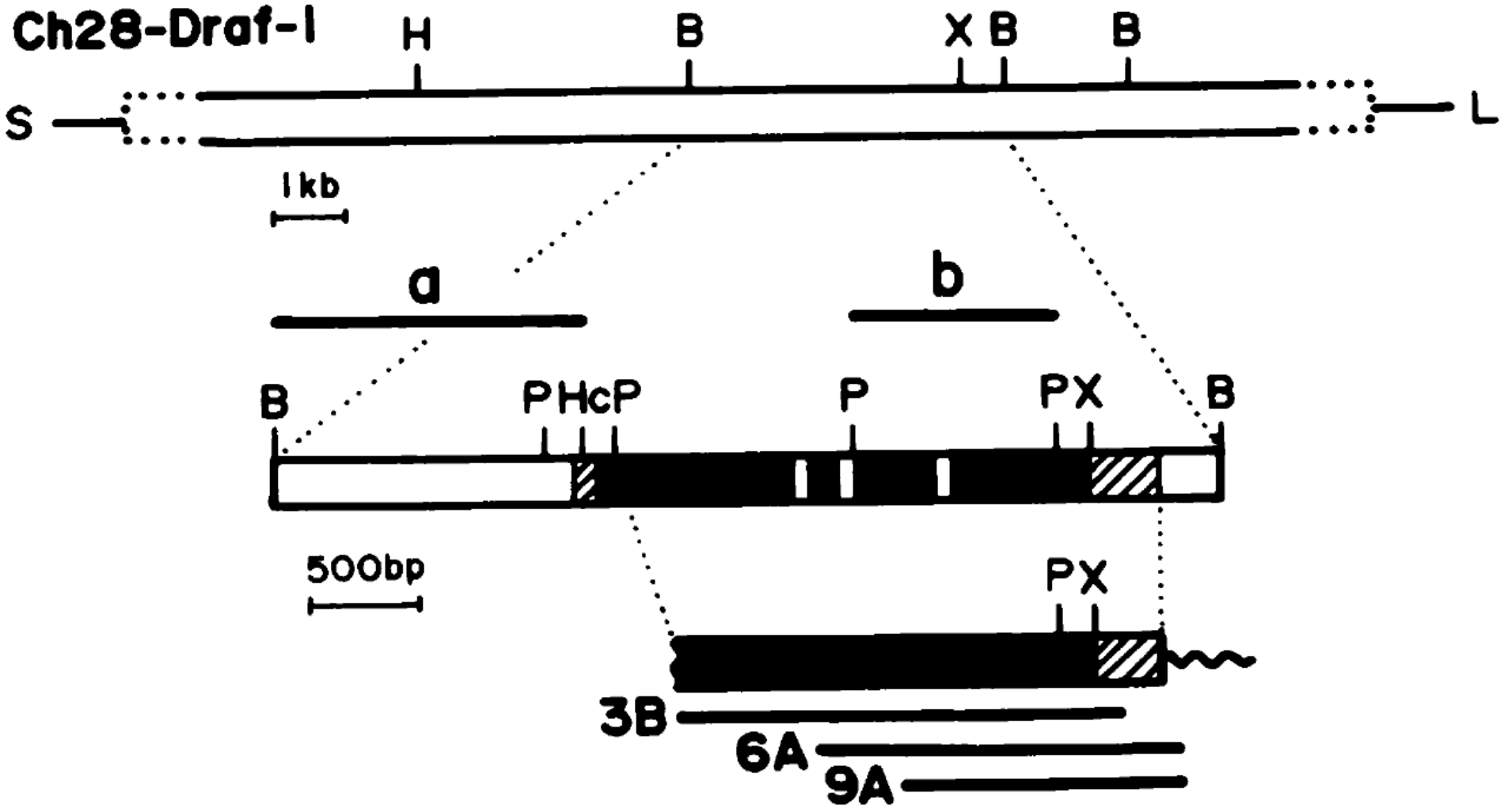
ショウジョウバエと共に28年

西田　育巧

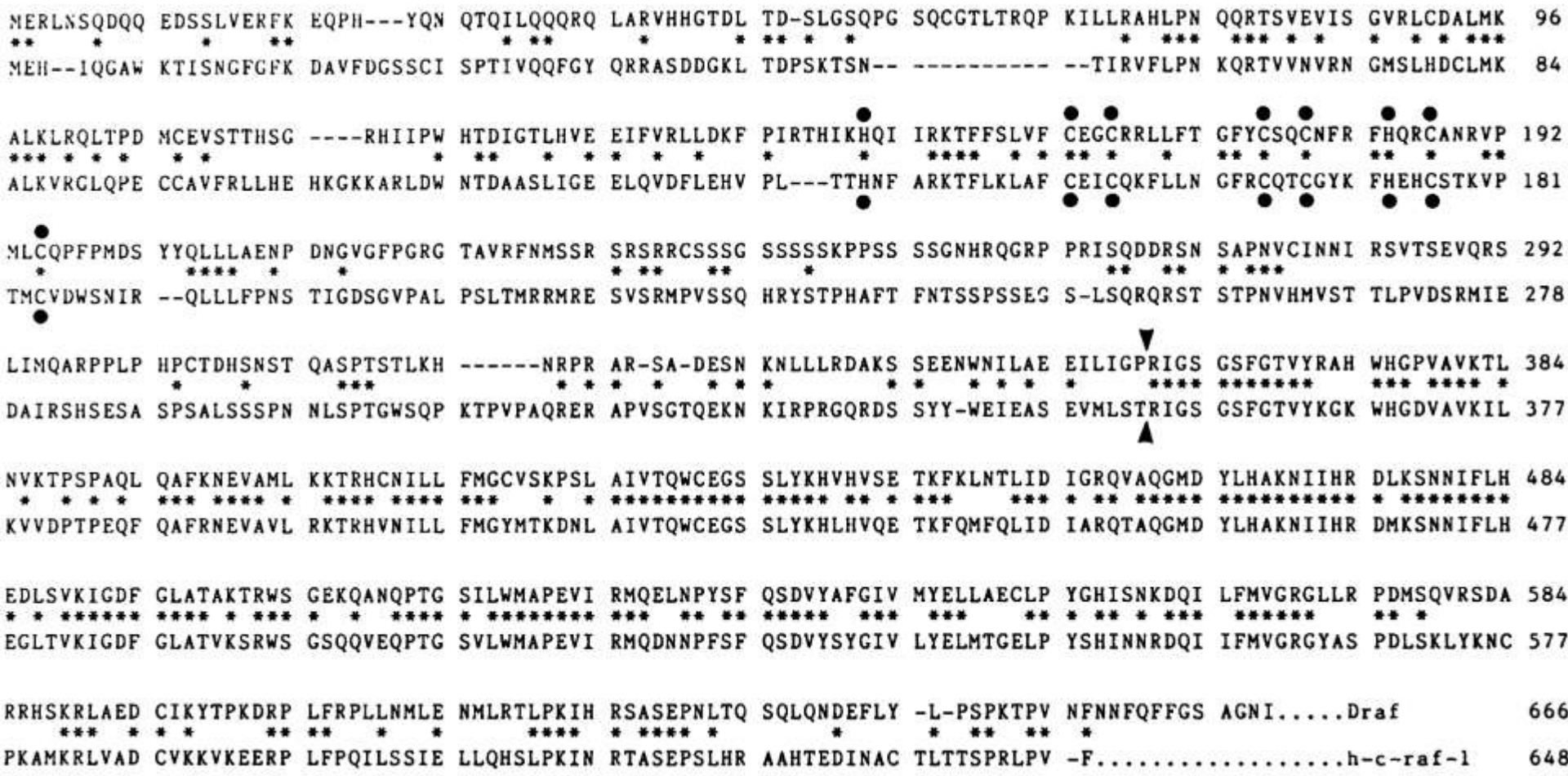
略　　歴

１９７１年３月　九州大学理学部生物学科　卒業
１９７１年４月　九州大学大学院理学研究科修士課程　入学
（九大山岳会ネパールヒマラヤ遠征隊に参加の為休学）
１９７４年３月　　同　　上　　修了
１９７４年４月　九州大学大学院理学研究科博士課程　進学
１９７６年８月　　同　　上　　中退
１９７６年９月　大阪大学医学部遺伝学教室　助手
１９８３年４月　The Institute for Cancer Research
（Beatrice Mintz 博士）
１９８５年８月　愛知県がんセンター研究所　分子生物学研究室　室長
１９９０年４月　愛知県がんセンター研究所　放射線部　部長
１９９４年４月　名古屋大学理学部　生物学科　教授

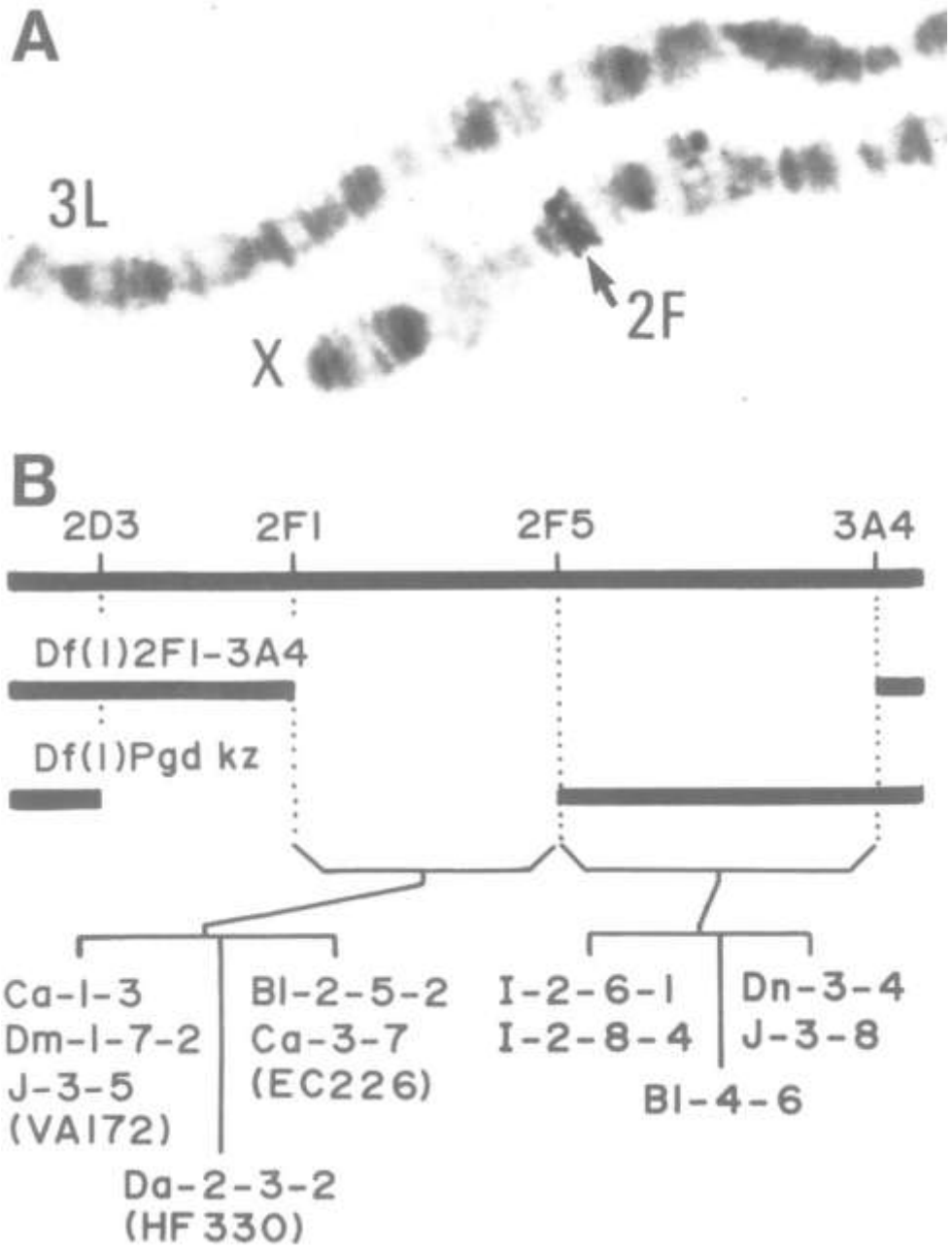
Cloning of the *Drosophila raf* gene and cDNAs



