

5. CONCLUSIONES

Las conclusiones que se pueden extraer del presente trabajo son:

1. La región de 1,944 Mb que rodea al locus *Adh* en *D. melanogaster* (elemento B) está representada en 6 posiciones cromosómicas distintas en las especies *D. repleta* y *D. buzzatii*. Los genes *Adh* y *Adhr* están incluidos en un segmento conservado de 366 kb. Sin embargo, el hecho de que un segmento esté conservado no excluye que en su interior se hayan producido microrreordenaciones que no pueden ser detectadas con la técnica de hibridación *in situ*.

2. La hibridación de 160 clones procedentes de la especie *D. melanogaster* en las especies *D. repleta* y *D. buzzatii* confirma una vez más las homologías cromosómicas establecidas en el género *Drosophila* y la gran reorganización del contenido genético de los elementos cromosómicos debida a la fijación de inversiones paracéntricas. Sólo 2 clones, el gen *Lsplalpha* y el cósmido 174F6, no hibridaron en el elemento cromosómico esperado y representan probablemente eventos de transposición. La estima de la tasa de transposición en el género *Drosophila* es de $4,9 \times 10^{-5}$ por gen y por millón de años. Esta cifra es una subestima ya que no incluye genes repetidos en tándem, que a menudo muestran transposición, ni transposiciones intracromosómicas.

3. La tasa de fijación de inversiones (\pm SD) durante la divergencia de las especies *D. melanogaster* y *D. repleta* es de 118 ± 17 para el elemento A; 30 ± 13 para el elemento B; y 56 ± 8 para el elemento D. La densidad de puntos de rotura varía hasta cuatro veces entre los elementos A, B, D y E. El elemento A es el que muestra la mayor densidad (10,83) aunque también existen diferencias entre las densidades de los tres autosomas analizados: el elemento E presenta la densidad más elevada (8,14), el elemento D una densidad intermedia (4,63) y el elemento B la densidad más baja (2,57). Estos resultados concuerdan con los obtenidos al comparar especies del grupo *virilis*, en las que el elemento A evoluciona más rápido que el E que a su vez evoluciona más rápido que el D sugiriendo que este patrón podría ser relativamente general.

4. Debido a los múltiples efectos de las inversiones parece poco probable que un único factor pueda explicar la variación en la tasa de evolución de los diferentes elementos cromosómicos observada en el género *Drosophila*. Es más probable que varios factores, entre ellos cantidad de DNA repetitivo, tasa de recombinación o densidad génica contribuyan a esta variación.
5. La estima para la tasa de fijación de inversiones en todo el genoma durante la divergencia de las especies *D. melanogaster* y *D. repleta* es de 393, es decir, 0,053 puntos de rotura fijados por Mb y por Ma. Esta estima es comparable a las obtenidas para otras especies del género *Drosophila* pero superior a la tasa estimada en varias especies de mamíferos y plantas. Esta mayor tasa evolutiva del género *Drosophila* podría ser debida a un tiempo de generación más corto y un menor efecto detrimental de las inversiones sobre la fertilidad en estas especies. Sólo la estima obtenida a partir de la comparación de las secuencias de dos especies de levadura es comparable a la estima para las especies del género *Drosophila*.
6. Se han identificado 9 segmentos cromosómicos conservados en el elemento A, 6 en la región *Adh* del elemento B y 13 en el elemento D. No hay evidencias de restricciones funcionales que puedan explicar la conservación de estos segmentos cromosómicos. Solo 1 segmento en el elemento A y 1 en el elemento D tienen un tamaño superior al esperado de acuerdo con la hipótesis de que los segmentos conservados son el resultado de la fijación de un número limitado de reordenaciones con puntos de rotura al azar desde la divergencia de las especies comparadas. Sin embargo, debido a que estos dos segmentos incluyen tan solo 2 marcadores es probable que dentro de ellos se hayan producido reorganizaciones que no han sido detectadas.
7. La conservación de tres complejos génicos en las especies *D. repleta* y *D. buzzatii*, complejo *achaete-scute*, complejo *iroquois* y complejo *knirps-knirps-related*, que en *D. melanogaster* muestran expresión corregulada sugiere que la selección natural puede jugar un papel en algunos casos para mantener juntos genes funcionalmente relacionados.

8. Los resultados obtenidos en el presente trabajo apuntan hacia una organización modular del genoma en las especies del género *Drosophila*. El genoma de *Drosophila* se puede considerar un mosaico de módulos independientes que pueden cambiar de localización cromosómica, la mayoría de veces dentro del mismo elemento cromosómico y solo ocasionalmente entre elementos, sin que estos cambios tengan consecuencias para su función.

9. La comparación de la organización molecular del cromosoma X en las especie *D. repleta* y *D. buzzatii* indica que los puntos de rotura de las inversiones Xb y Xc fijadas entre estas dos especies han sido mal asignados. De acuerdo a los resultados obtenidos en el presente trabajo las inversiones Xb y Xc no estarían dispuesta en tándem sino que serían inversiones solapantes. Los puntos de rotura de estas inversiones se han localizado en F1c-G1e y F1a-F2i.

