

Journey from extra-nuclear DNA to non-coding transcripts

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Extra-nuclear DNA in a Myxosporidian parasite (1966-67)

Significance?
Learn GENETICS

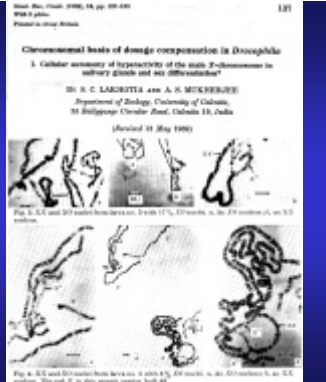


First encounter with "Fly Genetics"

Dosage compensation in *Drosophila*

Dosage compensation in *Drosophila* is cell autonomous (1969)

"In a very original study LAKHOTIA and MUKHERJEE (1969) show that the hyperactivity of the male X is cell autonomous" - M. Ashburner (1972)



The single X chromosome in polytene cells of male *Drosophila* completes replication earlier than autosomes (1970)



Further research interests originating from studies on dosage compensation in *Drosophila*

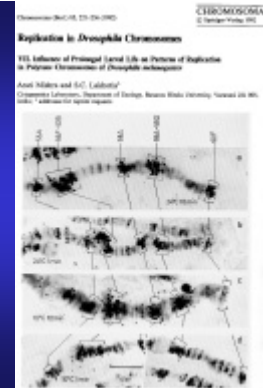
1. Replication in *Drosophila* chromosomes
1. Heterochromatin in *Drosophila*
2. Heat shock response in *Drosophila* and other insects
3. Non-coding *hsr-omega* gene in *Drosophila*

Replication in *Drosophila* chromosomes

This stemmed from the observations on transcription and replication patterns in X chromosome of male and female *Drosophila*

Ph. D. students:
 Dr. Mahesh Kumar
 Dr. Sabita Roy
 Dr. Jagat K. Roy
 Dr. Pradip Sinha
 Dr. Arati Mishra
 Dr. Pramod K. Tiwari
 Dr. Sujata Roy

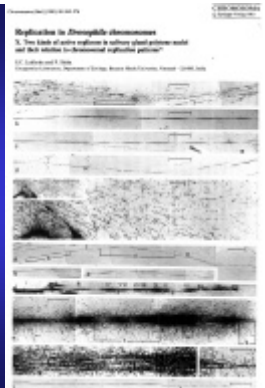
Temporal order of replication of specific bands in *Drosophila* cells is affected by specific developmental conditions



Cell division cycles in brain ganglia show certain unusual features including independent replication cycles in hetero- and eu-chromatin regions in mitotic cells (1978-1995)



DNA-Fibre autoradiography established existence of at least two kinds of active replicons in *Drosophila* cells (1983)



Heterochromatin in *Drosophila*

- Active and inactive chromatin regions replicate at different times
- Heterochromatin content varies in different species
- Review on heterochromatin

Reported from the journal of Zoology - International Research, Vol. 12, No. 4, September 2001, pp. 487-498
Nature of Heterochromatin*
 V. C. SHAR & S. C. LAKSHYMINI
 Department of Zoology, University School of Science, Sreejith University, Alambikad 4
 S. B. C. BAP
 Department of Zoology, University of Delhi, Delhi-1

Ph. D. students:
 Dr. Mahesh Kumar
 Dr. Jagat K. Roy
 Dr. Arati Mishra
 Dr. Sujata Roy

A Rat, *Rattus blanfordi*, has unusual chromosomes and abundant centromeric and sex-chromosomal heterochromatin



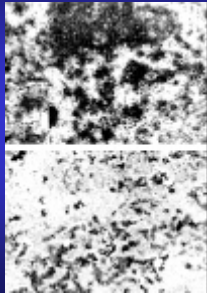
Chromosoma (1974) 3: 229-233
 Experimental Cell Research 84 (1974) 229-233

EM AUTORADIOGRAPHIC STUDIES ON POLYTENE NUCLEI OF *DROSOPHILA MELANOGASTER*
 II. Organization and Transcriptional Activity of the Chromosome

S. C. LAKHOTA and J. LACROIX

Department of Zoology, Bihar University, Muzaffarpur, India and
 Institute of Animal Sciences, University of Edinburgh, Edinburgh EH9 1QN, Scotland