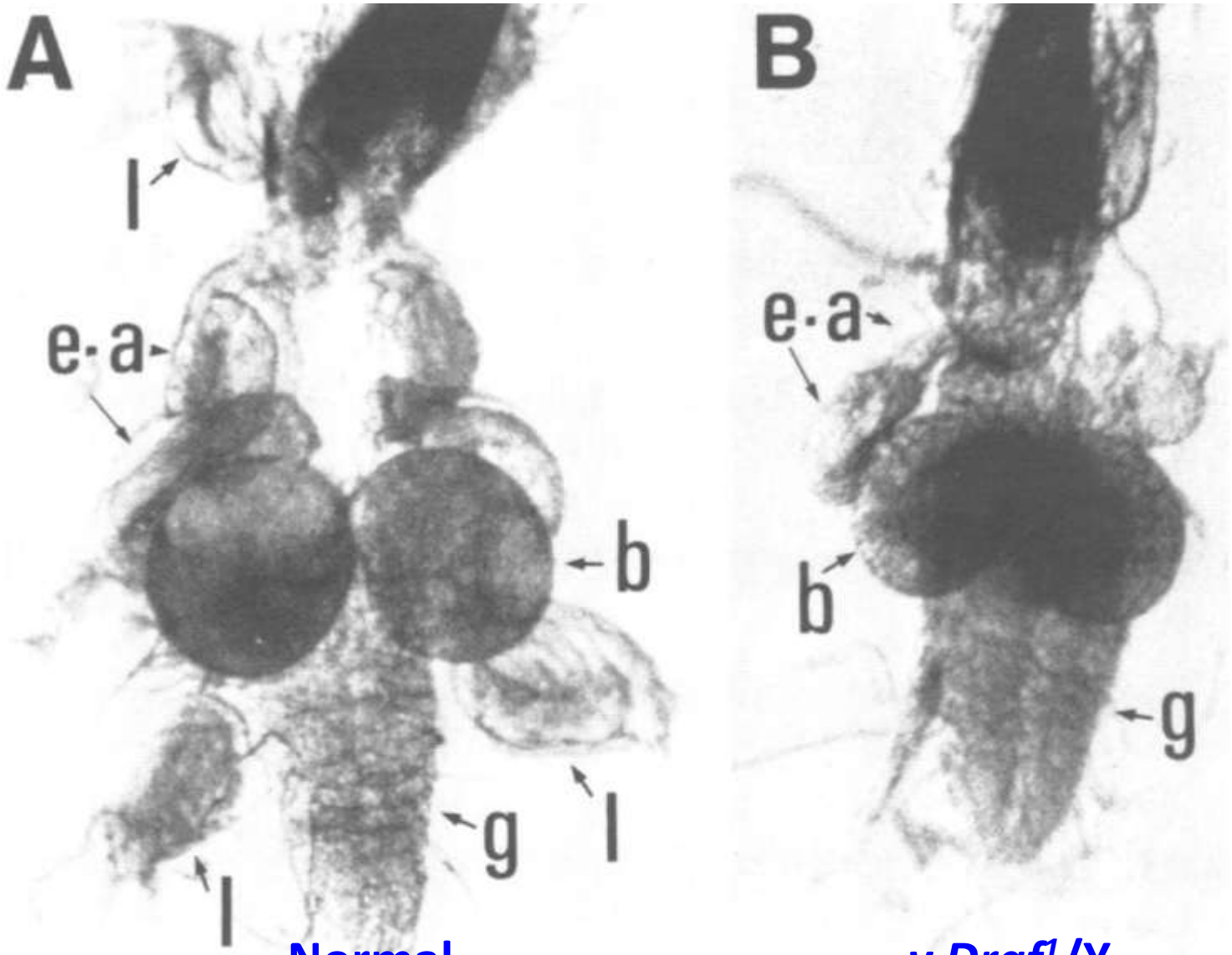
Comparison of Draf with human c-raf-1



Identification of the *Draf* mutants



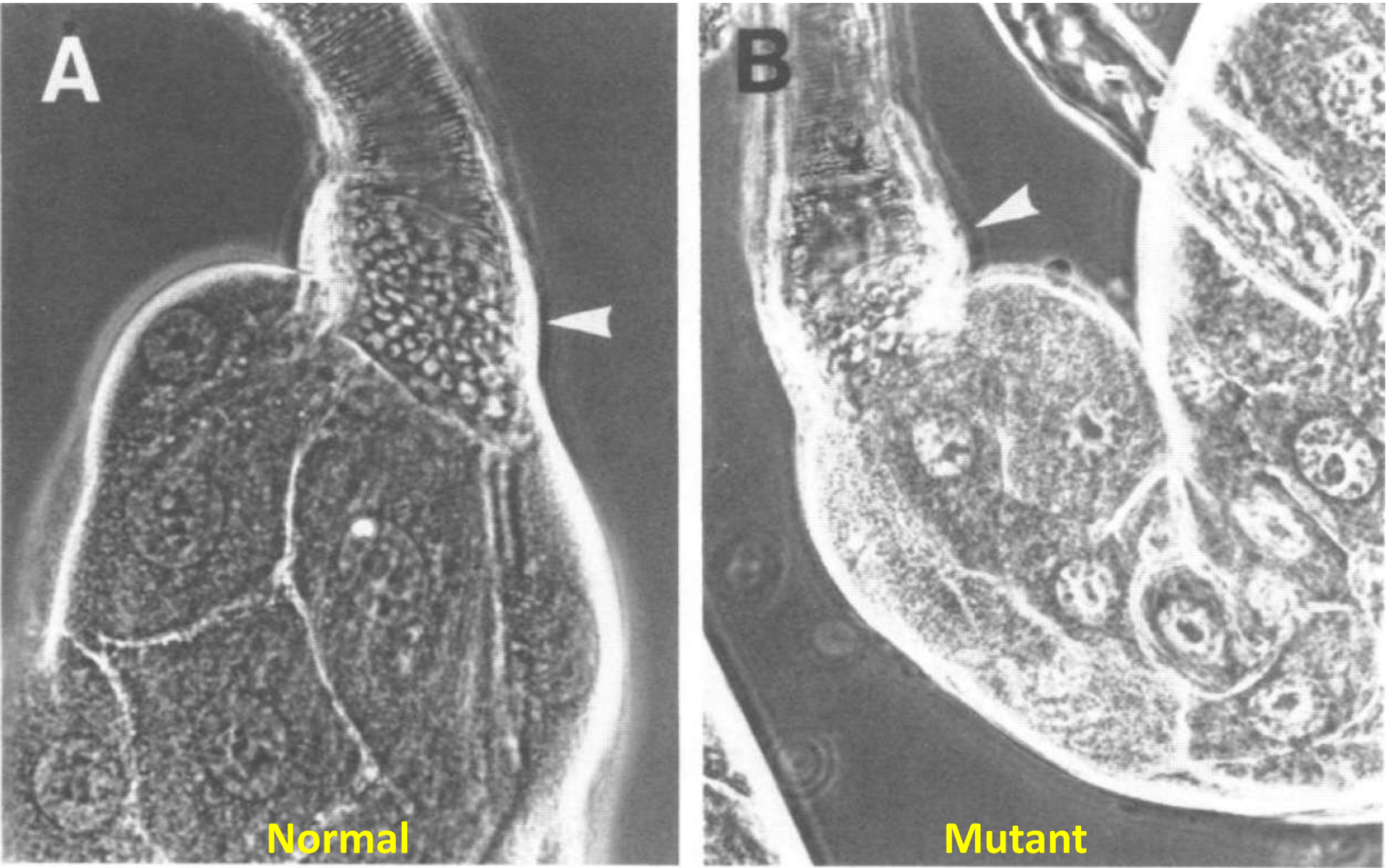
Growth defect of imaginal discs in *Draf*



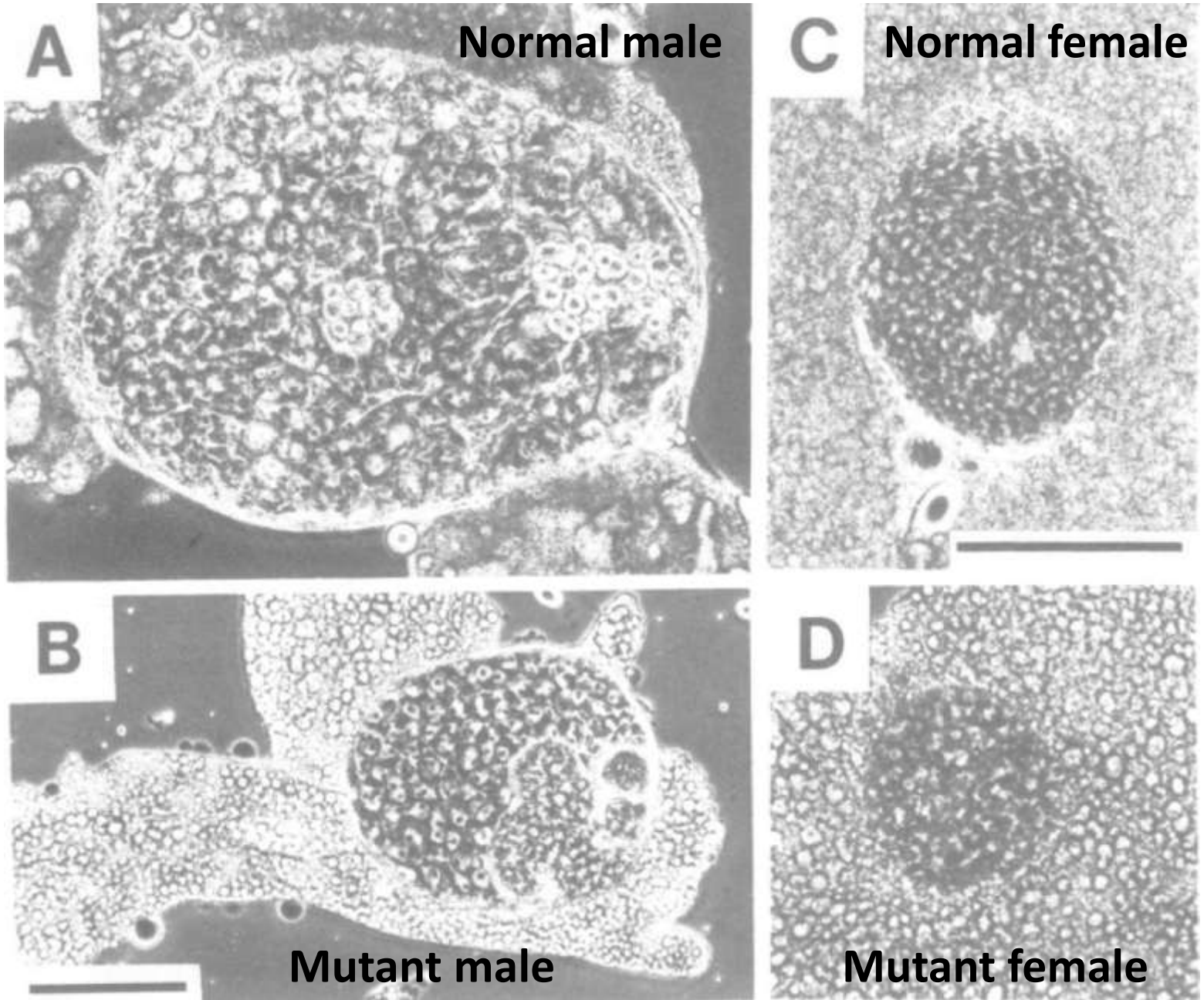
Normal

y Draf^{1}/Y

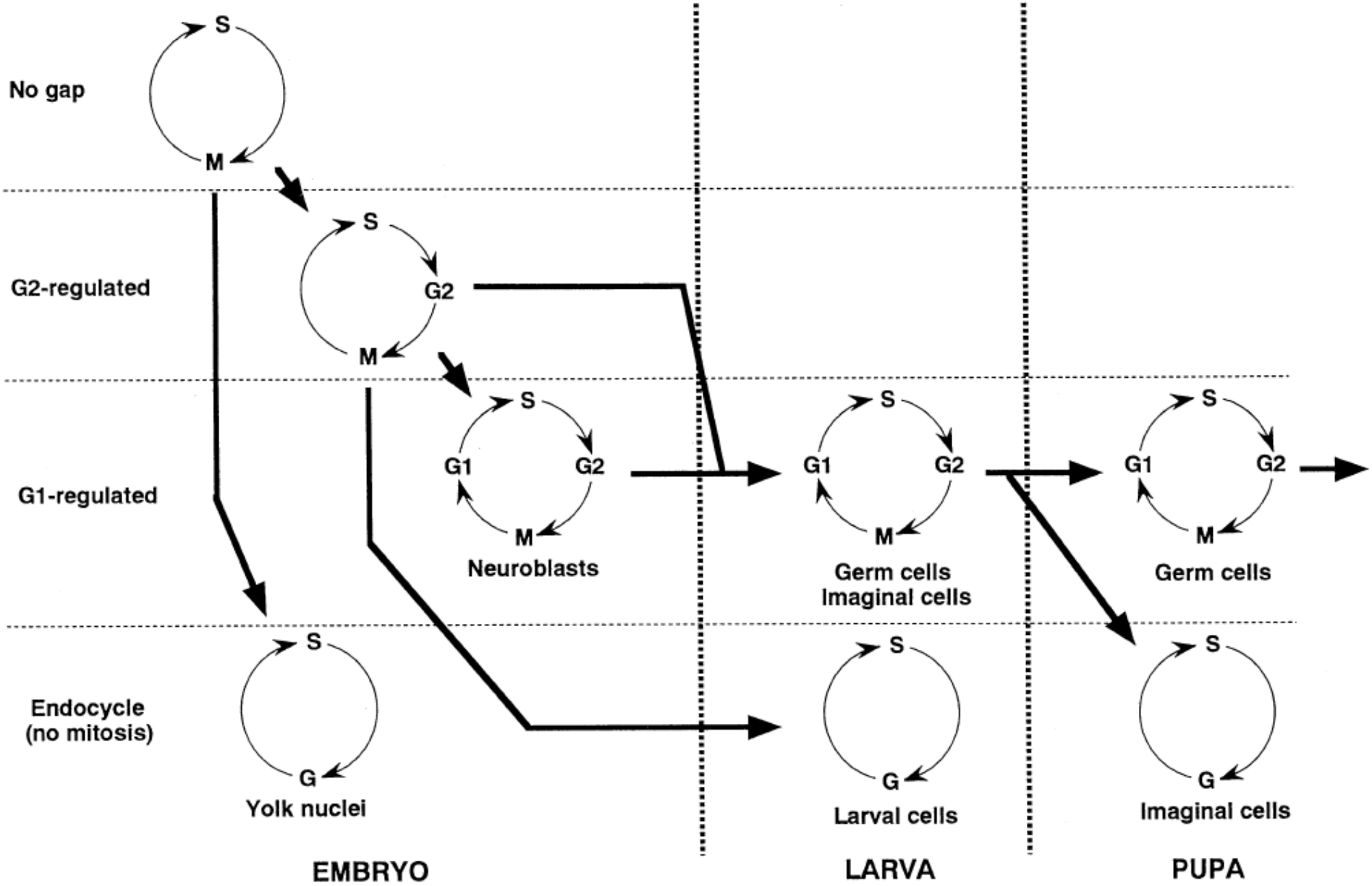
Imaginal salivary gland cells are reduced in *Draf*^{1} mutant



