comparison, between rice and sorghum [15], indicated conservation of gene presence and order for four loci. In sorghum, the *a1*-ortholog is tandemly duplicated as it is in some maize genomes. Differences in tandem gene number are found frequently when comparing cereal genomes, indicating that tandem genes are probably generated and lost frequently, often via unequal recombination [16,26,27,28•]. Interestingly, the first exon of the X2 gene is present only in the rice locus but not in the maize or sorghum genes. Expression data suggest that all of the putative X2 genes, which apparently encode transcription factors, are active. Because the exon that varies between the different cereal genomes appears to encode a zinc-finger domain of the protein–protein interaction type, it is likely that the rice gene can interact with more partners than can the maize or sorghum genes. Hence, an evolved change in function is possible at this locus although not proven by these data. Further functional characterizations are needed to resolve this issue. The difference in the X2 homologs may have been caused by the insertion of an exon in rice or by a deletion from a common ancestor of maize and sorghum. The latter scenario seems much more likely, but both possibilities could be tested by sequence analysis of the X2 homolog that has been partly characterized in wheat

Figure 2



Structures of the *sh2/a1*-homologous regions in four grass genomes. Open boxes depict exons, whereas gray boxes represent genes that have not been fully sequenced. Arrows show the positions, approximate sizes and transcriptional orientations of each candidate gene. The wheat region has homologs in four chromosomal segments: the long arm of chromosome 1 (1L), the long arm of chromosome 3 (3L), the short arm of chromosome 3 (3S) and the long arm of chromosome 7 (7L). The terms 'distal' and 'proximal' are indications of whether the locus is closer to the centromere (proximal) or telomere (distal) of the indicated chromosome arm.

(Figure 2; [29•]). If the exon is present in the wheat gene, it would suggest that the exon was lost from the Andropogoneae lineage.

Other than the apparent duplication of *a1* homologs in sorghum and the exon variation in X2, the content and order of genes in the orthologous *sh2/a1* regions are completely conserved between rice, sorghum and maize. However, the maize genes are separated by much larger amounts of DNA than those of rice and sorghum (Figure 2; [30]). These DNA sequences are primarily the long terminal repeat (LTR) retrotransposons that are commonly intermixed with genes in all of the large genome cereals studied so far [16,26,29•,30–33]. These LTR retrotransposons usually comprise different elements and are found in different places in each grass genome, a finding that concurs with the observation that they appear to be only a few million years old [26,34,35]. We believe that the relative youth of the LTR retrotransposons in all of the plant species that we have investigated is not primarily caused by unusual recent bursts in LTR retrotransposon activity. More likely, the LTR retrotransposons are rapidly removed from most or all plant species by illegitimate and unequal recombination [36,37]. Hence, older elements have either been completely removed or are no longer recognizable. None of the comparisons of rice with maize, rice with barley, rice with sorghum or rice with wheat have found the same transposable elements at the precisely same locations. Hence, the vast majority of these insertions postdate the divergence of the ancestors of rice from those of these other cereals.

Recently, Li and Gill [29•] demonstrated that the only X2 homolog in wheat is not linked to a X1 homolog. Figure 2 shows that the wheat X1 and *Sh2* homologs are linked, as are those of other grasses, but at a much greater physical and genetic distance than in other grasses. Similarly, the X2 and *A1* homologs are linked in wheat, but are located on a different chromosome from X1 and *Sh2*. A translocation breakpoint appear to have occurred between X1 and

X2 in an early Triticeae because the same rearrangement appears to be present in barley [29•].

The *alcohol dehydrogenase1* (*adh1*)-orthologous regions of maize, sorghum and rice are a second set of cereal chromosome segments that have been extensively studied by sequence analysis [19,38]. Comparison of the rice *adh1/adh2* region with the sequence of the same region from the maize genome suggested that *adh1* was transposed as a single gene to a new location in the Andropogoneae [11•,38]. No change in the basic exon/intron organization or alteration in the tissue specificity of *adh1* expression resulted from this transposition [11•,38].

