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

Some cytochemical observations on *Zschokkella auerbachi* (WEILL) CHAKRAVARTY, 1940 (myxosporidia, protozoa)

By S. C. LAKHOTIA and M. R. CHAKRAVARTY

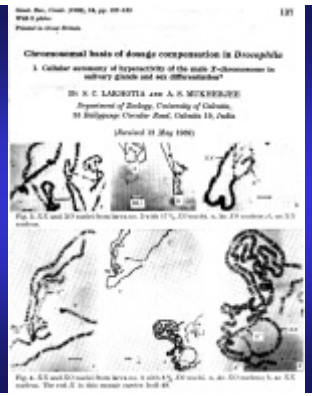
Department of Zoology, University of Calcutta

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)



Chromosomal basis of dosage compensation in *Drosophila*

I. Cellular autonomy of hyperactivity of the male X-chromosome in salivary glands and sex differentiation*

By S. C. LAKHOTIA and A. S. MUKHERJEE

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

CHROMOSOMAL BASIS OF DOSAGE COMPENSATION IN *DROSOPHILA*

III. Early Completion of Replication by the Polytene X-Chromosome in Male : Further Evidence and Its Implications

S. C. LAKHOTIA and A. S. MUKHERJEE

ABSTRACT

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

1. **Replication in *Drosophila* chromosomes**

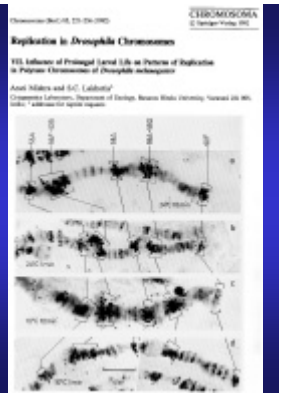
1. **Heterochromatin in *Drosophila***
2. **Heat shock response in *Drosophila* and other insects**
3. **Non-coding *hsr-omega* gene in *Drosophila***

Replication in *Drosophila* chromosomes

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

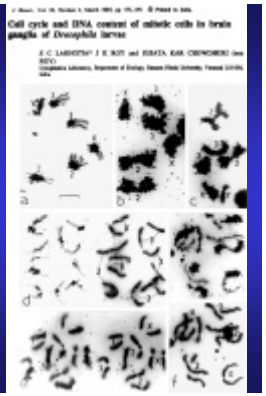
Ph. D. students :
Dr. Mahesh Kumar
Dr. Sabita Roy
Dr. Jagat K. Roy
Dr. Pradip Sinha
Dr. Arati Mishra
Dr. Pramod K. Tiwari
Dr. Sujata Roy

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

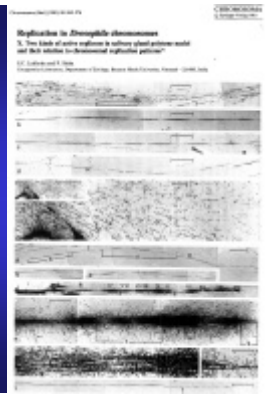

CHROMOSOMA

Replication in *Drosophila* Chromosomes

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

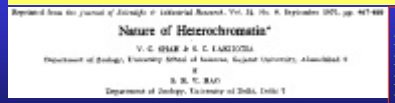

Cell cycle and DNA content of mitotic cells in brain ganglia of *Drosophila* larvae

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


Replication in *Drosophila* chromosomes

Heterochromatin in *Drosophila*

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


Nature of Heterochromatin*

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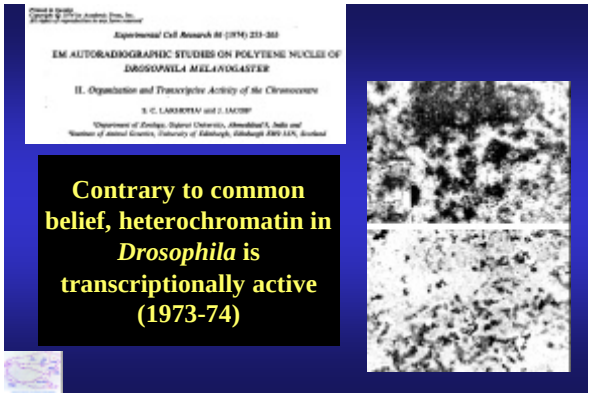
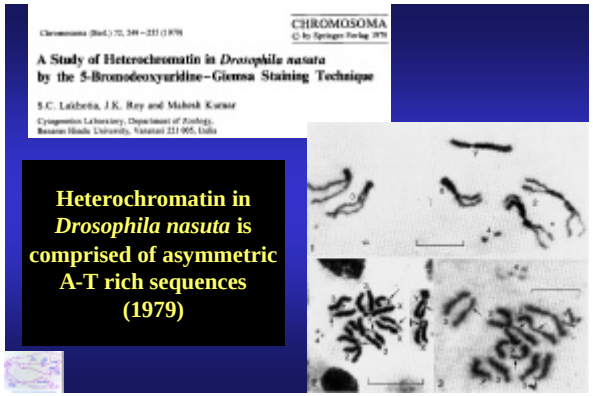
Dr. Arati Mishra
Dr. Sujata Roy