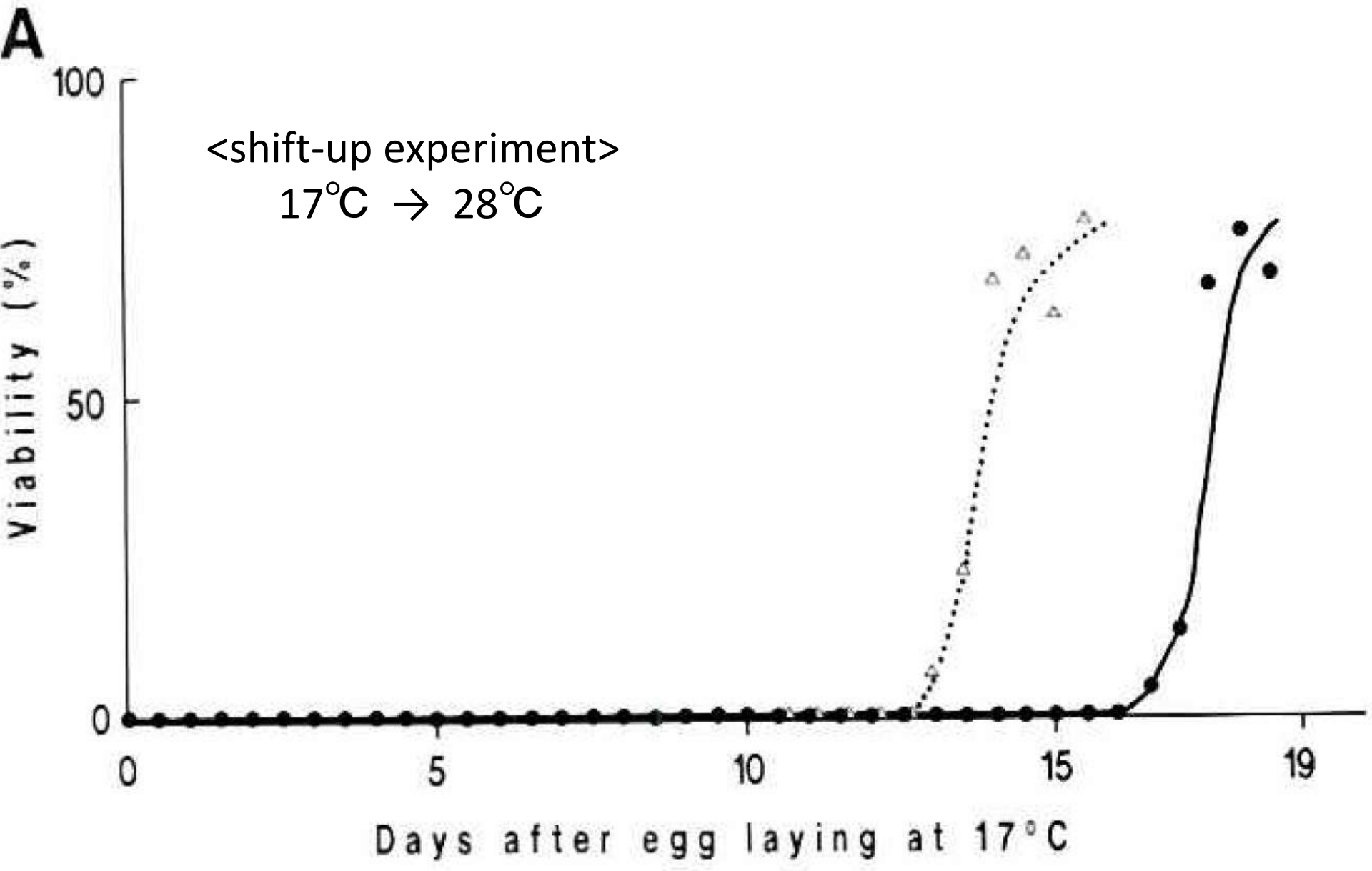
Germ cell proliferation is affected in *Draf*[1]



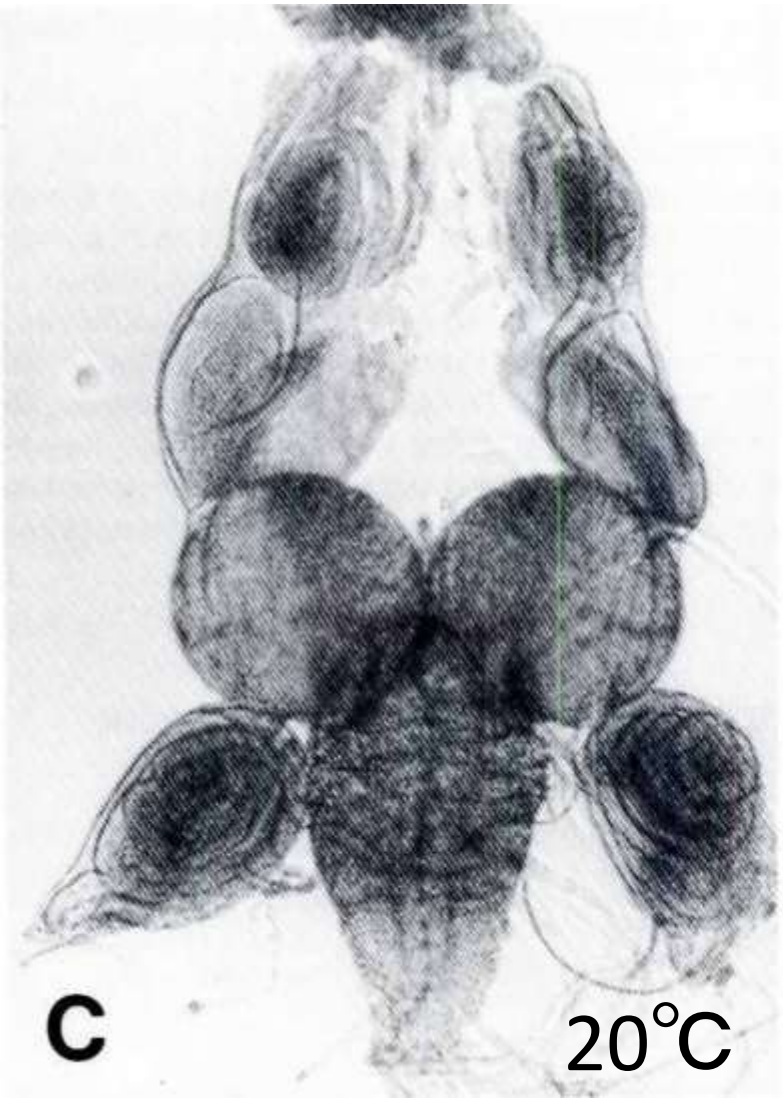
Different cell cycles are programmed during *Drosophila* development