Contrary to common belief, heterochromatin in *Drosophila* is transcriptionally active (1973-74)



Chromosoma (1979) 7: 249-251 (1979)
 CHROMOSOMA © by Springer Verlag 1979

A Study of Heterochromatin in *Drosophila nasuta* by the 5-Bromodeoxyuridine-Giemsa Staining Technique

S. C. Lakhota, J. K. Ray and Mihosh Kumar

Cytopgenetic Laboratory, Department of Zoology, Banskranthi University, Varanasi 221 005, India

Heterochromatin in *Drosophila nasuta* is comprised of asymmetric A-T rich sequences (1979)



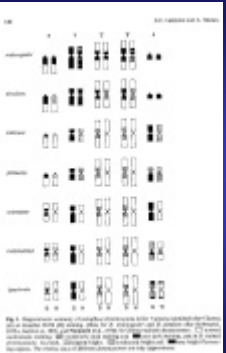
Chromosoma (1980) 10: 117-120 (1980)
 CHROMOSOMA © by Springer-Verlag 1980

Fluorescence Patterns of Heterochromatin in Mitotic and Polytene Chromosomes in Seven Members of Three Sub-groups of the melanogaster Species Group of *Drosophila*

S. C. Lakhota and Anil Mishra

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Heterochromatin in *Drosophila melanogaster* species group differs in repetitive sequences (1980)



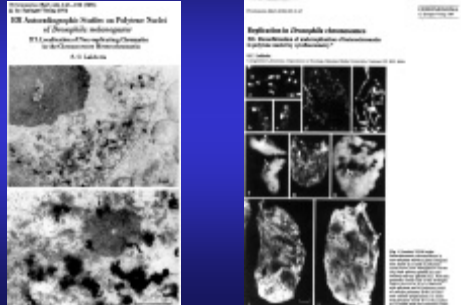
Bulk of heterochromatin does not replicate in polytene cells of *Drosophila* as originally suggested by Heitz in 1934 (1974, 1984)

Experimental Cell Research 84 (1974) 229-233
 Experimental Cell Research 104 (1984) 1-10

EM Autoradiographic Studies on Polytene Nuclei of *Drosophila melanogaster*
 III. Localization of Polytene Chromosomes in the Chromosome

S. C. Lakhota


Replication in *Drosophila* chromosomes: the localization of polytene chromosomes in the chromosome
 S. C. Lakhota



Heat shock response in *Drosophila*

Interest originated from the observation in 1969 that the benzamide-inducible 93D puff was a member of heat shock gene family

Ph. D. students:
 Dr. Tapas Mukhopadhyaya
 Dr. Ajit K. Singh
 Dr. B. B. Nath
 Dr. Abhay Sharma
 Dr. Bhupendra N. Singh
 Dr. K. V. Prasanth
 Ms. Priya Srivastava
 Mr. Surajit Sarkar



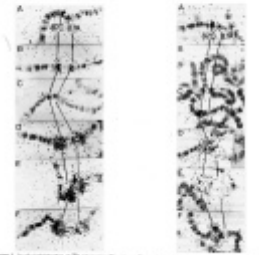
Chromosoma (1980) 10: 117-120 (1980)
 CHROMOSOMA © by Springer-Verlag 1980

In situ quantification of hsp70 and alpha-beta transcripts at 87A and 87C loci in relation to heat-shock gene activity in polytene cells of *Drosophila melanogaster*

A. Ghosh & S. C. Lakhota

Chromosoma (1980) 10: 117-120 (1980)
 CHROMOSOMA © by Springer-Verlag 1980

The RNA synthesis and turnover of hsp70 and $\alpha\beta$ transcripts (non-coding) at the 87A and 87C heat shock puffs is affected by the state of activity of the *hsw* or the 93D gene (1980-1995)



Heat shock induces the *hsp70* genes of 87A and 87C clusters very differently in different cell types (2002)

Inducibility of the different heat shock genes in *Chironomus* varies in summer and winter months in relation to the ambient temperature (1989)

The Malpighian tubules of *Drosophila* respond to heat shock in a manner very different from the other tissues (1989)

The heat shock induced 64 kDa polypeptide in Malpighian tubules is a member of the Hsp60 family (1998)

Research Articles

Synthesis of a ubiquitously present new HSP60 family protein is enhanced by heat shock only in the Malpighian tubules of *Drosophila*