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

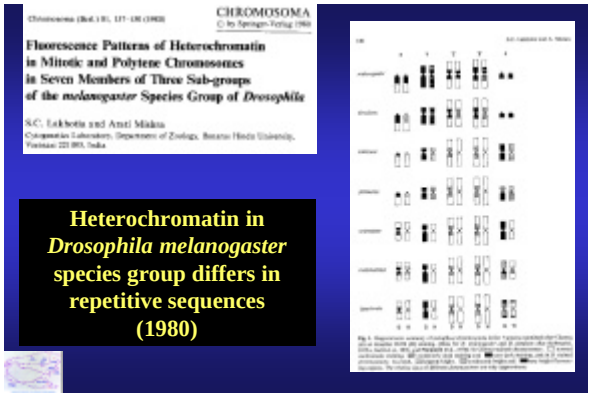

Chromosomes of *Rattus blanfordi*



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

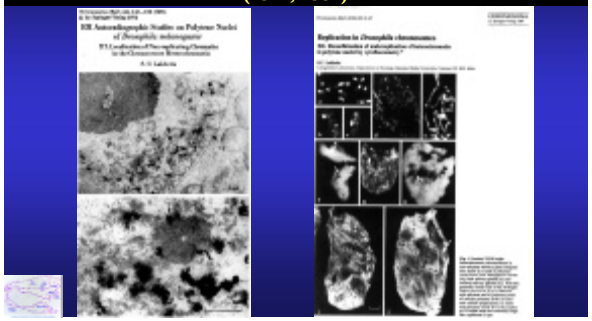


Heterochromatin in *Drosophila nasuta* is comprised of asymmetric A-T rich sequences (1979)



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)



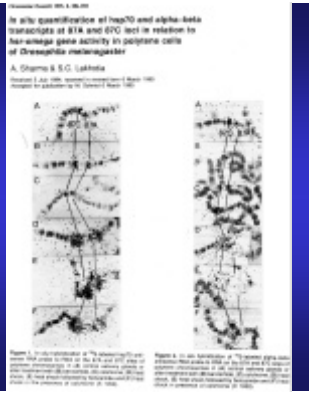
Heat shock response in *Drosophila*

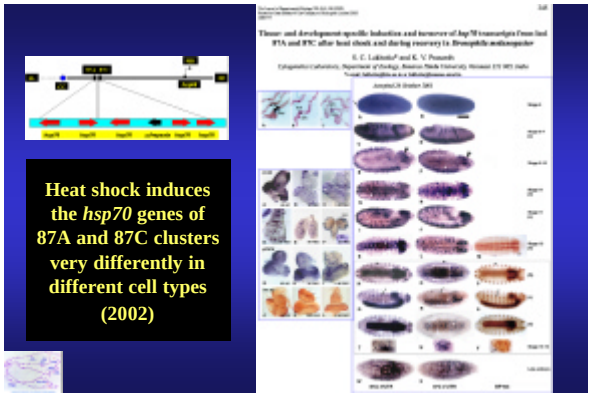
Interest originated from the observation in 1969 that the benzamide-inducible 93D puff was a member of heat shock gene family

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

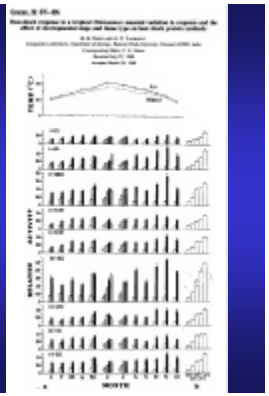
The RNA synthesis and turnover of hsp70 and αβ transcripts (non-coding) at the 87A and 87C heat shock puffs is affected by the state of activity of the *hsr*ω or the *93D* gene (1980-1995)