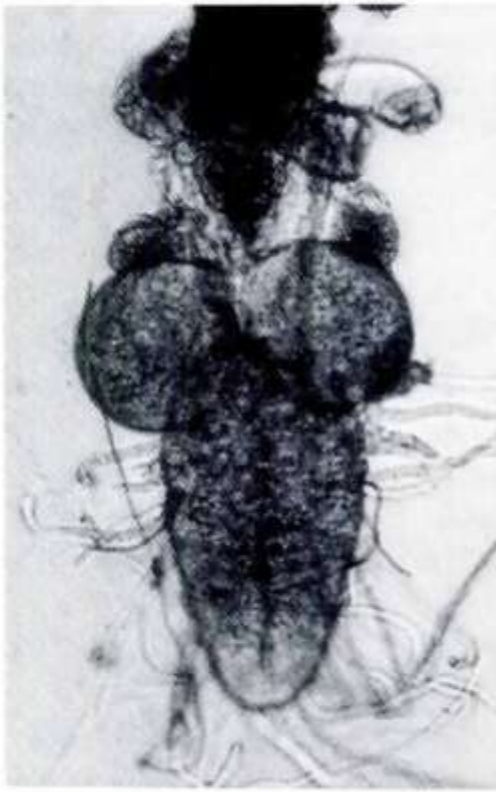


Draf is required throughout development

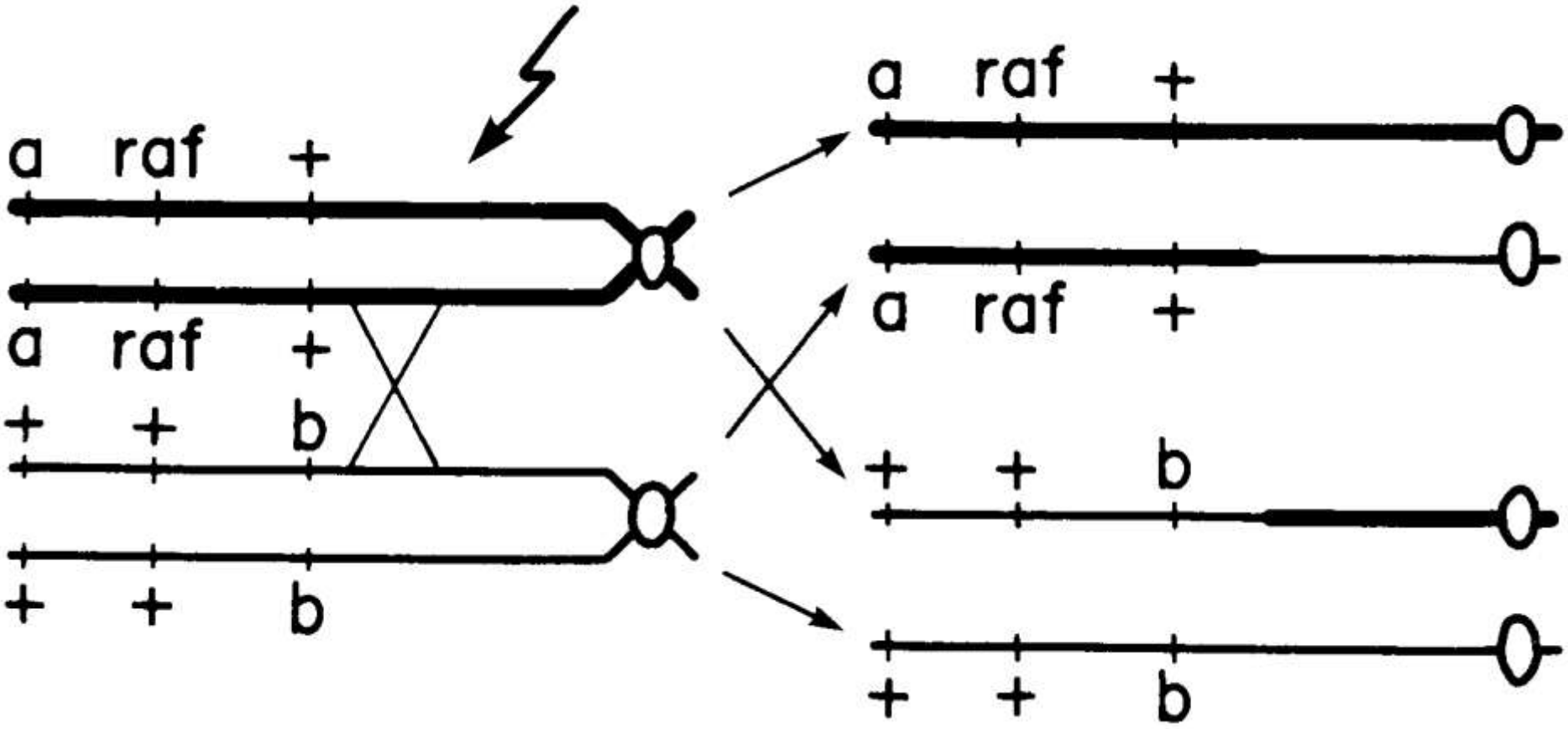


Temperature-sensitibity of imaginal disc growth in *Draf*^{E1}

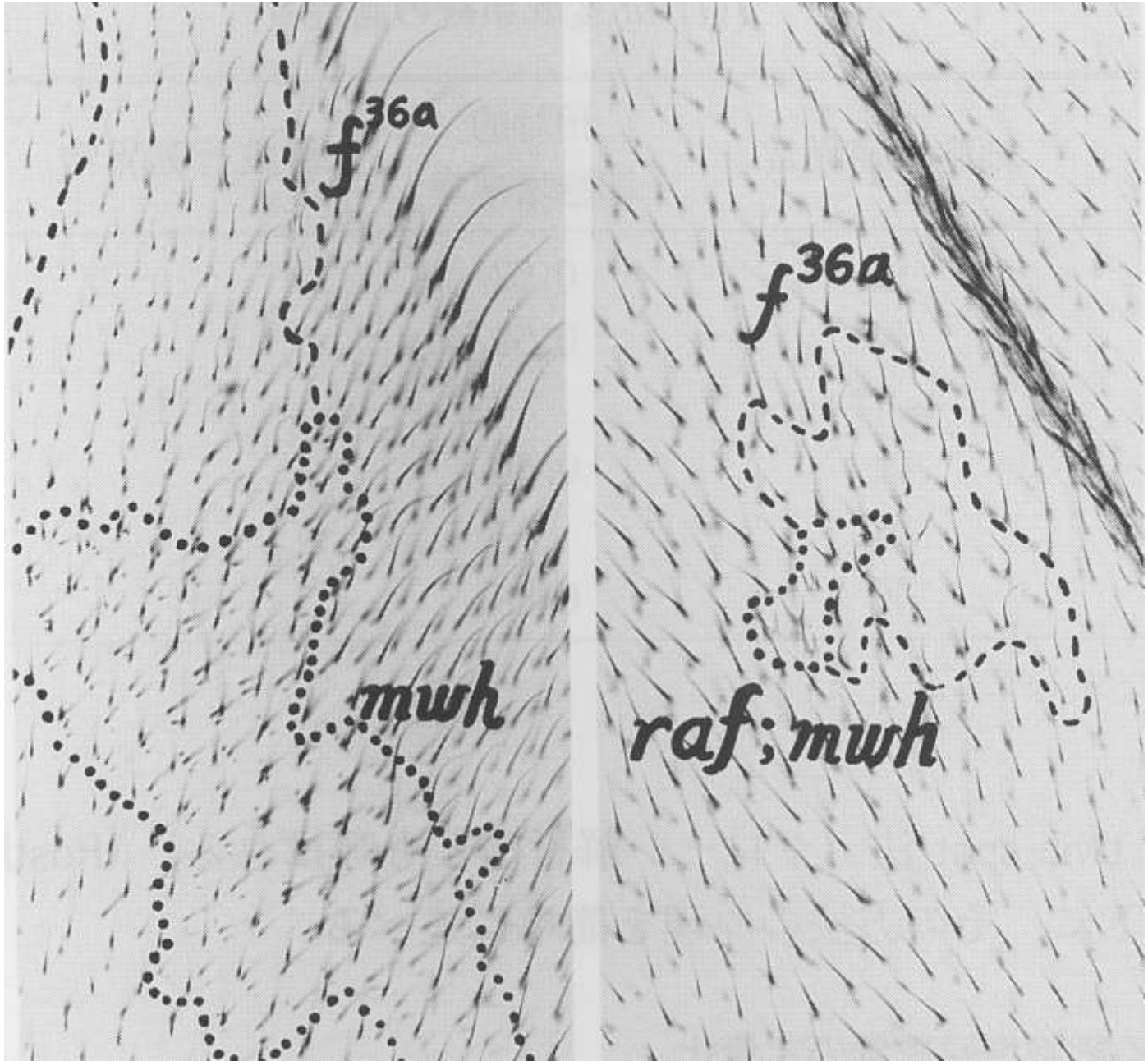




Twin-spot analysis



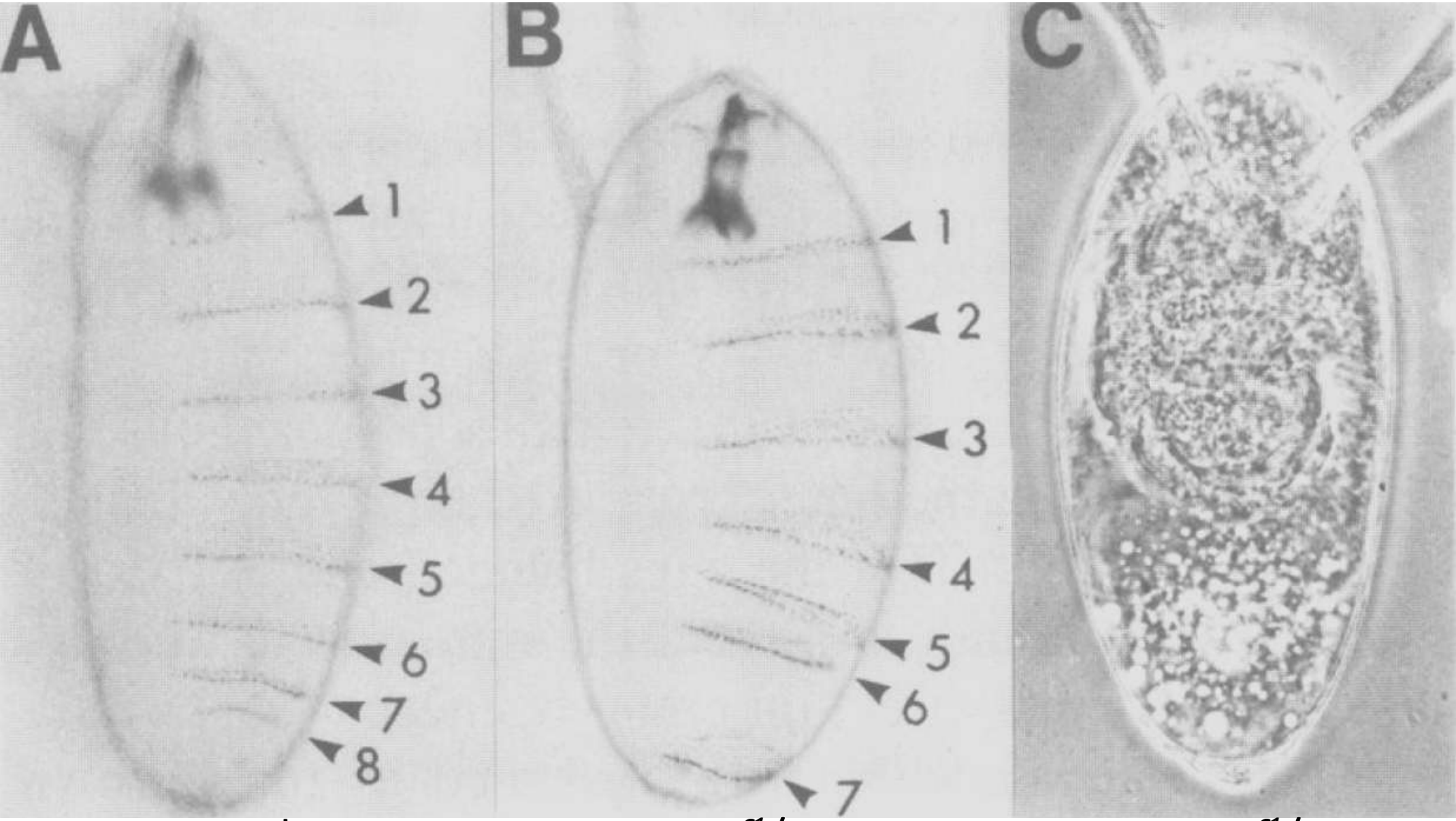
Twin-spots in the wing



TEMPERATURE-DEPENDENT DECREASE OF GROWTH RATES IN A ts MUTANT *D-raf^{E1}*

Genotype	Temperature (°C)	No. of twin spots analyzed	Mean No. of doubling *mwh* (A)	Mean No. of doubling *f^{36a}* (B)	Relative rate (A/B)	Normalized rate
+/M2'; mwh/mwh	25	57	6.63±1.47	7.07±1.51	0.946±0.126	1.00
D-raf^{E1}/M2'; mwh/mwh	17	36	6.07±1.21	7.13±0.89	0.850±0.127	0.90
	20	11	5.47±1.23	7.04±1.24	0.779±0.101	0.82
	25	24	4.16±1.33	6.05±1.14	0.696±0.200	0.74
	28	28	3.97±1.55	6.34±1.13	0.632±0.224	0.67
D-raf^{C110}/M2'; mwh/mwh	25	34	5.92±1.20	7.25±1.23	0.817±0.098	0.86
D-raf^{1}/M2'; mwh/mwh^{a}	25	79	3.41±1.07	5.79±0.99	0.588±0.161	0.62

Draf acts downstream of receptor tyrosine kinases



Normal *Draf*^{1}/+ *Draf*^{1}/Y

Screening of Downstream suppressors of *Draf* (*Dsor*)

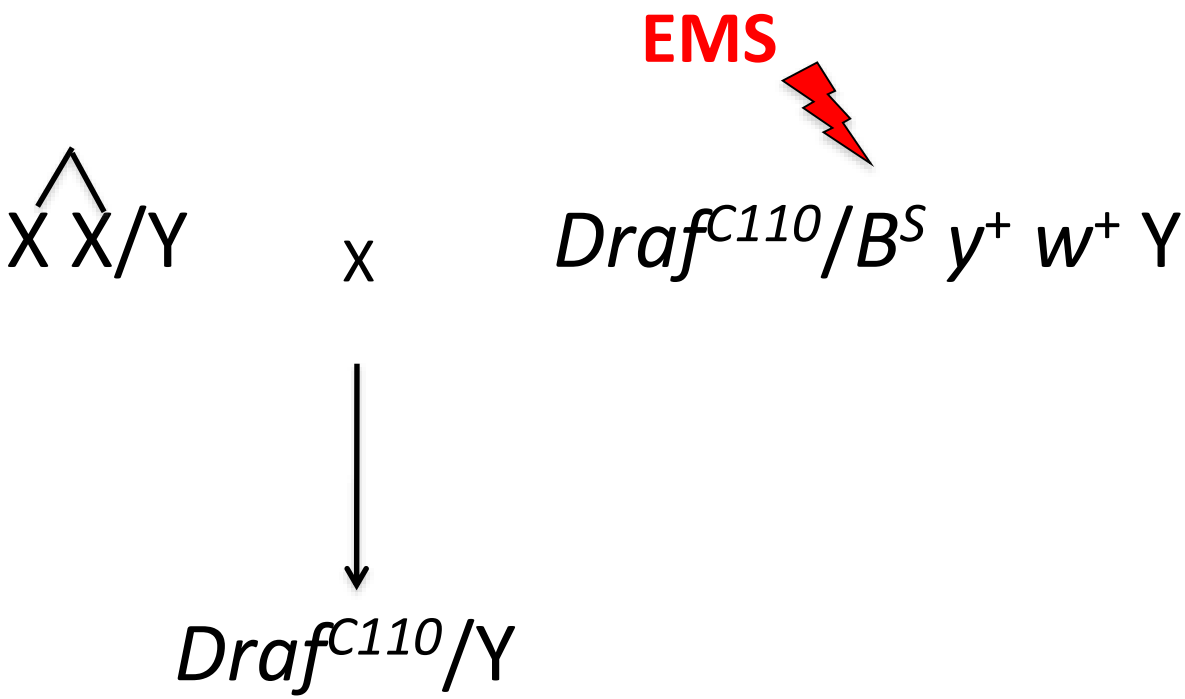
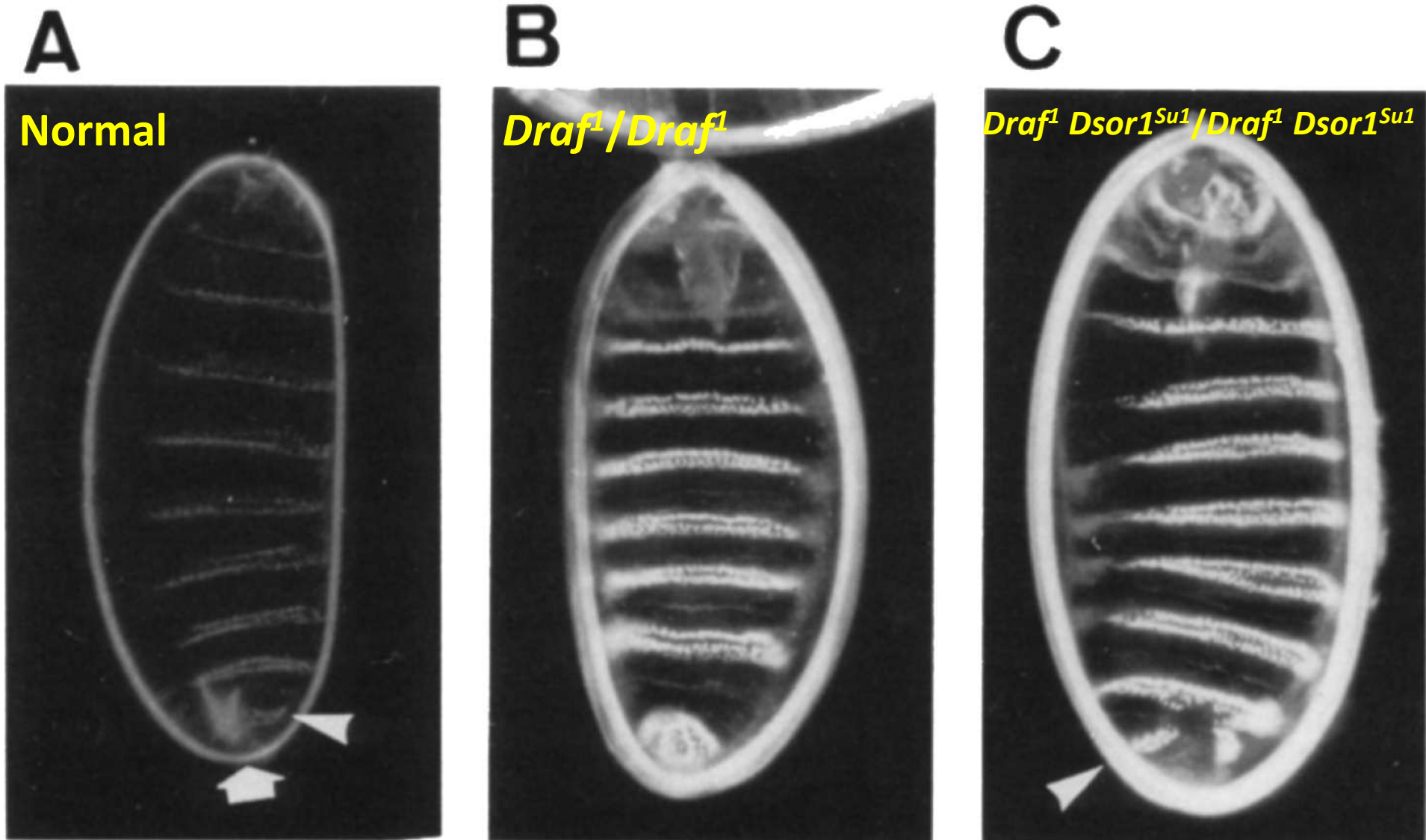