6. REFERENCIAS

- Abad, J. P., M. Carmena, S. Baars, R. D. C. Saunders D. M. Glover *et al.* (1992) Dodeca satellite: a conserved G+C-rich satellite from the centromeric heterochromatin of *Drosophila melanogaster* Proc. Natl. Acad. Sci. USA 89: 4663-4667.
- Abad, J. P. y A. Villasante (2000) Searching for a common centromeric structural motif: *Drosophila* centromeric satellite DNAs show propensity to form telomeric-like unusual DNA structures. *Genetica* 109: 71-75.
- Adams, M. D., S. E. Celniker, R. A. Holt, C. A. Evans, J. D. Gocayne *et al.* (2000) The genome sequence of *Drosophila melanogaster*. *Science* 287: 2185-2195.
- Alonso, C. y H. D. Berendes (1975) The location of 5S (ribosomal) RNA genes in *Drosophila hydei*. *Chromosoma* 51: 347-356.
- Andres, A. J., J. C. Fletcher, F. D. Karim y C. S. Thummel (1993) Molecular analysis of the initiation of insect metamorphosis: a comparative study of *Drosophila* ecdysteroid-regulated transcription. *Dev. Biol.* 160: 388-404.
- Ashburner, M. (1989) *Drosophila* a laboratory handbook. Cold Spring Harbor Laboratory Press.
- Ashburner M., S. Misra, J. Roote, S. E. Lewis, R. Blazej *et al* (1999) An exploration of the sequence of a 2.9-Mb region of the genome of *Drosophila melanogaster*: the *Adh* region. *Genetics* 153: 179-219.
- Bachtrog, D., S. Weiss, B. Zangerl, G. Brem y C. Schöletterer (1999) Distribution of dinucleotide microsatellites in the *Drosophila melanogaster* genome. *Mol. Biol. Evol.* 16: 602-610.
- Barnett, T., C. Pacht, J. P. Gergen y P. C. Wensink (1980) The isolation and characterization of *Drosophila* yolk protein genes. *Cell* 21: 729-738.

- Bauer, V. L. y C. F. Aquadro (1997) Rates of DNA sequence evolution are not sex-biased in *Drosophila melanogaster* and *D. simulans*. *Mol. Biol. Evol.* 14: 1252-1257.
- BDGP, *Berkeley Drosophila Genome Project*. <http://www.fruitfly.org/>
- Beamonte, D. (1990) Búsqueda y caracterización de genes homólogos a los del complejo *achaete-scute* de *Drosophila melanogaster*. Tesis doctoral. Universidad Autónoma de Madrid.
- Begun, D. J. (1997) Origin and evolution of a new gene descendent from *alcohol dehydrogenase* in *Drosophila*. *Genetics* 145: 375-382.
- Betrán, E., J. Rozas, A. Navarro y A. Barbadilla (1997) The estimation of the number and the length distribution of gene conversion tracts from population DNA sequence data. *Genetics* 146: 89-99.
- Beverly, S. M. y A. C. Wilson (1984) Molecular evolution in *Drosophila* and higher Dipterans. II. A time scale for fly evolution. *J. Mol. Evol.* 21: 1-13.
- Bondinas, G. P., M. G. Loukas, G. N. Goulielmos y D. Sperlich (2001) The *actin* loci in the genus *Drosophila*: establishment of chromosomal homologies among five palearctic species of the *Drosophila obscura* group by *in situ* hybridization. *Chromosoma* 110: 441-450.
- Bridges, C. B. (1935) Salivary chromosome maps, with a key to the banding of the chromosomes of *Drosophila melanogaster*. *J. Hered.* 26: 60-64.
- Brock, H. W. y D. B. Roberts (1983) Location of the *LSP-1* genes in *Drosophila* species by *in situ* hybridization. *Genetics* 103: 75-92.

- Brogna, S. y M. Ashburner (1997) The *Adh-related* gene of *Drosophila melanogaster* is expressed as a functional dicistronic messenger RNA: multigenic transcription in higher organism. EMBO J. 16: 2023-2031.
- Burt, D. W., C. Bruley, I. C. Dunn, C. T. Jones, A. Ramage *et al.* (1999) The dynamics of chromosome evolution in birds and mammals. Nature 402: 411-413.
- Cáceres, M., J. M. Ranz, A. Barbadilla, M. Long y A. Ruiz (1999a) A transposable element mediated the generation of a *Drosophila* widespread chromosomal inversion. Science 285: 415-418.
- Cáceres, M., A. Barbadilla y A. Ruiz (1999b) Recombination rate predicts inversion size in Diptera. Genetics 153: 251-259.
- Cáceres, M., M. Puig y A. Ruiz (2001) Molecular characterization of two natural hotspots in the *Drosophila buzzatii* genome induced by transposon insertions. Genome Res. 11: 1353-1364.
- Cai, H., P. Kiefel, J. Yee y I. Duncan (1994) A yeast artificial chromosome clone map of the *Drosophila* genome. Genetics 136: 1385-99.
- Campbell, S. D., A. Duttaroy, A. L. Katzen y A. Chovnick (1991) Cloning and characterization of the *scalloped* region of *Drosophila melanogaster*. Genetics 127: 367-380.
- Cavodeassi, F., J. Modolell y J. L. Gómez-Skarmeta (2001) The *iroquois* family of genes: from body building to neural patterning. Development 128: 2847-2855.
- Celniker, S. (2000) The *Drosophila* genome. Curr. Opin. Genet. Dev. 10: 612-616.
- Charlesworth, B., J. A. Coyne y N. H. Barton (1987) The relative rates of evolution of sex chromosomes and autosomes. Am. Nat. 130: 113-146.