Messing and coworkers [28•] undertook detailed studies of gene clusters that encode storage proteins in maize and sorghum, and compared them to the orthologous region in rice. The maize storage protein (zein) genes and the sorghum storage protein (kafirin) genes are closely related in structure and are tandemly duplicated at orthologous positions, although the copy numbers of these genes differ between the two species. Rice, however, has no homologous storage protein gene at this location. Rice also lacks additional orthologous gene candidates that are found within or tightly flanking the storage protein gene clusters in maize and sorghum. Some of these putative genes have been amplified either during or subsequent to their apparent insertion. Messing and coworkers [28•] speculate that the insertion and/or amplification of a storage protein gene at this location in a common ancestor of maize and sorghum was the cause of the additional gene insertions and amplifications in this region. In a similar vein, Ramakrishna and coworkers [26] found a cluster of 48 small nucleolar RNA genes in rice that were absent at the orthologous position in sorghum.

Comparative analysis between wheat and rice of a small orthologous segment has identified another region, containing three putative receptor-like kinase genes, in which duplicated genes are conserved [39]. The apparent stability of the location and content of candidate genes for disease resistance in these orthologous regions is often not seen for other resistance gene homologs, as demonstrated by recombinational mapping [40].

Dubcovsky and coworkers [16] compared the rice and barley genomes for gene content and arrangement in the area around the *Vernalization1* (*Vrn1*) locus of wheat. In the sequences analyzed, four genes were comparable and two genic rearrangements were detected. Subsequent investigations that included orthologous wheat and sorghum regions allowed prediction of the lineages in which and times at which these rearrangements probably occurred [26]. The duplication of gene 4 is shared by barley and wheat but is missing from rice and sorghum, presumably because the duplication event happened early in the Triticeae lineage. The detected inversion of gene 2 is found only in barley and is associated with flanking inverted repeats; so it is likely that this inversion was caused by unequal recombination within the last 10–14 million years.

Chromosome walking in questionably colinear grasses

Probably the most comprehensive application of colinearity between rice and another cereal species was the attempt by Kleinhofs and coworkers [41,42] to clone specific barley disease resistance genes by chromosome walking in rice. The regions that they investigated were highly colinear for most genes, but homologs of the targeted barley disease resistance genes were not found in the orthologous region of the rice genome. Hence, the project was much more challenging than might have been anticipated. The colinearity provided numerous DNA markers from rice that facilitated the chromosome walk in barley, leading to the isolation of the desired resistance genes [43]. Disease resistance genes in plants are unusually unstable in their chromosomal location [40], but this exception to colinearity could also occur in any chromosome walk using a small genome surrogate.

Conclusions

Many more studies to compare orthologous genome organization in rice and other cereals are needed. With the deluge of high quality genomic sequence data for rice ([3]; http://rgp.dna.affrc.go.jp), these studies are becoming more and more feasible. Numerous local rearrangements differentiate the structures of different cereal genomes. On average, any comparison of a ten-gene segment between rice and a distant grass relative such as barley, maize, sorghum or wheat shows one or two rearrangements that involve genes. A simple extrapolation to the rice genome of about 40 000 genes [2•] suggests that about 6000 genic rearrangements will differentiate rice from these other cereals. Most of these rearrangements appear to be tiny and thus would not interfere with the macrocolinearity observed by recombinational mapping. There are exceptions, however, which include chromosomal arm translocations and movements of single genes to different chromosomes.

Most of the rearrangements that have been detected in comparisons between rice and another cereal have occurred in the other cereal rather than in rice. Hence, rice may contain a relatively stable genome that reflects the ancestral grass genome better than do the genomes of other cereals. Further studies are needed to test this theory.