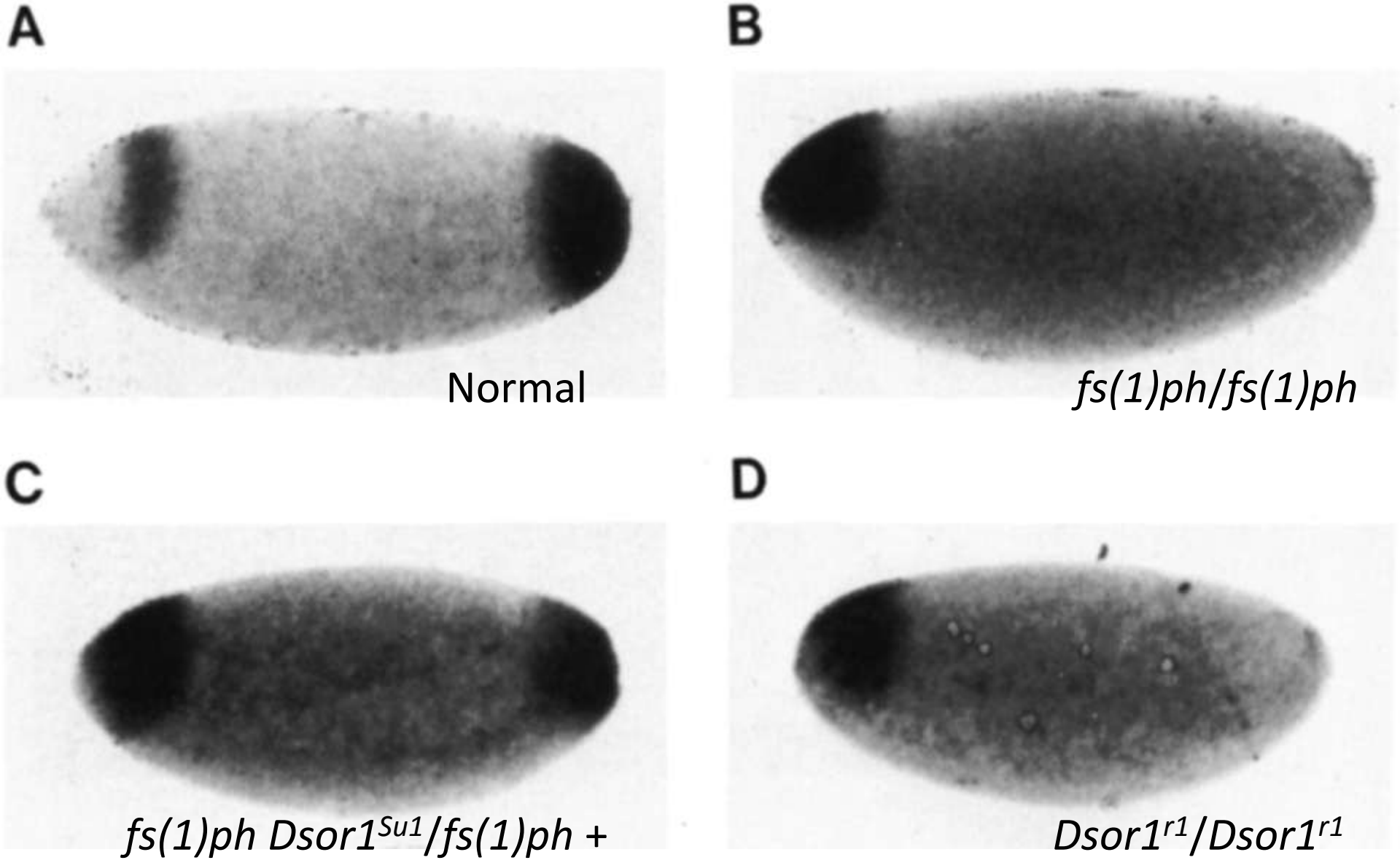
Table 1. Effects of the *D-raf* and *Dsor1* Mutations on the Rate of Proliferation

Genotype	Number of Twin Spots Analyzed	Mean Number of Cell Divisions		Relative Rate (A/B)	Normalized Rate
		mwh (A)	f^{36a} (B)		
+/M2'	57	6.63 ± 1.47	7.07 ± 1.51	0.946 ± 0.126	1.00
Dsor1^{Su1}/M2'	38	6.37 ± 1.39	6.74 ± 1.29	0.944 ± 0.098	1.00
D-raf^{1}/M2'	79	3.41 ± 1.07	5.79 ± 0.99	0.588 ± 0.161	0.62
D-raf^{1} Dsor1^{Su1}/M2'	74	5.01 ± 1.28	6.34 ± 1.20	0.793 ± 0.133[a]	0.84
Dsor1^{r1}/M2'	13	4.82 ± 1.67	8.28 ± 1.77	0.585 ± 0.166	0.62
Dsor1^{r2}/M2'	28	4.80 ± 1.61	8.40 ± 1.30	0.568 ± 0.162	0.60