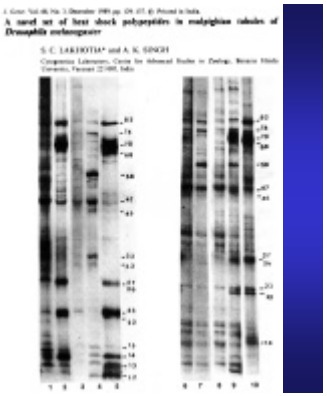


Heat shock induces the *hsp70* genes of 87A and 87C clusters very differently in different cell types (2002)

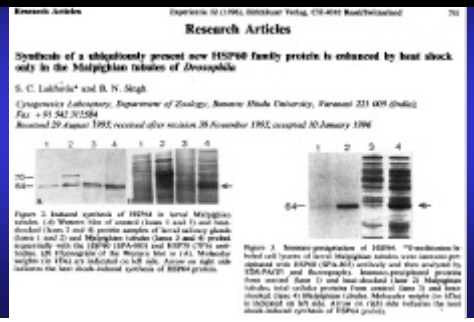
Inducibility of the different heat shock genes in *Chironomus* varies in summer and winter months in relation to the ambient temperature (1989)



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



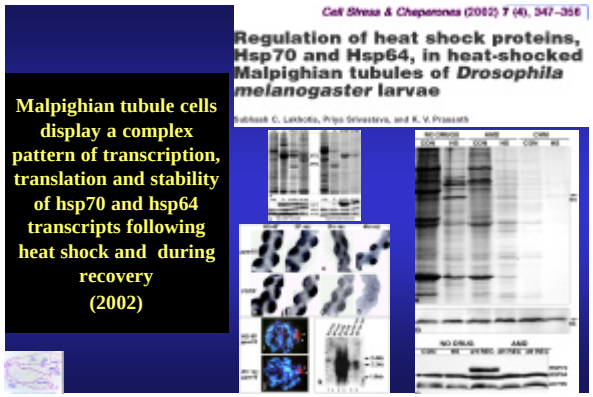
The heat shock induced 64 kDa polypeptide in Malpighian tubules is a member of the Hsp60 family (1998)



Research Articles

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

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

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)

Ph. D. students :

Dr. Tapas Mukhopadhyaya
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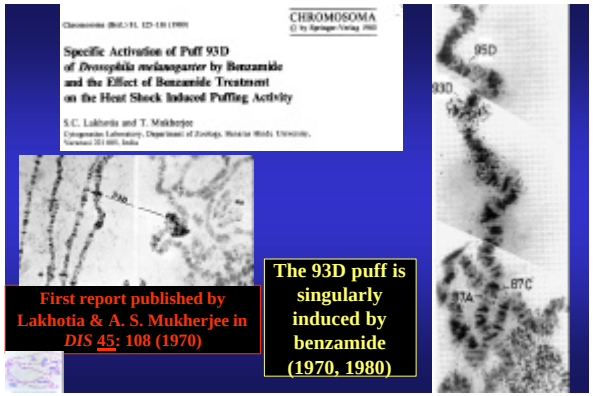
Dr. Debpratim Kar Chowdhury
Dr. Pradeep K. Burma
Dr. Abhay Sharma
Dr. Mousumi Mutsuddi
Dr. Pritha Ray
Dr. K. V. Prasanth
Dr. T. K. Rajendra
Ms. Sonali Sengupta
Mr. Saripalle Srikrishna

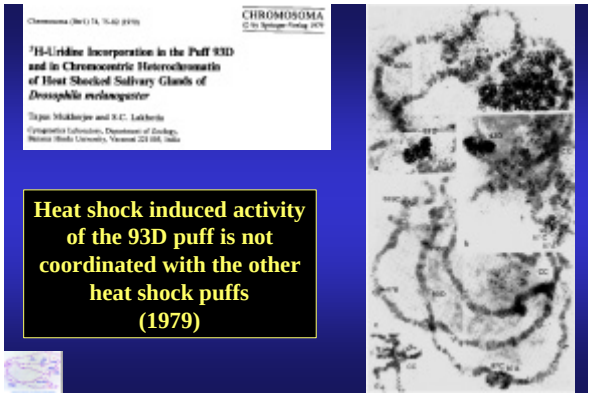


First report published by Lakhotia & A. S. Mukherjee in *DIS* 45: 108 (1970)

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

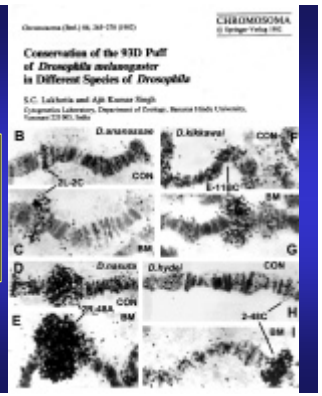
Could the 93D puff provide a good model system to examine the relation between puffs, gene activity and proteins?