S. C. Lakhotia* and B. N. Singh
 Zoology Laboratory, Department of Zoology, Banarus Hindu University, Varanasi 221 005 (India)
 Fax: +91 542 372584
 Received 20 August 1995; received after revision 26 November 1995; accepted 10 January 1996

Malpighian tubule cells display a complex pattern of transcription, translation and stability of *hsp70* and *hsp64* transcripts following heat shock and during recovery (2002)

Cell Stress & Chaperones (2002) 7 (4), 347-356

Regulation of heat shock proteins, Hsp70 and Hsp64, in heat-shocked Malpighian tubules of *Drosophila melanogaster* larvae

Sukhesh C. Lakhotia, Pooja Srivastava, and K. V. Prasanth

Non-coding 93D or *hsrω* gene in *Drosophila*

Inhibition of chromosomal transcription with benzamide in salivary glands revealed unique and singular induction of the 93D puff (1969)

P.N. K. srivastava :
 Dr. Tapas Mukhopadhyaya
 Dr. Ajit K. Singh
 Dr. B. B. Nath
 Dr. Debpratin Kar Chowdhury
 Dr. Pradeep K. Burma
 Dr. Abhay Sharma
 Dr. Mousumi Mutsuddi
 Dr. Pritha Ray
 Dr. K. V. Prasanth
 Dr. T. K. Rajendra
 Ms. Sonali Sengupta
 Mr. Saripalle Srikrishna

Chromosoma (Berl.) 11, 127-131 (1976)

CHROMOSOMA
© by Springer-Verlag 1976

Specific Activation of Puff 93D of *Drosophila melanogaster* by Benzamide and the Effect of Benzamide Treatment on the Heat Shock Induced Puffing Activity

S.C. Lakhota and T. Mukherjee
Cytogenetics Laboratory, Department of Zoology, Banarus Hindu University, Varanasi 221 002, India



The 93D puff is singularly induced by benzamide (1970, 1980)

First report published by Lakhota & A. S. Mukherjee in *DIS* 45: 108 (1970)

Could the 93D puff provide a good model system to examine the relation between puffs, gene activity and proteins?

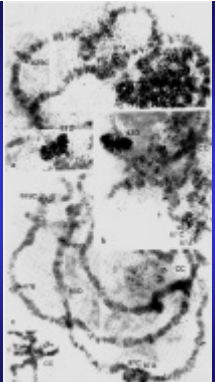
In the early 1970s, this relationship was still not well established

Chromosoma (Berl.) 13, 15-20 (1978)

CHROMOSOMA
© by Springer-Verlag 1978

³H-Uridine Incorporation in the Puff 93D and in Chromocentric Heterochromatin of Heat Shocked Salivary Glands of *Drosophila melanogaster*

Tilraj Mukherjee and S.C. Lakhota
Cytogenetics Laboratory, Department of Zoology, Banarus Hindu University, Varanasi 221 002, India



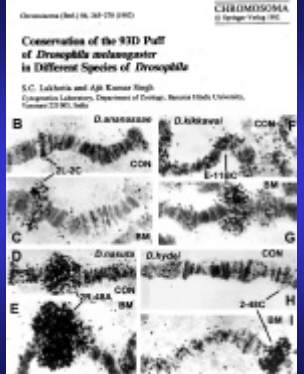
Heat shock induced activity of the 93D puff is not coordinated with the other heat shock puffs (1979)

Chromosoma (Berl.) 16, 347-370 (1982)

CHROMOSOMA
© Springer-Verlag 1982

Conservation of the 93D Puff of *Drosophila melanogaster* in Different Species of *Drosophila*

S.C. Lakhota and Ajit Kumar Singh
Cytogenetics Laboratory, Department of Zoology, Banarus Hindu University, Varanasi 221 002, India



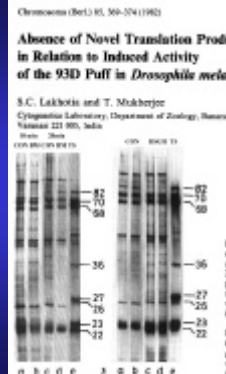
A homologue of the 93D puff is present in all species of *Drosophila* (1982)

Chromosoma (Berl.) 15, 509-524 (1982)

CHROMOSOMA
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Absence of Novel Translation Products in Relation to Induced Activity of the 93D Puff in *Drosophila melanogaster*