Suppression of the terminal defect of *Draf* by *Dsor1*^{Su1}



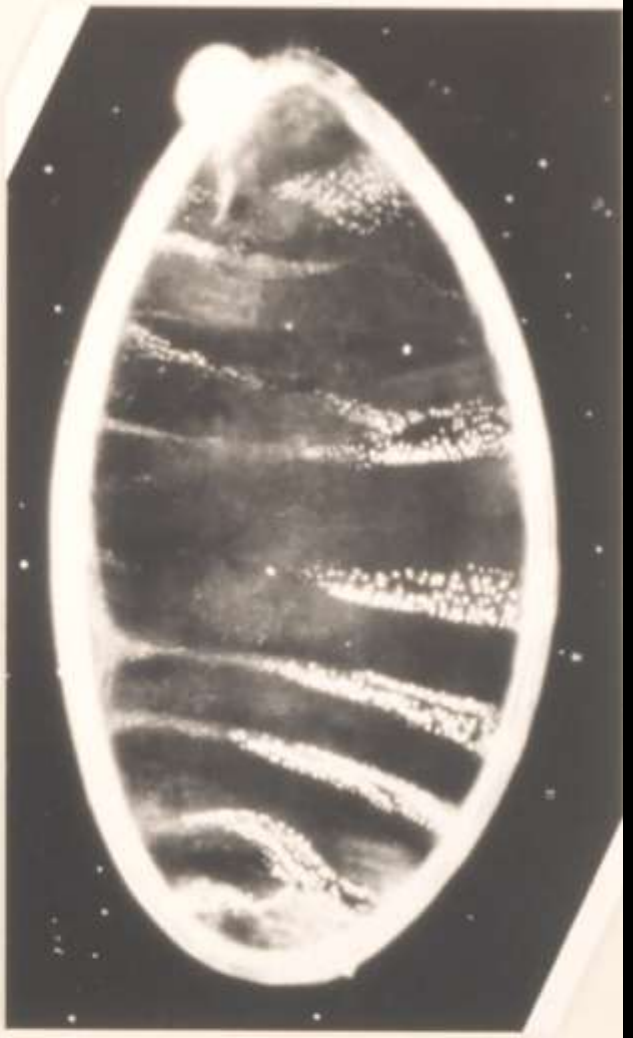
tailless expression patterns



Interaction between *Dsor1*^{r1} and *tor*^{RL3}

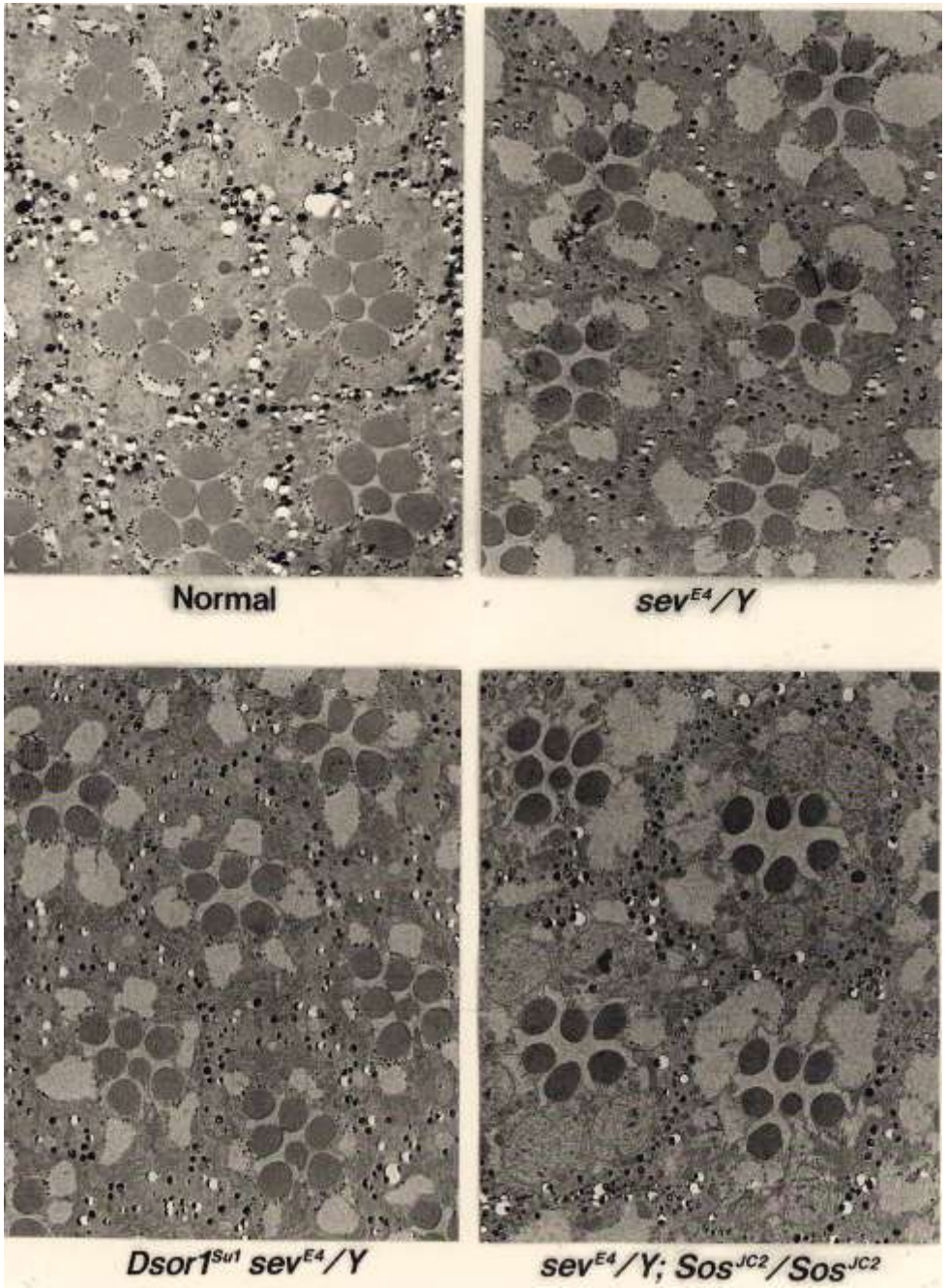
Dsor1^{r1}/*Dsor1*^{r1}; +/+

+/+; *tor*^{RL3}/*tor*^{RL3}

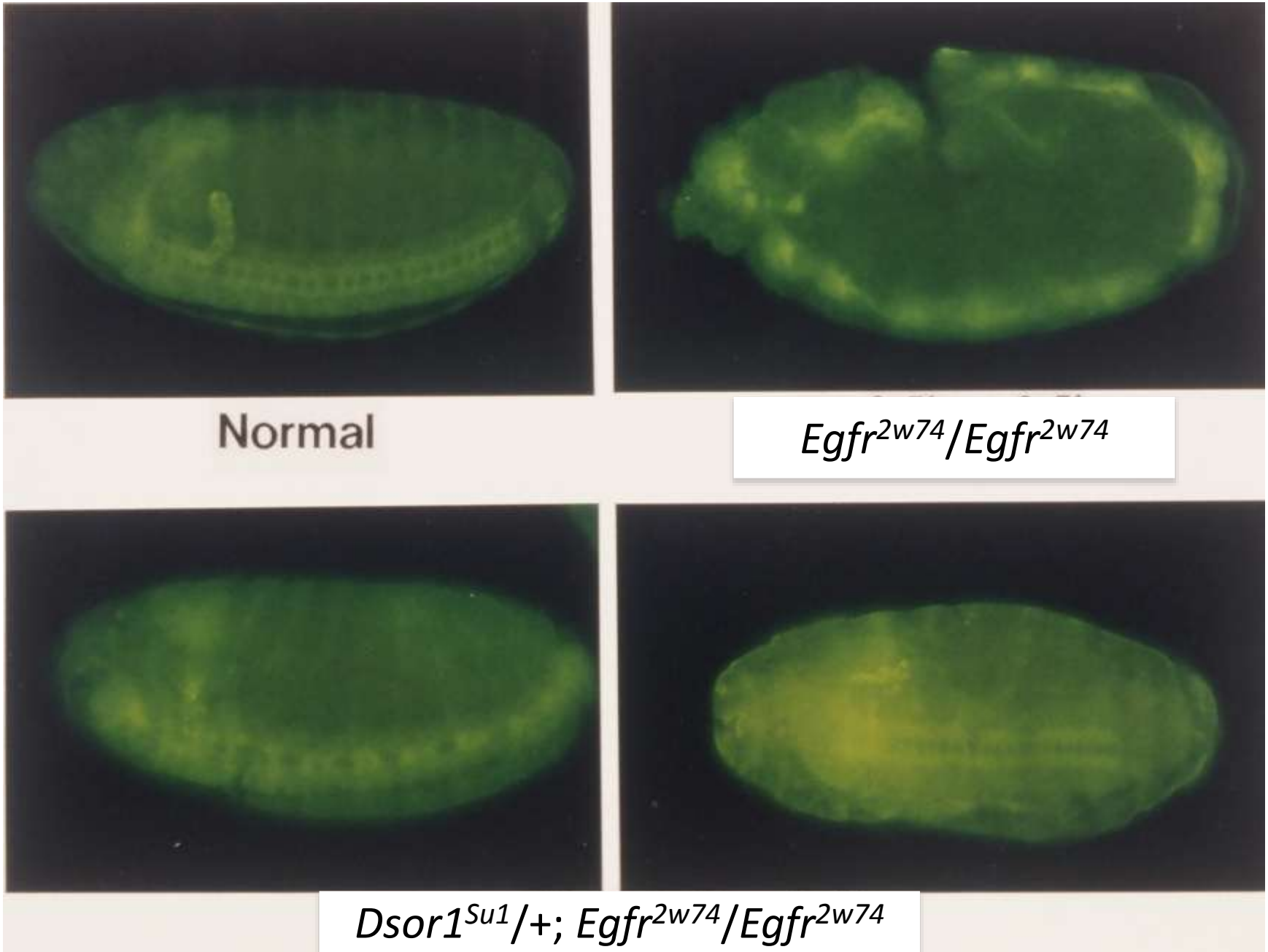


Dsor1^{r1}/*Dsor*^{r1}; *tor*^{RL3}/*tor*^{RL3}

Suppression of *sev* by *Dsor1* and *Sos*



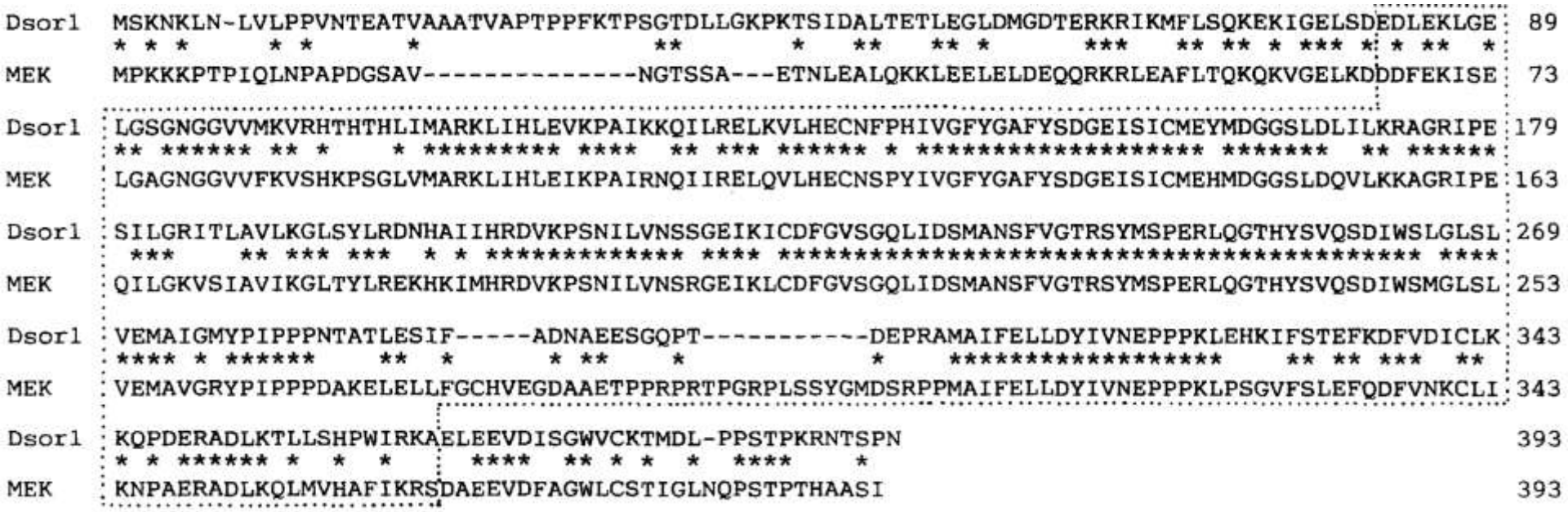
Suppression of *Egfr* by *Dsor1*^{Su1}



Effects of *Dsor1*^{Su1} on *Sos*

+/+; SF15/DM7 Su1/+; SF15/DM7

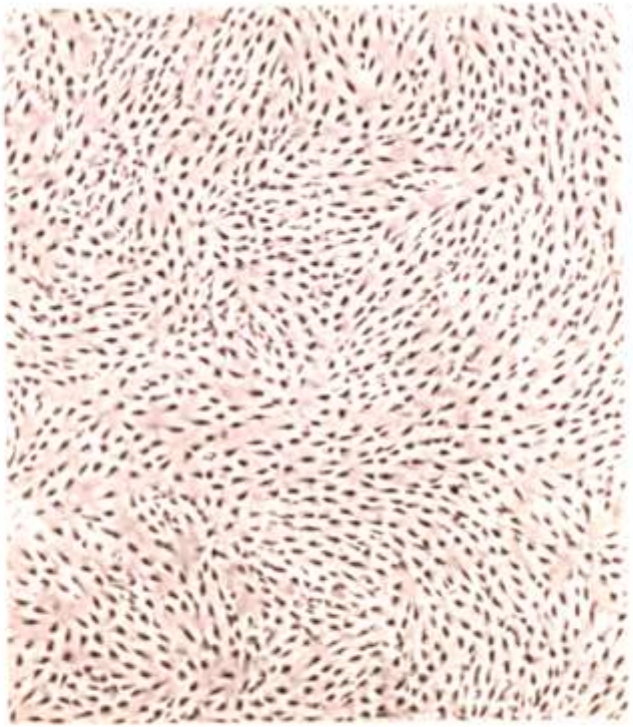
Dsor1 is homologous to hMAPKK



Drosophila MAPKK Mutations

Morphological Change of MEK^{Su1} -transfected Cells

NIH 3T3



MEK

MEK^{Su1}

Downstream suppressors of *Draf* (*Dsor*)

Dsor1 : MAPKK (MEK)

Dsor2a : *rl* (MAPK)