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



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

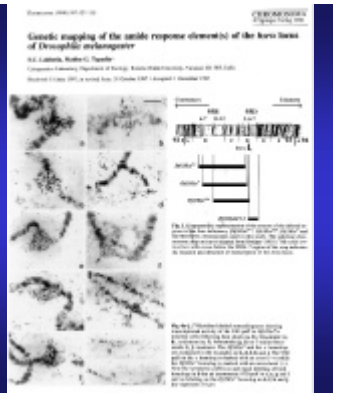
A homologue of the 93D puff is present in all species of *Drosophila* (1982)



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

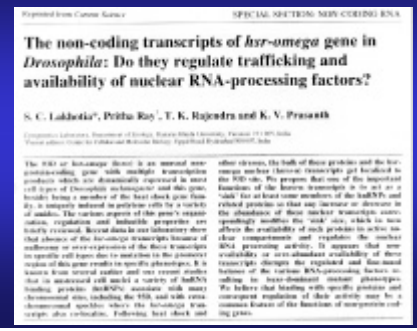
Transgenic flies used for analysing promoter of the *hsrω* gene (1995)

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



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

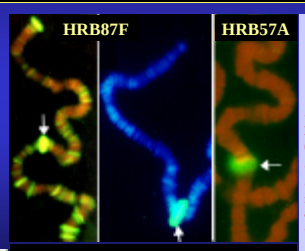
A new insight into functions of the non-coding large transcript of the *hsr*ω gene (1999)



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

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*

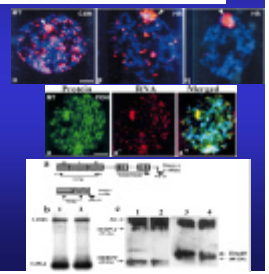
- hnRNPs: Hrp40 (hnRNPA), HRB87F (hnRNP A1/A2), Hrb57A (hnRNP K), S5 (hnRNP M)
- Sxl
- nuclear non-histone proteins recognized hy Q14, Q16, T29, P75 antibodies
- Snf

(review in Lakhotia et al, 1999)

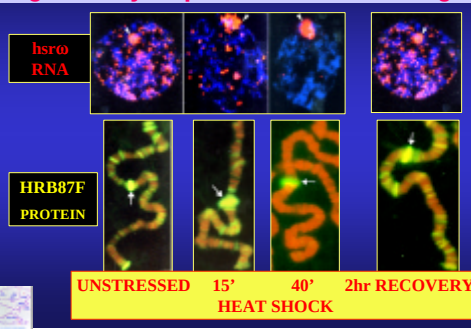
Omega speckles – a novel class of nuclear speckles containing hnRNPs associated with noncoding hsr-omega RNA in *Drosophila*

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

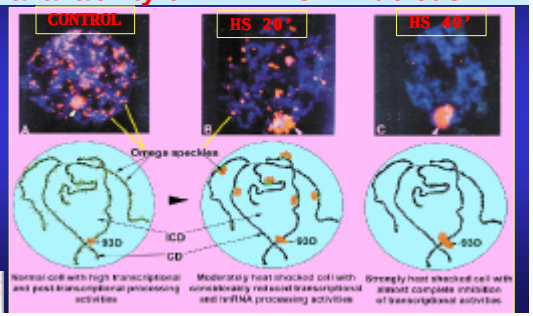
hsrω-n transcripts essential for organizing *OMEGA SPECKLES*, which regulate the availability of hnRNPs for RNA processing (2000)