Most of the many potential uses [8,9] of colinearity within the grass family require a reasonable amount of local genomic colinearity (microcolinearity). There is no way to predict whether microcolinearity is present, even in areas that exhibit recombinational map colinearity. Investigators will need to use colinearity with caution, for

instance when using rice as a surrogate for the map-based cloning of genes from large genome cereals such as barley. As additional grass genome sequences become available, more quantitative assessments of colinearity will be possible and predictive patterns may emerge. Until then, each comparison will need to directly assess colinearity in the studied region before making a major investment in the approach.

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References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1. • Yu J, Hu S, Wang J, Wong GK, Li S, Liu B, Deng Y, Dai L, Zhou Y, Zhang X *et al.*: **A draft sequence of the rice genome (*Oryza sativa* L. ssp. *indica*)**. *Science* 2002, **296**:79-92.
See annotation for [2•].

2. • Goff SA, Ricke D, Lan TH, Presting G, Wang R, Dunn M, Glazebrook J, Sessions A, Oeller P, Varma H *et al.*: **A draft sequence of the rice genome (*Oryza sativa* L. ssp. *japonica*)**. *Science* 2002, **296**:92-100.
This paper and [1•] provide a dramatic demonstration of the efficiency, value and limitations of full-genome shotgun sequencing. The short sequence contigs provide essentially 100% gene discovery, but are not usually useful for characterizing the organization or evolution of multigene segments.

3. Sasaki T, Burr B: **International rice genome sequencing project: the effort to completely sequence the rice genome**. *Curr Opin Plant Biol* 2000, **3**:138-141.

4. Ahn S, Tanksley SD: **Comparative linkage maps of the rice and maize genomes**. *Proc Natl Acad Sci USA* 1993, **90**:7980-7984.

5. Ahn S, Anderson JA, Sorrells ME, Tanksley SD: **Homoeologous relationships of rice, wheat and maize chromosomes**. *Mol Gen Genet* 1993, **241**:483-490.

6. Moore G, Devos KM, Wang Z, Gale MD: **Cereal genome evolution. Grasses, line up and form a circle**. *Curr Biol* 1995, **5**:737-739.

7. Devos KM, Gale MD: **Genome relationships: the grass model in current research**. *Plant Cell* 2000, **12**:637-646.

8. Bennetzen JL, Freeling M: **Grasses as a single genetic system: genome composition, collinearity and compatibility**. *Trends Genet* 1993, **9**:259-261.

9. Bennetzen JL, Freeling M: **The unified grass genome: synergy in synteny**. *Genome Res* 1997, **7**:301-306.

10. Freeling M: **Grasses as a single genetic system: reassessment**. *Plant Physiol* 2001, **125**:1191-1197.

11. • Bennetzen JL, Ramakrishna W: **Numerous small rearrangements of gene content, order and orientation differentiate grass genomes**. *Plant Mol Biol* 2002, **48**:821-827.
See annotation for [12•].

12. • Feuillet C, Keller B: **Comparative genomics in the grass family: molecular characterization of grass genome structure and evolution**. *Ann Bot* 2002, **89**:3-10.
The authors of this paper and of [11•] provide the most recent reviews of microcolinearity, its exceptions, and its significance in the cereals.

13. Hardison RC: **Conserved noncoding sequences are reliable guides to regulatory elements**. *Trends Genet* 2000, **16**:369-372.

14. Kaplinsky NJ, Braun DM, Penterman J, Goff SA, Freeling M: **Utility and distribution of conserved noncoding sequences in the grasses**. *Proc Natl Acad Sci USA* 2002, **99**:6147-6151.

15. Chen M, SanMiguel P, Bennetzen JL: **Sequence organization and conservation in *sh2/a1*-homologous regions of sorghum and rice**. *Genetics* 1998, **148**:435-443.