- Cirera, S., J. M. Martín-Campos, C. Segarra y M. Aguadé (1995) Molecular characterization of the breakpoints of an inversion fixed between *Drosophila melanogaster* and *D. subobscura*. *Genetics* 139: 321-326.
- Clayton, F. E. y W. C. Guest (1986) Overview of chromosomal evolution in the family *Drosophilidae*. En: *The Genetics and Biology of Drosophila*, vol. 3e, pp. 1-38. Editado por: M. Ashburner, H. L. Carson y J. N. Thompson. Academic Press, London.
- Csink, A. K. y S. Henikoff (1998) Something from nothing: the evolution and utility of satellite repeats. *Trends Genet.* 14: 200-204
- Currie, P. D. y D. T. Sullivan (1994) Structure, expression and duplication of genes which encode phosphoglyceromutase of *Drosophila melanogaster*. *Genetics* 138: 352-363.
- Devos, K. M. y M. D. Gale (2000) Genome relationships: the grass model in current research. *Plant Cell* 12: 637-646.
- DiBartolomeis, S. M., K. D. Tartof y F. R. Jackson (1992) A superfamily of *Drosophila* satellite related (SR) DNA repeats restricted to the X chromosome euchromatin. *Nucleic Acids Res.* 20: 1113-1116.
- Dowsett, A. P. y M. W. Young (1982) Differing levels of dispersed repetitive DNA among closely related species of *Drosophila*. *Proc. Natl. Acad. Sci. USA* 79: 4570-4574.
- Drosopoulou, E. y Z. G. Scouras (1995) The *beta-tubulin* gene family evolution in the *Drosophila montium* subgroup of the *melanogaster* species group. *J. Mol. Evol.* 41: 293-298.
- Durando, C. M., R. H. Baker, W. J. Etges, W. B. Heed, M. Wasserman y R. DeSalle (2000) Phylogenetic analysis of the *repleta* species group of the genus

- Drosophila* using multiple sources of characters. *Mol. Phylogenet. Evol.* 16: 296-307.
- Ehrlich, J., D. Sankoff y J. H. Nadeau (1997) Synteny conservation and chromosome rearrangements during mammalian evolution. *Genetics* 147: 289-296.
- Fitch, H .A., L. D. Strausbaugh y V. Barret (1990) On the origins of tandemly repeated genes: Does histone gene copy number in *Drosophila* reflect chromosomal location? *Chromosoma* 99: 118-124.
- FlyBase (1999) The FlyBase database of the *Drosophila* genome projects and community literature. *Nucleic Acids Research* 27: 85-88.
<http://flybase.bio.indiana.edu/>
- Frönicke, L. y J. Wienberg (2001) Comparative chromosome painting defines the high rate of karyotype changes between pigs and bovids. *Mammalian Genome* 12: 442-449.
- Ganguly, R., N. Ganguly y J. E. Manning (1985) Isolation and characterization of the *glucose-6-phosphate dehydrogenase* gene of *Drosophila melanogaster*. *Gene* 35: 91-101.
- Gerasimova, T. I., K. Byrd y V. G. Corces (2000) A chromatin insulator determines the nuclear localization of DNA. *Mol. Cell* 6: 1025-1035.
- Gibson, T. J., A. Rosenthal y R. H. Waterston (1987) Lorist6, a cosmid vector with *Bam*HI, *Not*I, *Sca*I and *Hind*III cloning sites and altered neomycin phosphotransferase gene expression. *Gene* 53: 283-286.
- Gómez-Skarmeta, J. L., R. Díez del Corral, E. de la Calle-Mustienes, D. Ferrés-Marcó y J. Modolell (1996) *araucan* and *caupolican*, two members of the novel *Iroquois* complex, encode homeoproteins that control proneural and vein-forming genes. *Cell* 85: 95-105.

- Gorman, M., A. Franke y B. S. Baker (1995) Molecular characterization of the *male-specific lethal-3* gene and investigations of the regulation of dosage compensation in *Drosophila*. *Development* 121: 463-475.
- Graves, J. A. M. (1996) Mammals that break the rules: Genetics of Marsupials and Monotremes. *Annu. Rev. Genet.* 30: 233-260.
- Hartl D. L. y E. R. Lozovskaya (1994) Genome evolution: between the nucleosome and the chromosome. *EXS.* 69: 579-592.
- Hartl, D. L., D. I. Nurminsky, R. W. Jones y E. R. Lozovskaya (1994) Genome structure and evolution in *Drosophila*: applications of the framework P1 map. *Proc. Natl. Acad. Sci. USA* 91: 6824-6829.
- Hartl, D. L. y E. R. Lozovskaya (1995) The *Drosophila* genome map: a practical guide. Springer-Verlag, Heidelberg, Germany.
- Heckel, D. G. (1993) Comparative genetic linkage mapping in insects. *Annu. Rev. Entomol.* 38: 381-408.
- Hennig, W. (1999) Heterochromatin. *Chromosoma* 108: 1-9.
- Hill, R. J. y G. T. Rudkin (1987) Polytene chromosomes: the status of the band-interband question. *BioEssays* 7: 35-40.
- Hooper, J. E., M. Pérez-Alonso, J. R. Bermingham, M. Prout y B. A. Rocklein (1992) Comparative studies of *Drosophila* Antennapedia genes. *Genetics* 132: 453-469.
- Huijser, P., W. Hennig y R. Dijkhof (1987) Poly (dC-dA/ dG-dT) repeats in the *Drosophila* genome: a key function for dosage compensation and position effects? *Chromosoma* 95: 209-215.