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



hsrω RNA dynamically regulates the availability of hnRNPs in nucleus

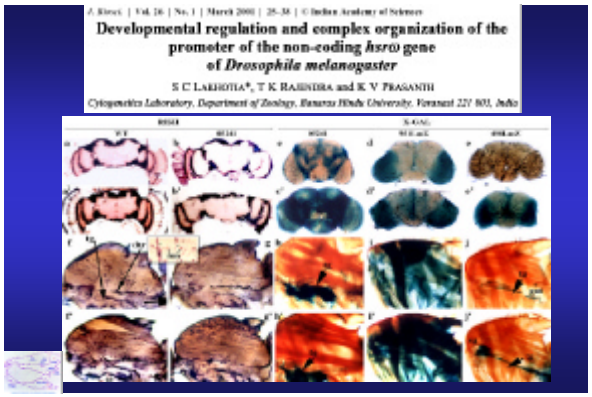


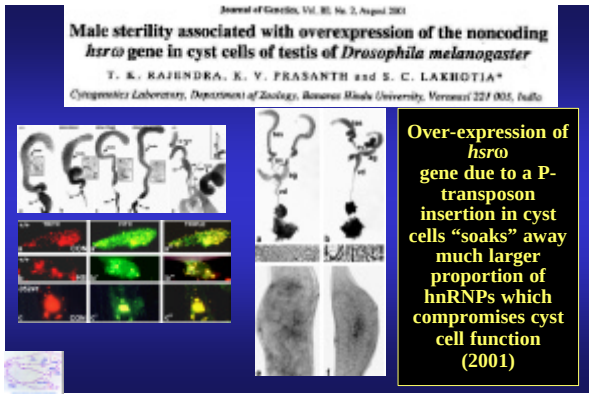
The non-coding, developmentally active and stress inducible *hsrω* gene of *Drosophila melanogaster* integrates post-transcriptional processing of other nuclear transcripts

Subhash C. Lakhotia

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

hsrω gene expression is developmentally regulated with multiple tissue-specific regulatory elements in the promoter (2001)





Over-expression of *hsrω* gene due to a P-transposon insertion in cyst cells "soaks" away much larger proportion of hnRNPs which compromises cyst cell function (2001)

Over-expression of hsrω-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 DM1 and DM2 human disorders which sequester CUG-BP, involved in processing of several other transcripts)

MOST TISSUES, OTHER THAN GUT, IN *hsrw*^{pl10} MUTANT LARVAE ARE SMALLER AND LARVAL LIFE IS PROLONGED

hsrw^{pl10}/*hsrw*^{pl10} LARVAE

- IMAGINAL DISCS ARE SMALL & DISORGANIZED
- hsrω-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

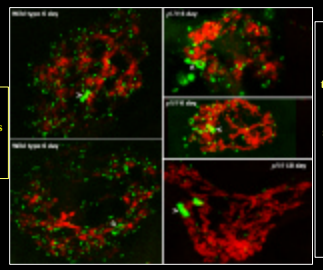
Sonali Sengupta & Lakhotia, unpublished

ABERRANT EXPRESSION OF *hsrw* IN *hsrw* ^{pl10} IS ASSOCIATED WITH CLUSTERING OF *hsrw* TRANSCRIPTS AND hnRNPs IN NUCLEI

Confocal images (projection) of Malpighian tubule cells

RED- chromatin

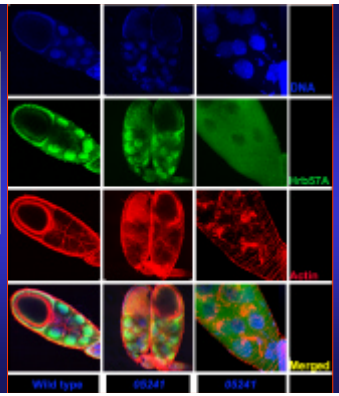
GREEN- hsrω-n RNA



Excessive sequesteration of hnRNPs by hsrω 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 *pl10* larvae and their ultimate death

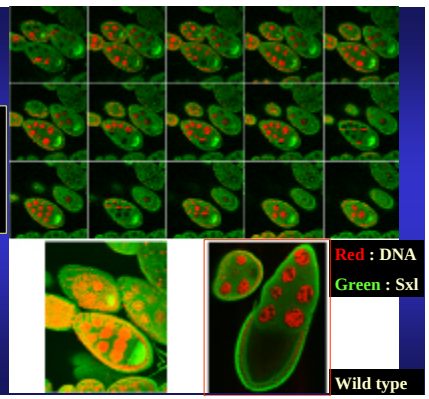
Sonali Sengupta & Lakhotia, unpublished

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



Srikrishna & Lakhotia, unpublished

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



Red : DNA

Green : Sxl

Wild type

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)