16. Dubcovsky J, Ramakrishna W, SanMiguel PJ, Busso CS, Yan L, Shiloff BA, Bennetzen JL: **Comparative sequence analysis of colinear barley and rice bacterial artificial chromosomes**. *Plant Physiol* 2001, **125**:1342-1353.

17. Chen M, SanMiguel P, de Oliveira AC, Woo SS, Zhang H, Wing RA, Bennetzen JL: **Microcolinearity in *sh2*-homologous regions of the maize, rice, and sorghum genomes**. *Proc Natl Acad Sci USA* 1997, **94**:3431-3435.

18. Bennetzen JL, SanMiguel P, Chen M, Tikhonov A, Francki M, Avramova Z: **Grass genomes**. *Proc Natl Acad Sci USA* 1998, **95**:1975-1978.

19. Tikhonov AP, SanMiguel PJ, Nakajima Y, Gorenstein NM, Bennetzen JL, Avramova Z: **Colinearity and its exceptions in orthologous *adh* regions of maize and sorghum**. *Proc Natl Acad Sci USA* 1999, **96**:7409-7414.

20. van Dodeweerd AM, Hall CR, Bent EG, Johnson SJ, Bevan MW, Bancroft I: **Identification and analysis of homoeologous segments of the genomes of rice and *Arabidopsis thaliana***. *Genome* 1999, **42**:887-892.

21. Liu H, Sachidanandam R, Stein L: **Comparative genomics between rice and *Arabidopsis* shows scant collinearity in gene order**. *Genome Res* 2001, **11**:2020-2026.

22. Mayer K, Murphy G, Tarchini R, Wambutt R, Volckaert G, Pohl T, Dusterhoft A, Stiekema W, Entian KD, Terryn N *et al.*: **Conservation of microstructure between a sequenced region of the genome of rice and multiple segments of the genome of *Arabidopsis thaliana***. *Genome Res* 2001, **11**:1167-1174.

23. Salse J, Piegu B, Cooke R, Delseny M: **Synteny between *Arabidopsis thaliana* and rice at the genome level: a tool to identify conservation in the ongoing rice genome sequencing project**. *Nucleic Acids Res* 2002, **30**:2316-2328.

24. Blanc G, Barakat A, Guyot R, Cooke R, Delseny M: **Extensive duplication and reshuffling in the *Arabidopsis* genome**. *Plant Cell* 2000, **12**:1093-1101.

25. Ku HM, Vision T, Liu J, Tanksley SD: **Comparing sequenced segments of the tomato and *Arabidopsis* genomes: large-scale duplication followed by selective gene loss creates a network of synteny**. *Proc Natl Acad Sci USA* 2000, **97**:9121-9126.

26. Ramakrishna W, Dubcovsky J, Park Y-J, Busso CS, Emberton J, SanMiguel P, Bennetzen JL: **Different types and rates of genome evolution detected by comparative sequence analysis of orthologous segments from four cereal genomes**. *Genetics* 2002, **162**:1389-1400.

27. Yuan Q, Hill J, Hsiao J, Moffat K, Ouyang S, Cheng Z, Jiang J, Buell CR: **Genome sequencing of a 239-kb region of rice chromosome 10L reveals a high frequency of gene duplication and a large chloroplast DNA insertion**. *Mol Genet Genomics* 2002, **267**:713-720.

28. • Song R, Llaca V, Messing J: **Mosaic organization of orthologous sequences in grass genomes**. *Genome Res* 2002, **12**:1549-1555.
This paper provides a comparison of more than 435 kb of maize DNA with orthologous regions in rice and sorghum. Although all of the candidate rice genes in the region are present and colinear in sorghum and maize, the latter two species have apparently acquired and often tandemly amplified several additional genes in this region.

29. • Li W, Gill BS: **The colinearity of the *Sh2/A1* orthologous region in rice sorghum and maize is interrupted and accompanied by genome expansion in the Triticeae**. *Genetics* 2002, **160**:1153-1162.
The authors compare an orthologous four-gene segment from rice and wheat. They find a translocation between two genes and huge differences in physical linkage.