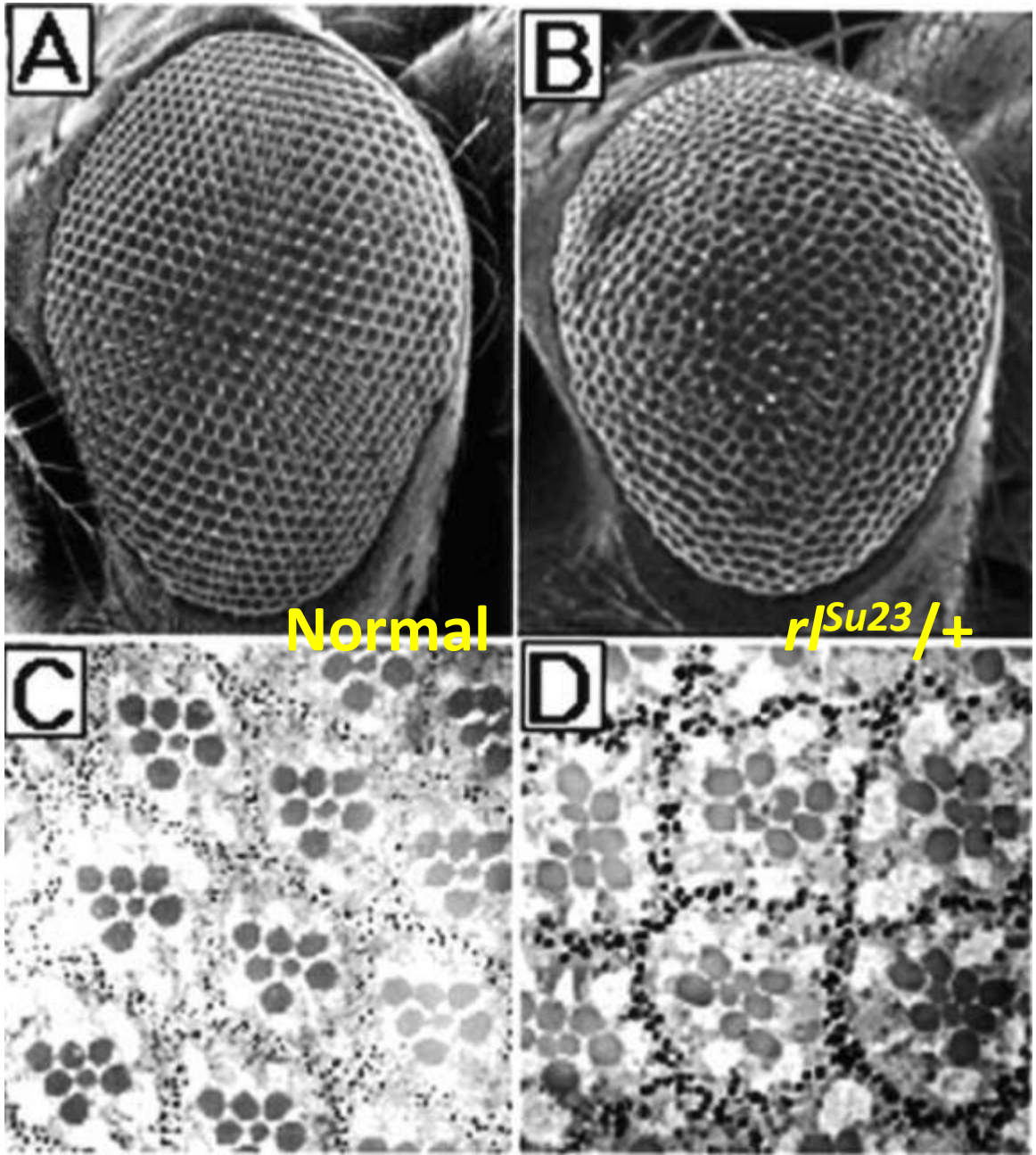
Dsor2b : *Dsrc42A*

Dsor3 : not identified

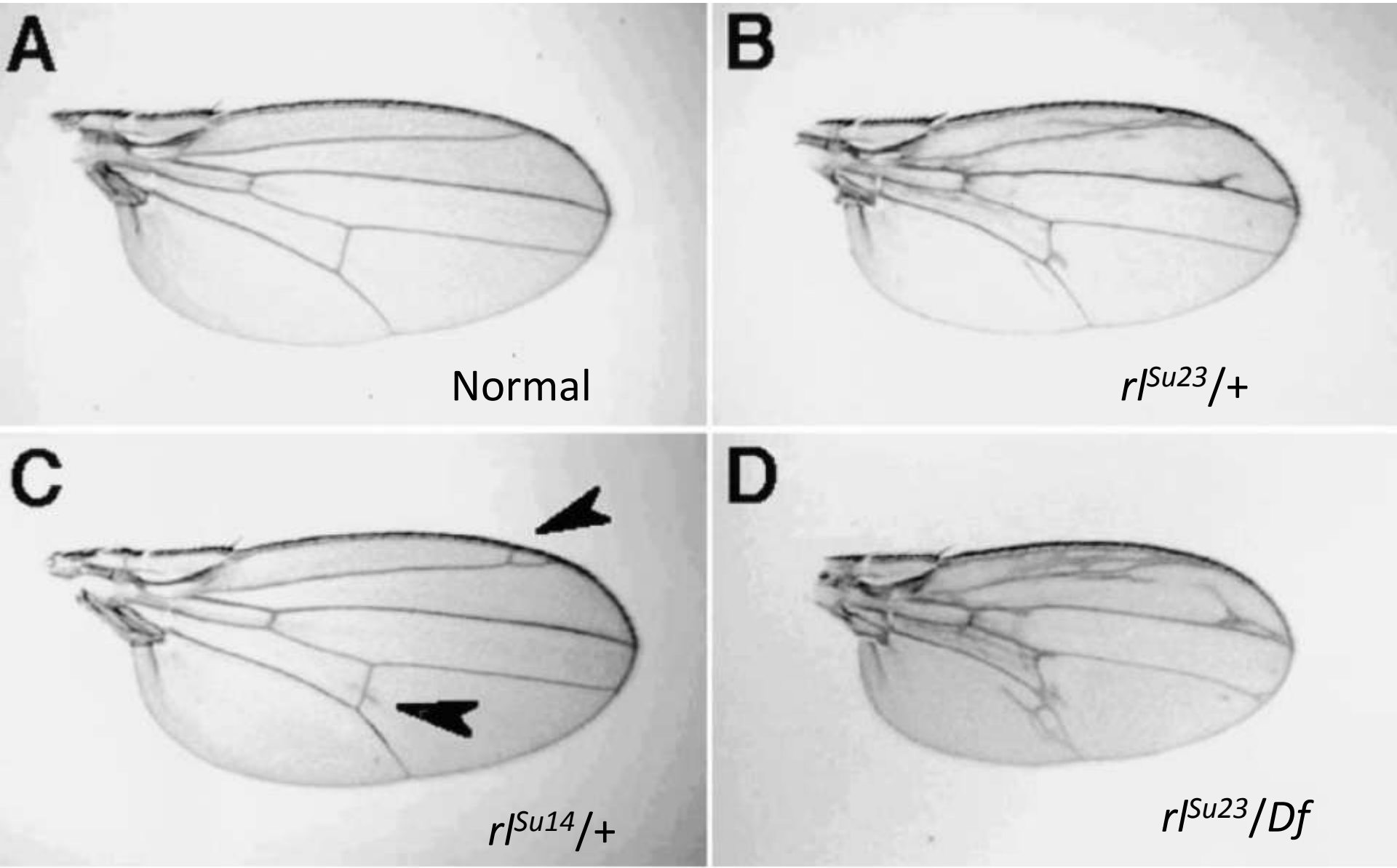
Proliferation defects in loss-of-function mutations of *Dsor1* and *D-raf* and their suppression by a gain-of-function mutation in *rl*

Genotype[a]	No. of twin spots analyzed	Mean no. of doubling		Relative rate (A/B)	Normalized rate
		mwh (A)	f^{36a} (B)		
+/M2′; mwh/mwh	24	7.28 ± 1.56	7.87 ± 1.48	0.930 ± 0.141	1.00
+/M2′; rl^{Su23}/+; mwh/mwh	13	7.52 ± 0.86	7.87 ± 1.38	0.974 ± 0.138	1.05
D-raf^{l}/M2′; mwh/mwh	24	3.37 ± 1.73	5.89 ± 0.60	0.572 ± 0.190	0.62
D-raf^{l}/M2′; rl^{Su23}/+; mwh/mwh	13	7.52 ± 0.86	7.87 ± 1.38	0.947 ± 0.138	1.02
$Dsor1^{Gp158}$/M2′; mwh/mwh	44	2.06 ± 1.46	6.66 ± 1.22	0.304 ± 0.227	0.33
$Dsor1^{Gp158}$/M2′; rl^{Su23}/+; mwh/mwh	14	4.48 ± 1.43	6.91 ± 1.56	0.661 ± 0.193	0.71
$Dsor1^{rl}$/M2′; mwh/mwh	13	4.82 ± 1.67	8.28 ± 1.77	0.585 ± 0.166	0.63
$Dsor1^{rl}$/M2′; rl^{Su23}/+; mwh/mwh	13	8.65 ± 0.32	8.91 ± 0.33	0.977 ± 0.031	1.05

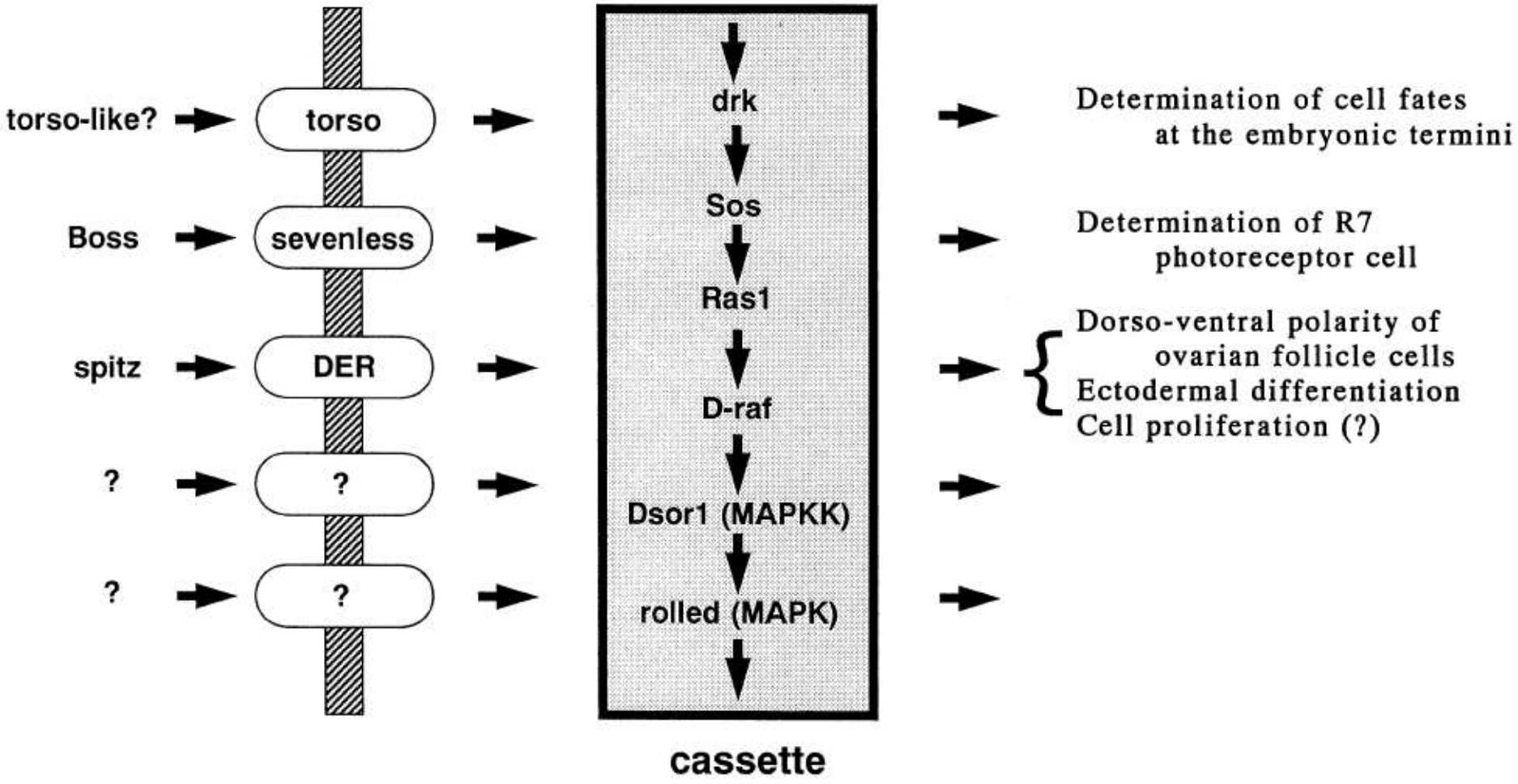
Extra R7 cells in *rl*^{Su23}



Extra wing veins in the *rl* ^{Su} mutants



Signaling cassette of MAPK cascade under multiple receptor tyrosine kinases

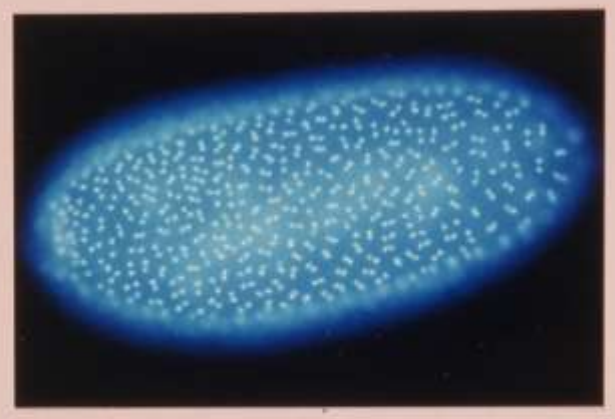


Mutations suppressed by *Dsor1*^{Su1}

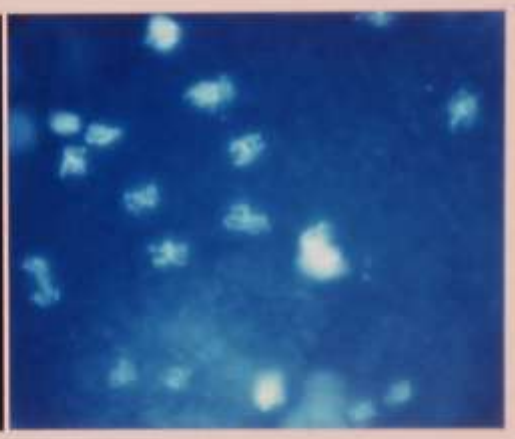
- Gp9 : *sqh* (myosin regulatory light chain)
- Gp99 : *ttm50*
- Gp126: *raptor*
- Hp126: *Dwhn* (*nude* gene homolog)