- Huynen, M. A., B. Snel y P. Bork (2001) Inversions and the dynamics of eukaryotic gene order. *Trends Genet.* 17: 304-306.
- Jabbari, K. y G. Bernardi (2000) The distribution of genes in the *Drosophila* genome. *Gene* 247: 287-292.
- Jeffs, P. S., E. C. Holmes y M. Ashburner (1994) The molecular evolution of the *alcohol dehydrogenase* and *alcohol dehydrogenase-related* genes in the *Drosophila melanogaster* species subgroup. *Mol. Biol. Evol.* 11: 287-304.
- Karpen, G. H. y R. C. Allshire (1997) The case for epigenetic effects on centromere identity and function. *Trends Genet.* 13: 489-496.
- Katti, M. V., P. K. Ranjekar y V. S. Gupta (2001) Differential distribution of simple sequence repeats in eukaryotic genome sequences. *Mol. Biol. Evol.* 18: 354-358.
- Kay, M. A., J. Y. Zhang y M. Jacobs-Lorena (1988) Identification and germline transformation of the ribosomal protein *rp21* gene of *Drosophila*: complementation analysis with the Minute QIII locus reveals nonidentity. *Mol. Gen. Genet.* 213: 354-358.
- Kehl, B. T., K. O. Cho y K. W. Choi (1998) *mirror*, a *Drosophila* homeobox gene in the *Iroquois* complex, is required for sensory organ and alula formation. *Development* 125: 1217-1227.
- Kelley, R. L. y M. I. Kuroda (1995) Equality for X chromosomes. *Science* 270: 1607-1610.
- Kimmerly, W., K. Stultz, S. Lewis, K. Lewis, V. Lustre *et al.* (1996) P1-based physical map of the *Drosophila* euchromatic genome. *Genome Res.* 6: 414-430.
- Kokoza, E. B., E. S. Belyaeva y I. F. Zhimulev (1992) Localization of genes *ecs*, *dor* and *swi* in eight *Drosophila* species. *Genetica* 87: 79-85.

- Koryakov, D. E., A. A. Alekseyenko y I. F. Zhimulev (1999) Dynamic organization of the beta-heterochromatin in the *Drosophila melanogaster* polytene X chromosome. *Mol. Gen. Genet.* 260: 503-509.
- Kraemer, C., B. Weil, M. Christmann y E. R. Schmidt (1998) The new *DmX* from *Drosophila melanogaster* encodes a novel WD-repeat protein. *Gene* 216: 267-276.
- Kress, H. (1993) The salivary gland chromosomes of *Drosophila virilis*: a cytological map, pattern of transcription and aspects of chromosome evolution. *Chromosoma* 102: 734-742.
- Krimbas, C. B. y J. R. Powell (1992) *Drosophila Inversion Polymorphism*. CRC Press, Boca Raton.
- Kumar, S., S. R. Gadagkar, A. Filipski y X. Gu (2001) Determination of the number of conserved chromosomal segments between species. *Genetics* 157: 1387-1395.
- Laayouni, H., M. Santos y A. Fontdevila (2000) Toward a physical map of *Drosophila buzzatii*. Use of randomly amplified polymorphic DNA polymorphisms and sequence-tagged site landmarks. *Genetics* 156: 1797-1816.
- Lagercrantz, U. (1998) Comparative mapping between *Arabidopsis thaliana* and *Brassica nigra* indicates that *Brassica* genomes have evolved through extensive genome replication accompanied by chromosome fusions and frequent rearrangements. *Genetics* 150: 1217-1228.
- Laird, C. D. (1973) DNA of *Drosophila* chromosomes. *Annu. Rev. Genet* 7: 177-204.
- Lander, E. S., L. M. Linton, B. Birren, C. Nusbaum, M. C. Zody *et al.* (2001) Initial sequencing and analysis of the human genome. *Nature* 409: 860-921.

- Leach, T. J., H. L. Chotkowski, M. G. Wotring, R. L. Dilwith y R. L. Glaser (2000) Replication of heterocromatin and structure of polytene chromosomes. *Mol. Cel. Biol.* 20: 6308-6316.
- Leitch, A. R., T. Schwarzacher, D. Jackson y I. J. Leitch (1994) *In situ* hybridization: a practical guide. Bios Scientific Publishers, Oxford.
- Lefevre, G. Jr. (1976) A photographic representation and interpretation of the polytene chromosomes of *D. melanogaster* salivary glands. En: *The Genetics and Biology of Drosophila*, vol 1a, pp 31-66. Editado por M. Ashburner y E. Novitski. Academic Press, London.
- Lemeunier, F. y F. Aulard (1992) Inversion polymorphism in *Drosophila melanogaster*. En: *Drosophila Inversion Polymorphism*, pp 339-405. Editado por C. B. Krimbas y J. R. Powell. CRC Press, Boca Raton, Florida.
- Lepesant, J. A., M. Levine, A. Garen, J. Lepesant-Kejzlarova, L. Rat *et al.* (1982) Developmentally regulated gene expression in *Drosophila* larval fat bodies. *J. Mol. Appl. Genet.* 1: 371-383.
- Lim, J. K. y M. J. Simmons (1994) Gross chromosome rearrangements mediated by transposable elements in *Drosophila melanogaster*. *Bioessays* 16: 269-275.
- Lindsley, D. L. y G. G. Zimm (1992) *The genome of Drosophila melanogaster*. Academic Press, Inc. San Diego, California.
- Llorente, B., A. Malpertuy, C. Neuvéglise, J. Montigny, M. Aigle *et al.* (2000) Genomic exploration of the hemiascomycetous yeasts: 18. Comparative analysis of chromosome maps and synteny with *Saccharomyces cerevisiae*. *FEBS Lett.* 487: 101-112.