S.C. Lakhota and T. Mukherjee
Cytogenetics Laboratory, Department of Zoology, Banarus Hindu University, Varanasi 221 002, India



The 93D puff in *Drosophila* is unlikely to code for a protein (1982)

DEVELOPMENTAL GENETICS 13:389-411 (1995)

Spatial Expression of the *hsc-omega* (93D) Gene in Different Tissues of *Drosophila melanogaster* and Identification of Promoter Elements Controlling Its Developmental Expression

MEERUNDE MISHRA AND S.C. LAKHOTA
Cytogenetics Laboratory, Dept. of Zoology, Banarus Hindu University, Varanasi, India



Transgenic flies used for analysing promoter of the *hscw* gene (1995)

The amide-response element on the *hsr ω* gene is more than 21kb upstream of the transcription start point (Promoter mapping using chromosomal deletions) (1998)

*Genetic mapping of the amide response element(s) of the hsr-omega gene of *Drosophila melanogaster**
 A. C. Lakhotia, R. K. Rajendra
 Department of Zoology, University of Lucknow, Lucknow-226007, India
 Received 15 June 2000; accepted 15 July 2000; first published online 15 August 2000

Does a non-coding gene like the 93D have any function or is it “junk”?

A new insight into functions of the non-coding large transcript of the *hsr ω* gene (1999)

*The non-coding transcripts of *hsr-omega* gene in *Drosophila*: Do they regulate trafficking and availability of nuclear RNA-processing factors?*
 S. C. Lakhotia*, Pritha Ray*, T. K. Rajendra and K. V. Prasanth
 Cytogenetics Laboratory, Department of Zoology, Banarus Hindu University, Varanasi-221 005, India
 *Present address: Institute of Cellular and Molecular Biology, Agricultural University, Ludhiana

A VARIETY OF hnRNPs AND RELATED NUCLEAR PROTEINS SPECIFICALLY BIND WITH THE 93D PUFF FOLLOWING HEAT SHOCK

Antibodies to the following proteins specifically bind with the 93D puff in heat shocked polytene nuclei of *Drosophila melanogaster*

- hnRNPs: Hrp40 (hnRNPA), HRB87F (hnRNP A1/A2), Hrb57A (hnRNP K), SS (hnRNP M)
- *Sxl*
- nuclear non-histone proteins recognized by Q14, Q16, T29, P75 antibodies
- Snf

(review in Lakhotia et al, 1999)

Omega speckles – a novel class of nuclear speckles containing hnRNPs associated with noncoding hsr-omega RNA in *Drosophila*

K. V. Prasanth, T. K. Rajendra, A. K. Lal and S. C. Lakhotia*

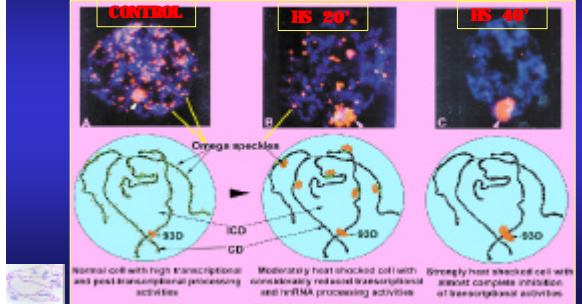
Cytogenetics Laboratory, Department of Zoology, Banarus Hindu University, Varanasi-221 005, India
 *Present address: Institute of Cellular and Molecular Biology, Agricultural University, Ludhiana

hsr ω -n transcripts essential for organizing OMEGA SPECKLES, which regulate the availability of hnRNPs for RNA processing (2000)

Under heat shock condition, all the hnRNPs get progressively sequestered at the *hsr ω* gene site

UNSTRESSED 15' 40' 2hr RECOVERY
 HEAT SHOCK

hsr ω RNA dynamically regulates the availability of hnRNPs in nucleus

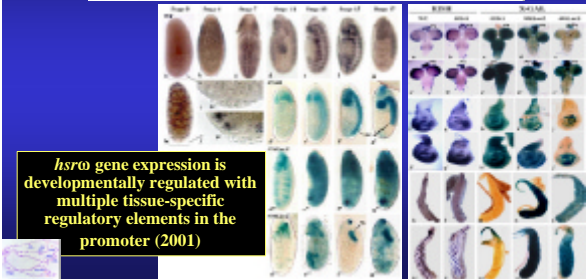


The non-coding, developmentally active and stress inducible *hsr ω* gene of *Drosophila melanogaster* integrates post-transcriptional processing of other nuclear transcripts