30. Yao H, Zhou Q, Li J, Smith H, Yandeau M, Nikolau BJ, Schnable PS: **Molecular characterization of meiotic recombination across the 140-kb multigenic *a1–sh2* interval of maize**. *Proc Natl Acad Sci USA* 2002, **99**:6157-6162.

31. SanMiguel P, Tikhonov A, Jin YK, Motchoulskaia N, Zakharov D, Melake-Berhan A, Springer PS, Edwards KJ, Lee M, Avramova Z,

Bennetzen JL: **Nested retrotransposons in the intergenic regions of the maize genome**. *Science* 1996, **274**:765-768.

32. Wicker T, Stein N, Albar L, Feuillet C, Schlagenhauf E, Keller B: **Analysis of a contiguous 211 kb sequence in diploid wheat (*T. monococcum* L.) reveals multiple mechanisms of genome evolution**. *Plant J* 2001, **26**:307-316.

33. Fu H, Zhang Z, Dooner HK: **Recombination rates between adjacent genic and retrotransposon regions in maize vary by 2 orders of magnitude**. *Proc Natl Acad Sci USA* 2002, **99**:1082-1087.

34. SanMiguel PJ, Ramakrishna W, Bennetzen JL, Busso CS, Dubcovsky J: **Transposable elements genes, and recombination in a 215-kb contig from wheat chromosome 5A(m)**. *Funct Integr Genomics* 2002, **2**:70-80.

35. SanMiguel P, Gaut BS, Tikhonov A, Nakajima Y, Bennetzen JL: **The paleontology of intergene retrotransposons of maize**. *Nat Genet* 1998, **20**:43-45.

36. Vicient CM, Suoniemi A, Anamthawat-Jonsson K, Tanskanen J, Beharav A, Nevo E, Schulman AH: **Retrotransposon *BARE-1* and its role in genome evolution in the genus *Hordeum***. *Plant Cell* 1999, **11**:1769-1784.

37. Devos KM, Brown JK, Bennetzen JL: **Genome size reduction through illegitimate recombination counteracts genome expansion in *Arabidopsis***. *Genome Res* 2002, **12**:1075-1079.

38. Tarchini R, Biddle P, Wineland R, Tingey S, Rafalski A: **The complete sequence of 340 kb of DNA around the rice *Adh1–adh2* region reveals interrupted colinearity with maize chromosome 4**. *Plant Cell* 2000, **12**:381-391.

39. Feuillet C, Keller B: **High gene density is conserved at syntenic loci of small and large grass genomes**. *Proc Natl Acad Sci USA* 1999, **96**:8265-8270.

40. Leister D, Kurth J, Laurie DA, Yano M, Sasaki T, Devos K, Graner A, Schulze-Lefert P: **Rapid reorganization of resistance gene homologues in cereal genomes**. *Proc Natl Acad Sci USA* 1998, **95**:370-375.

41. Kilian A, Chen J, Han F, Steffenson B, Kleinhofs A: **Towards map-based cloning of the barley stem rust resistance genes *Rpg1* and *rpg4* using rice as an intergenomic cloning vehicle**. *Plant Mol Biol* 1997, **35**:187-195.

42. Han F, Kilian A, Chen JP, Kudrna D, Steffenson B, Yamamoto K, Matsumoto T, Sasaki T, Kleinhofs A: **Sequence analysis of a rice BAC covering the syntenous barley *Rpg1* region**. *Genome* 1999, **42**:1071-1076.

43. Brueggeman R, Rostoks N, Kudrna D, Kilian A, Han F, Chen J, Druka A, Steffenson B, Kleinhofs A: **The barley stem rust-resistance gene *Rpg1* is a novel disease-resistance gene with homology to receptor kinases**. *Proc Natl Acad Sci USA* 2002, **99**:9328-9333.