- Long, M. y C. H. Langley (1993) Natural selection and the origin of *jingwei*, a chimeric processed functional gene in *Drosophila*. *Science* 260: 91-95.
- Loukas, M. y F. C. Kafatos (1986) The *actin* loci in the genus *Drosophila*: establishment of chromosomal homologies among distantly related species by *in situ* hybridization. *Chromosoma* 94: 297-308.
- Loukas, M. y F. C. Kafatos (1988) Chromosomal locations of *actin* genes are conserved between the *melanogaster* and *obscura* groups of *Drosophila*. *Genetica* 76: 33-41.
- Lovering, R., N. Harden y M. Ashburner (1991) The molecular structure of *TE146* and its derivatives in *Drosophila melanogaster*. *Genetics* 128: 357-372.
- Lowenhaupt, K., A. Rich y M. L. Pardue (1989) Nonrandom distribution of long mono- and dinucleotide repeats in *Drosophila* chromosomes: correlation with dosage compensation, heterochromatin and recombination. *Mol. Cell. Biol.* 9: 1173-1182.
- Lozovskaya, E. R, D. A. Petrov y D. L. Hartl (1993) A combined molecular and cytogenetic approach to genome evolution in *Drosophila* using large-fragment DNA cloning. *Chromosoma* 102: 253-266.
- Lucchesi, J. C. y D. T. Suzuki (1968) The interchromosomal control of recombination. *Annu. Rev. Genet.* 2: 53-86.
- Lunde, K., B. Biehs, U. Nauber y E. Bier (1998) The *knirps* and *knirps-related* genes organize development of the second wing vein in *Drosophila*. *Development* 125: 4145-4154.
- Madueño, E., G. Papagiannakis, G. Remington, R. D. C. Saunders, C. Savakis *et al.* (1995) A physical map of the X chromosome of *D. melanogaster*: cosmid contigs and sequence tagged sites. *Genetics* 139: 1631-1647.

- Maier, D., B. M. Marte, W. Schafer, Y. Yu y A. Preiss (1993) *Drosophila* evolution challenges postulated redundancy in the *E(spl)* gene complex. Proc. Natl. Acad. Sci. USA 90: 5464-5468.
- Martínez-Cruzado, J. C., C. Swimmer, M. G. Fenerjian y F. C. Kafatos (1988) Evolution of the autosomal chorion locus in *Drosophila*. I. General organization of the locus and sequence comparisons of genes *s15* and *s19* in evolutionary distant species. Genetics 119: 663-677.
- McClelland, A., D. F. Smith y D. M. Glover (1981) Short intervening sequences close to the 5' ends of the three *Drosophila larval serum protein 1* genes. J. Mol. Biol. 153: 257-272.
- McGinnis, W., A. W. Shermoen y S. K. Beckendorf (1983) A transposable element inserted just 5' to a *Drosophila* glue protein gene alters gene expression and chromatin structure. Cell 34: 75-84.
- Menotti-Raymond, M., W. T. Starmer y D. T. Sullivan (1991) Characterization of the structure and evolution of the *Adh* region of *Drosophila hydei*. Genetics 127: 355-366.
- Merriam, J., Ashburner, M., D. L. Hartl y F. C. Kafatos (1991) Toward cloning and mapping the genome of *Drosophila*. Science 254: 221-225.
- Mitas, M. (1997) Trinucleotide repeats associated with human disease. Nucleic Acids Res. 25: 2245-2253.
- Modolell, J. y S. Campuzano (1998) The *achaete-scute* complex as an integrating device. Int. J. Dev. Biol. 42: 275-282.
- Mongelard, F. y V. G. Corces (2001) Two insulators are not better than one. Nature Structural Biology 8: 192-194.

- Montell, C., K. Jones, C. Zuker y G. Rubin (1987) A second *opsin* gene expressed in the ultraviolet-sensitive R7 photoreceptor cells of *Drosophila melanogaster*. *J. Neurosci.* 7: 1558-1566.
- Montgomery, E., B. Charlesworth y C. H. Langley (1987) A test for the role of natural selection in the stabilization of transposable element copy number in a population of *Drosophila melanogaster*. *Genet Res.* 49: 31-41.
- Montgomery, E. A., S. M. Huang, C. H. Langley y B. H. Judd (1991) Chromosome rearrangement by ectopic recombination in *Drosophila melanogaster*: genome structure and evolution. *Genetics* 129: 1085-1098.
- Moore, H., P. W. Greenwell, C. -P. Liu, N. Arnheim y T. Petes (1999) Triplet repeats form secondary structures that escape DNA repair in yeast. *Proc. Natl. Acad. Sci. USA* 96: 1504-1509.
- Moriyama, E. N., D. A. Petrov y D. L. Hartl (1998) Genome size and intron size in *Drosophila*. *Mol. Biol. Evol.* 15: 770-773.
- Morrow, J. F., S. N. Cohen, A. C. Chang, H. W. Boyer, H. M. Goodman y R. B. Helling (1974) Replication and transcription of eukaryotic DNA in *Escherichia coli*. *Proc. Natl. Acad. Sci. USA* 71: 1743-1747.
- Muller, J. H. (1940) Bearings of the *Drosophila* work on systematics. En: *New Systematics*, pp 185-268. Editado por J. Huxley. Clarendon Press, Oxford.
- Müller, S., R. Stanyon, P. Finelli, N. Archidiacono y J. Wienberg (2000) Molecular cytogenetic dissection of human chromosomes 3 and 21 evolution. *Proc. Natl. Acad. Sci. USA* 97: 206-211.
- Murphy, W. J., S. Sun, Z. Chen, N. Yuhki, D. Hirschmann *et al.* (2000) A radiation hybrid map of the cat genome: implications for comparative mapping. *Genome Res.* 10: 691-702.