Subhash C. Lakhota
In: "Non-protein-coding RNAs" (edited by J. Barciszewski and Volker A. Erdmann), Landes Biosciences, 2002 (in press)

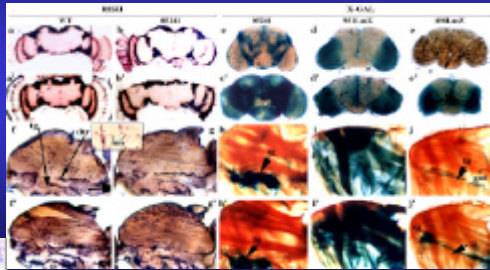
Developmental regulation and complex organization of the promoter of the non-coding *hsr ω* gene of *Drosophila melanogaster*

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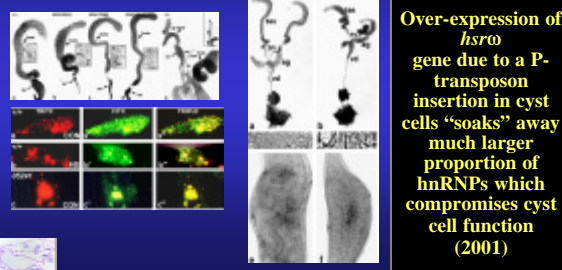
Developmental regulation and complex organization of the promoter of the non-coding *hsr ω* gene of *Drosophila melanogaster*

S. C. LAKHOTIA*, T. K. RAJENDRA and K. V. PRASANTH
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Male sterility associated with overexpression of the noncoding *hsr ω* gene in cyst cells of testis of *Drosophila melanogaster*

T. K. RAJENDRA, K. V. PRASANTH and S. C. LAKHOTIA*
Cytogenetics Laboratory, Department of Zoology, Banaras Hindu University, Varanasi 221 005, India



Over-expression of *hsr ω -n* transcripts in cyst cells of *05241* mutant testes excessively sequesters hnRNPs into the inactive compartment (clusters of omega speckles) and this affects processing of a variety of other nuclear transcripts
Compromise in cyst cell function prevents sperm maturation and individualization
(interesting parallel with the RNA-foci in DMI and DM2 human disorders which sequester CUG-BP, involved in processing of several other transcripts)

MOST TISSUES, OTHER THAN GUT, IN *hsrw^{p110}* MUTANT LARVAE ARE SMALLER AND LARVAL LIFE IS PROLONGED

***hsrw^{p110}/hsrw^{p110}* LARVAE**

- IMAGINAL DISCS ARE SMALL & DISORGANIZED
- *hsrw*-TRANSCRIPTS CLUSTERED AT THE GENE SITE IN MOST TISSUES
- *hsrw* IS NOT EXPRESSED IN PROTHORACIC GLANDS OF MUTANT LARVAE
- MUTANT LARVAE PUPATE AFTER 11-12 DAYS BUT ALL DIE

Sonali Sengupta & Lakhotia, unpublished

ABERRANT EXPRESSION OF *hsrw* IN *hsrw^{p110}* IS ASSOCIATED WITH CLUSTERING OF *hsrw* TRANSCRIPTS AND hnRNPs IN NUCLEI

Confocal images (projection) of Malpighian tubule cells
 RED- chromatin
 GREEN- *hsrw*-n RNA

Excessive sequestration of hnRNPs by *hsrw* transcripts at the *hsrw* gene site (>) and in clusters of omega speckles compromises processing of various nuclear transcripts in affected cells, resulting in the various anomalies in *p110* larvae and their ultimate death

Sonali Sengupta & Lakhotia, unpublished

Distribution of an hnRNP and Actin in wild type and 05241 mutant egg chambers

Srikrishna & Lakhotia, unpublished

The Sxl Protein in *hsrw* nullisomic egg chambers moves in the oocyte

Srikrishna & Lakhotia, unpublished

Developmental Genetics

The *Bar* gene, besides its role in ommatidial differentiation, acts as a proximal-distal selector gene in antennal and leg disks of *Drosophila*
 S.Mandal & Lakhotia (1999)