- Murphy, W. J., R. Stanyon y S. J. O'Brien (2001) Evolution of mammalian genome organization inferred from comparative gene mapping. *Genome Biol* 2: reviews0005.1-0005.8.
- Nadeau, J. H. y B. A. Taylor (1984) Lengths of chromosomal segments conserved since divergence of man and mouse. *Proc. Natl. Acad. Sci. USA* 81: 814-818.
- Nadeau, J. y D. Sankoff (1998a) Counting on comparative maps. *Trends Genet.* 14: 495-501.
- Nadeau, J. y D. Sankoff (1998b) The lengths of undiscovered conserved segments in comparative maps. *Mammalian Genome* 9: 491-495.
- Navarro, A., E. Betrán, A. Barbadilla y A. Ruiz (1997) Recombination and gene flux caused by gene conversion and crossing over in inversion heterokaryotypes. *Genetics* 146: 695-709.
- Naveira, H., C. Pla y A. Fontdevila (1986) The evolutionary history of *Drosophila buzzatii* XI. A new method for cytogenetic hybrids of *Drosophila*. *Genetica* 71: 199-212.
- Neufeld, T. P., R. W. Carthew y G. M. Rubin (1991) Evolution of gene position: chromosomal arrangement and sequence comparison of the *Drosophila melanogaster* and *Drosophila virilis sina* and *Rh4* genes. *Proc. Natl. Acad. Sci. USA* 88: 10203-10207.
- Nurminsky, D. I., E. N. Moriyama, E. R. Lozovskaya y D.L. Hartl (1996) Molecular phylogeny and genome evolution in the *Drosophila virilis* species group: duplications of the *alcohol dehydrogenase* gene. *Mol. Biol. Evol.* 13: 132-149.
- O'Brien, S. J., M. Menotti-Raymond, W. J. Murphy, W. G. Nash, J. Wienberg *et al.* (1999) The promise of comparative genomics in mammals. *Science* 286: 458-481.

- Orr, H. A. (1997) Haldane's rule. *Annu. Rev. Ecol. Syst.* 28: 195-218.
- Papaceit, M. y E. Juan (1993) Chromosomal homologies between *Drosophila lebanonensis* and *D. melanogaster* determined by *in situ* hybridization. *Chromosoma* 102: 361-368.
- Pardue, M. L., S. A. Gerbi, R. A. Eckhardt y J. G. Gall (1970) Cytological localization of DNA complementary to ribosomal RNA in polytene chromosomes of Diptera. *Chromosoma* 29: 268-290.
- Pardue, M. L., K. Lowenhaupt, A. Rich y A. Nordheim (1987) (dC-dA)_n (dG-dT)_n sequences have evolutionary conserved chromosomal locations in *Drosophila* with implication for roles in chromosome structure and function. *EMBO J.* 6: 1781-1789.
- Paterson, J. y K. O'Hare (1991) Structure and transcription of the *singed* locus of *Drosophila melanogaster*. *Genetics* 129: 1073-1084.
- Perkins, L. A., I. Larsen y N. Perrimon (1992) *Corkscrew* encodes a putative protein tyrosine phosphatase that functions to transduce the terminal signal from the receptor tyrosine kinase torso. *Cell* 70: 225-236.
- Pimpinelli, S., M. Berloco, L. Fanti, P. Dimitri, S. Bonaccorsi *et al.* (1995) Transposable elements are stable structural components of *Drosophila melanogaster* heterochromatin. *Proc. Natl. Acad. Sci. USA* 92: 3804-3808.
- Pletcher, M. T., B. A. Roe, F. Chen, T. Do, A. Do *et al.* (2000) Chromosome evolution: the junction of mammalian chromosomes in the formation of mouse chromosome 10. *Genome Res.* 10: 1463-1467.
- Postlethwait, J. H., I. G. Woods, P. Ngo-Hazelett, Y. L. Yan, P. D. Kelly *et al.* (2000) Zebrafish comparative genomics and the origins of vertebrate chromosomes. *Genome Res.* 10: 1890-1902.

- Powell, J. R. (1997) Progress and prospects in evolutionary biology. The *Drosophila* model. Oxford University Press, New York.
- Puttagunta R., L. A. Gordon, G. E. Meyer, D. Kapfhamer, J. E. Lamerdin, *et al.* (2000) Comparative maps of human 19p13.3 and mouse chromosome 10 allow identification of sequences at evolutionary breakpoints. *Genome Res.* 10: 1369-1380.
- Randazzo, F. M., M. A. Seeger, C. A. Huss, M. A. Sweeney, J. K. Cecil *et al.* (1993) Structural changes in the *Antennapedia* complex of *Drosophila pseudoobscura*. *Genetics* 133: 319-330.
- Ranz, J. M., C. Segarra y A. Ruiz (1997) Chromosomal homology and molecular organization of Muller's element D and E in the *Drosophila repleta* species group. *Genetics* 145: 281-295.
- Ranz, J. M. (1998) Cartografía física comparada de los elementos cromosómicos E y D en el género *Drosophila*. Tesis doctoral. Universitat Autònoma de Barcelona.
- Ranz, J. M., M. Cáceres y A. Ruiz (1999) Comparative mapping of cosmids and gene clones from a 1.6 Mb chromosomal region of *Drosophila melanogaster* in three species of the distantly related subgenus *Drosophila*. *Chromosoma* 108: 32-43.
- Ranz, J. M., F. Casals y A. Ruiz (2001) How malleable is the eukaryotic genome? Extreme rate of chromosomal rearrangements in the genus *Drosophila*. *Genome Res.* 11: 230-239.
- Rice, W. R. (1984) Sex chromosomes and the evolution of sexual dimorphism. *Evolution* 38: 735-742.
- Rizzon, C., G. Marais, M. Gouy y C. Biémont (2002) Recombination rate and the distribution of transposable elements in the *Drosophila melanogaster* genome. *Genetics* (en prensa).

- Rodriguez-Trelles, F., L. Alarcón y A. Fontdevila (2000) Molecular evolution and phylogeny of the *buzzatii* complex (*Drosophila repleta* group): a maximum-likelihood approach. *Mol. Biol. Evol.* 17 :1112-1122.
- Rubin, G. M. y A. C. Spradling (1982) Genetic transformation of *Drosophila* with transposable element vectors. *Science* 218:348-353.
- Rubin, G. M. y E. B. Lewis (2000) A brief history of *Drosophila*'s contributions to genome research. *Science* 287: 2216-2218.
- Rubin, G. M., M. D. Yandell, J. R. Wortman, G. L. G. Miklos, C. R. Nelson *et al.* (2000a) Comparative genomics of the eukaryotes. *Science* 287: 2204-2215.
- Rubin, G. M., L. Hong, P. Brokstein, M. Evans-Holm, E. Frise *et al.* (2000b) A *Drosophila* complementary resource. *Science* 287: 2222-2224.
- Ruiz, A. y M. Wasserman (1993) Evolutionary cytogenetics of the *Drosophila buzzatii* species complex. *Heredity* 70: 582-596.
- Russo, C. A. M., N. Takezaki y M. Nei (1995) Molecular phylogeny and divergence times of Drosophilid species. *Mol. Biol. Evol.* 12: 391-404.
- Sambrook, J., E. F. Fritsch y T. Maniatis (1989) *Molecular cloning, a laboratory manual*. Cold Spring Harbor Laboratory Press, New York.
- Schafer, D. J., D. K. Fredline, W. R. Knibb, M. M. Green y J. S. F. Barker (1993) Genetics and linkage mapping of *Drosophila buzzatii*. *J. Hered.* 84: 188-194.
- Schneuwly, S., A. Kuroiwa y W. J. Gehring (1987) Molecular analysis of the dominant homeotic Antennapedia phenotype. *EMBO J.* 6: 201-206.

- Schoen, D. J. (2000) Comparative genomics, marker density and statistical analysis of chromosome rearrangements. *Genetics* 154: 943-952.
- Schulze, D. H. y C. S. Lee (1986) DNA sequence comparison among closely related *Drosophila* species in the *mulleri* complex. *Genetics* 113: 287-303.
- Segarra, C. y M. Aguadé (1992) Molecular organization of the X chromosome in different species of the *obscura* group of *Drosophila*. *Genetics* 130: 513-521.
- Segarra, C., E. R. Lozovskaya, G. Ribó, M. Aguadé y D.L. Hartl (1995) P1 clones from *Drosophila melanogaster* as markers to study the chromosomal evolution of Muller's A element in two species of the *obscura* group of *Drosophila*. *Chromosoma* 104: 129-136.
- Segarra C, G. Ribó y M. Aguadé (1996) Differentiation of Muller's chromosomal elements D and E in the *obscura* group of *Drosophila*. *Genetics* 144: 139-146.
- Seoighe, C., N. Federspiel, T. Jones, N. Hansen, V. Bivolarovic *et al.* (2000) Prevalence of small inversions in yeast gene order evolution. *Proc. Natl. Acad. Sci. USA* 97: 14433-14437.
- Sidén-Kiamos, I., R. D. Saunders, L. Spanos, T. Majerus, J. Treanear *et al.* (1990) Towards a physical map of the *Drosophila melanogaster* genome: mapping of cosmid clones within defined genomic divisions. *Nucleic Acids Res.* 18: 6261-6270.
- Smith, D. F., A. McClelland, B. N. White, C. F. Addison y D. M. Glover (1981) The molecular cloning of a dispersed set of developmentally regulated genes which encode the major larval serum protein of *D. melanogaster*. *Cell* 23: 441-449.
- Sperlich, D. y P. Pfriem (1986) Chromosomal polymorphism in natural and experimental populations. En: *The Genetics and Biology of Drosophila*, vol. 3e,

pp 257-309. Editado por: M. Ashburner, H. L. Carson y J. N. Thompson. Academic Press, London.

Spicer, G. S. (1988) Molecular evolution among some *Drosophila* species groups as indicated by two-dimensional electrophoresis. *J. Mol. Evol.* 27: 250-260.

Spicer, G. S. (1995) Phylogenetic utility of the mitochondrial *cytochrome oxidase* gene: molecular evolution of the *Drosophila buzzatii* species complex. *J. Mol. Evol.* 41: 749-759.

Spradling, A. C. y G. M. Rubin (1982) Transposition of cloned P elements into *Drosophila* germ line chromosomes. *Science* 218: 341-347.

Stathakis, D. S., E. S. Pentz y M. E. Freeman (1995) The genetic and molecular organization of the *dopa decarboxilase* gene cluster of *Drosophila melanogaster*. *Genetics* 141: 629-655.

Steinemann, M. (1982) Analysis of chromosomal homologies between two species of the subgenus *Sophophora*: *D. miranda* and *D. melanogaster* using cloned DNA segments. *Chromosoma* 87: 77-88.

Steinemann, M., W. Pinsker y D. Sperlich (1984) Chromosome homologies within the *Drosophila obscura* group probed by *in situ* hybridization. *Chromosoma* 91: 46-53.

Sternberg, N. (1990) Bacteriophage P1 cloning system for the isolation, amplification, and recovery of DNA fragments as large as 100 kilobase pairs. *Proc. Natl. Acad. Sci. USA* 87: 103-107.

Strachan, T. y A. P. Read (1996) *Human Molecular Genetics*. Oxford Bios Scientific Publishers.

- Stuckenholz, C., Y. Kageyama y M. I. Kuroda (1999) Guilt by association: non-coding RNAs, chromosome-specific proteins and dosage compensation in *Drosophila*. Trends Genet. 15: 454-458.
- Sturtevant, A. H. y E. Novitski (1941) The homologies of the chromosome elements in the genus *Drosophila*. Genetics 26: 517-541.
- Sullivan, D. T., P. W. Atkinson y W.T. Starmer (1990) Molecular evolution of the *alcohol dehydrogenase* genes in the genus *Drosophila*. Evolut. Biol. 24: 107-147.
- Sullivan, D. T., W. T. Starmer, S. W. Curtiss, M. Menotti-Raymond y J. Yum (1994) Unusual molecular evolution of an *Adh* pseudogen in *Drosophila*. Mol. Biol. Evol. 11: 443-458.
- Sun, H. -F. S., C. W. Ernst, M. Yerle, P. Pinton, M. F. Rothschild *et al.* (1999) Human chromosome 3 and pig chromosome 13 show complete synteny conservation but extensive gene-order differences. Cytogenet. Cell. Genet. 85: 273-278.
- Tanksley, S. D., M. W. Ganal, J. P. Prince, M. C. de Vicente, M. W. Bonierbale *et al.* (1992) High density molecular linkage maps of the tomato and potato genomes. Genetics 132: 1141-1160.
- Tanksley, S. D., M. W. Ganal y G. B. Martin (1995) Chromosome landing: a paradigm for map-based gene cloning in plants with large genomes. Trends Genet. 11: 63-68.
- Throckmorton, L. H. (1982) The *virilis* species group. En: *The Genetics and Biology of Drosophila*, vol. 3e, pp. 1-38. Editado por: M. Ashburner, H. L. Carson y J. N. Thompson. Academic Press, London.

- Tonzetich, J., T. W. Lyttle y H. L. Carson (1988) Induced and natural break sites in the chromosomes of Hawaiian *Drosophila*. Proc. Natl. Acad. Sci. USA 85: 1717-1721.
- Tonzetich, J., S. Hayashi y T. A. Grigliatti (1990) Conservatism of sites of *tRNA* loci among the linkage groups of several *Drosophila* species. J. Mol. Evol. 30: 182-188.
- True, J. R., J. M. Mercer y C. C. Laurie (1996) Differences in crossover frequency and distribution among three sibling species of *Drosophila*. Genetics 142: 507-523.
- Tudor, M., A. Mitchelson y K. O'Hare (1996) A 1.5 kb repeat sequence flanks the *suppressor of forked* gene at the euchromatin-heterochromatin boundary of the *Drosophila melanogaster* X chromosome. Genet. Res. 68: 191-202.
- Vieira, J., C. P. Vieira, D. L. Hartl y E. R. Lozovskaya (1997a) Discordant rates of chromosome evolution in the *Drosophila virilis* species group. Genetics 147: 223-230.
- Vieira, C. P., J. Vieira y D. L. Hartl (1997b) The evolution of small gene clusters: evidence for an independent origin of the *maltase* gene cluster in *Drosophila virilis* and *Drosophila melanogaster*. Mol. Biol. Evol. 14: 985-993.
- Vieira, J., C. P. Vieira, D. L. Hartl y E. R. Lozovskaya (1997c) A framework physical map of *D. virilis* based on P1 clones: applications in genome evolution. Chromosoma 106: 99-107.
- Wang, P. J., J. R. McCarrey, F. Yang y D. C. Page (2001) An abundance of X-linked genes expressed in spermatogonia. Nature Genetics 27: 422-426.
- Waring, G. L. y J. C. Pollack (1987) Cloning and characterization of a dispersed, multicopy X chromosome sequence in *Drosophila melanogaster*. Proc. Natl. Acad. Sci. USA 84: 2843-2847.

- Wasserman, M. (1962) Cytological studies of the *repleta* group of the genus *Drosophila*. V. The *mulleri* subgroup. The University of Texas Publication 6205: 85-117.
- Wasserman, M. (1992) Cytological evolution of the *Drosophila repleta* species group. En *Drosophila inversion polymorphism*, pp 455-552. Editado por C. B. Krimbas y J. R. Powell. CRC Press, Boca Raton, Florida.
- Wharton, L. T. (1942) Analysis of the *repleta* group of *Drosophila*. Univ. Texas Publ. 4228: 23-52.
- Whiting, J. H., M. D. Pliley, J. L. Farmer y D. E. Jeffery (1989) *In situ* hybridization analysis of chromosomal homologies in *Drosophila melanogaster* and *Drosophila virilis*. Genetics: 122: 99-109.
- Wright, T. R. F. (1996) Phenotypic analysis of the *dopa decarboxylase* gene cluster mutants in *Drosophila melanogaster*. Journal of Heredity 87: 175-190.
- Yi, S. y B. Charlesworth (2000) A selective sweep associated with a recent gene transposition in *Drosophila miranda*. Genetics 156: 1753-1763.
- Yuan, X., M. Miller y J. M. Belote (1996) Duplicated proteasome subunit genes in *Drosophila melanogaster* encoding testes-specific isoforms. Genetics 144: 147-157.