Maternal effects of the *Gp99* mutation

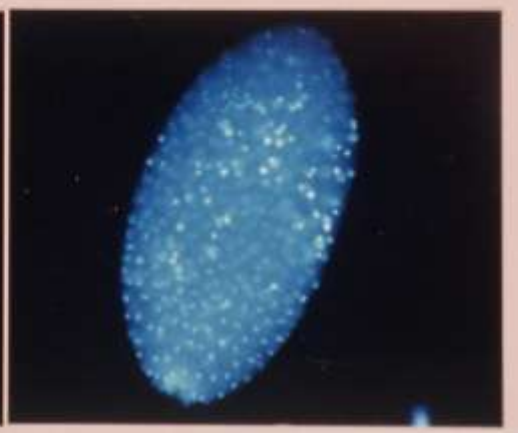
normal



Gp99



Gp99 Dsor1^{Su1}



Growth defects in the *ttm50* mutants

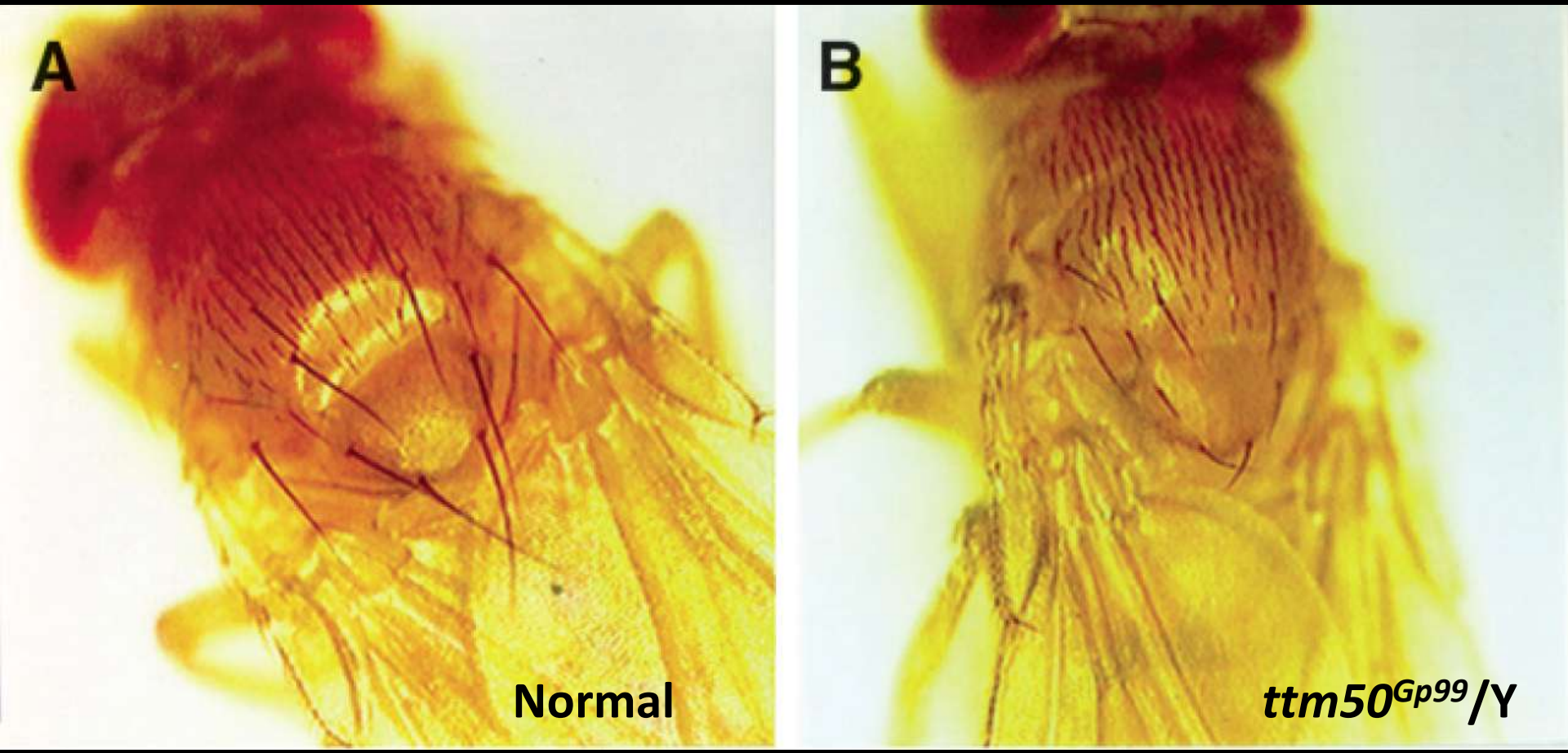
***y* /Y (normal)**

y ttm50^{IE1}/Y

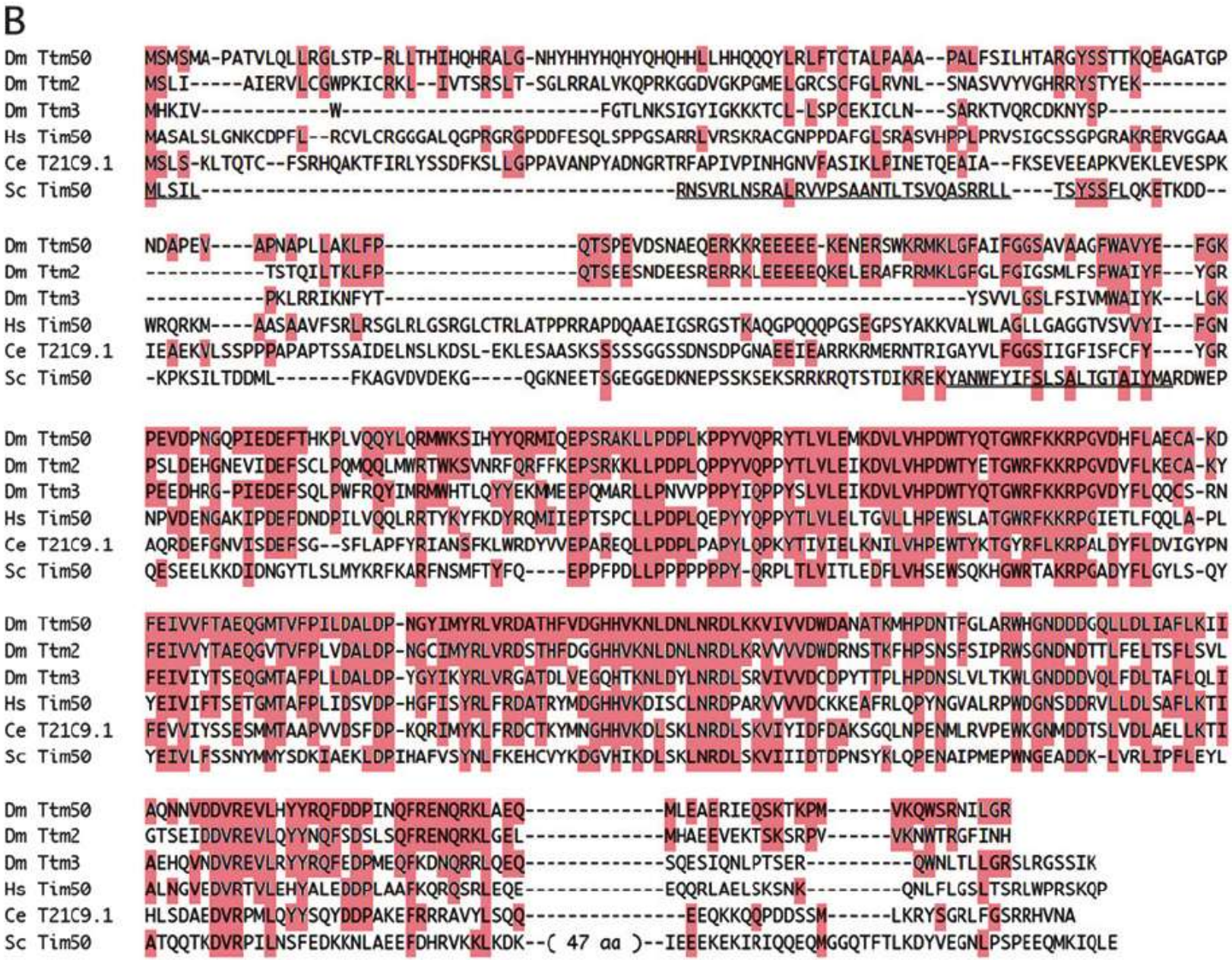
y ttm50^{IE2}/Y

y ttm50^{Gp99}/Y

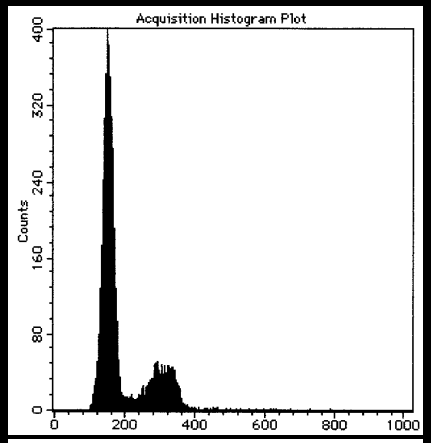
Adult phenotypes of a hypomorph of *ttm50*



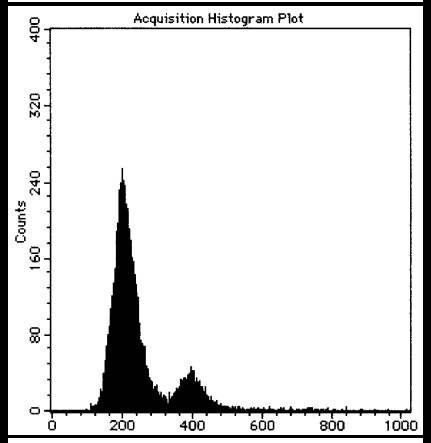
Three *Tim50*-like genes in *Drosophila*



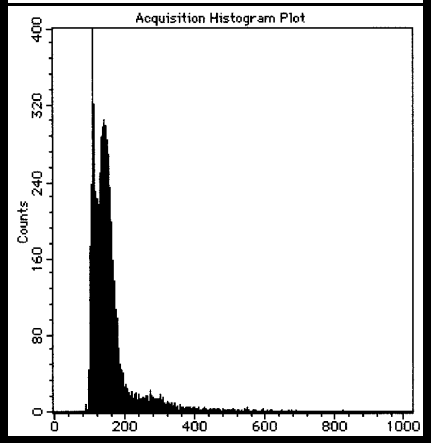
G1 arrest in Δgcc disruptant



15D (WT)

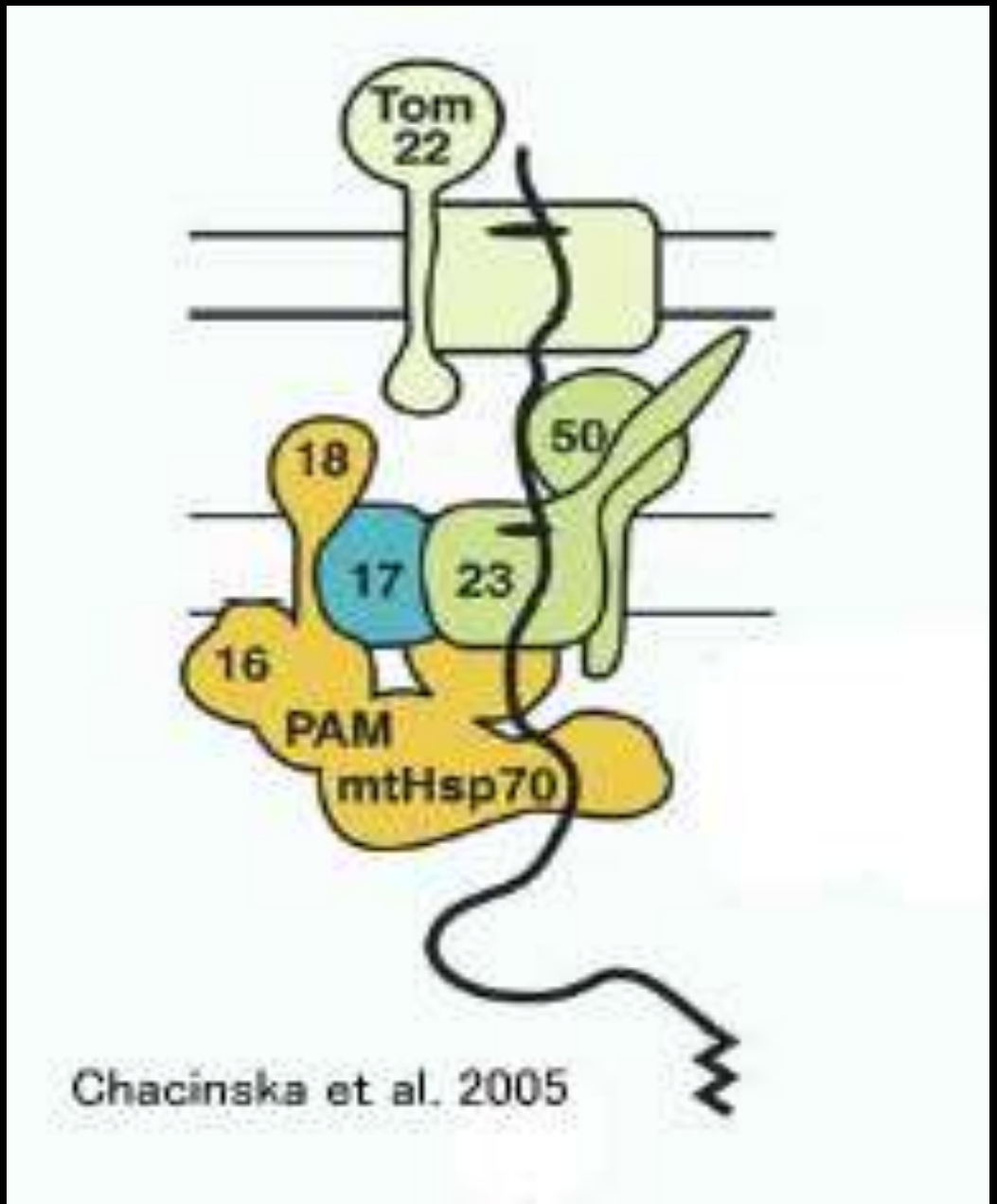


Δ gcc-a::URA
yCPG22-GCC
+ galactose
(on)

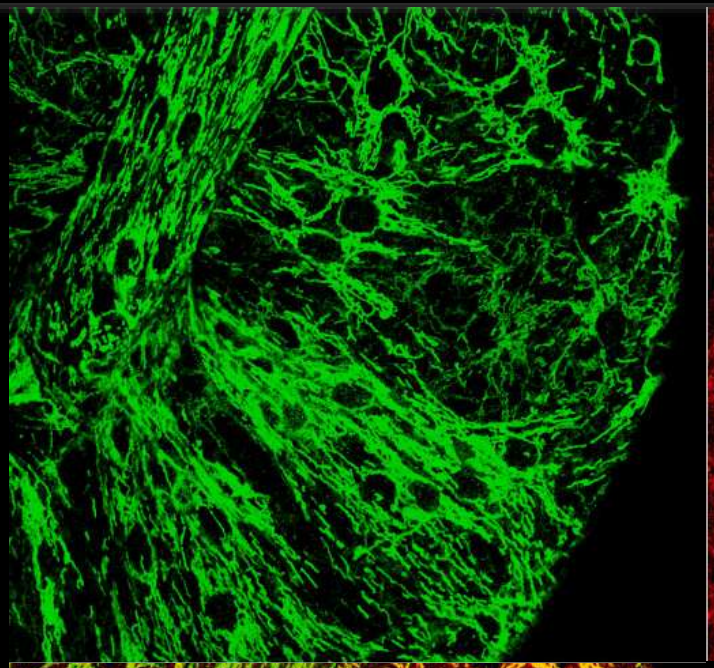


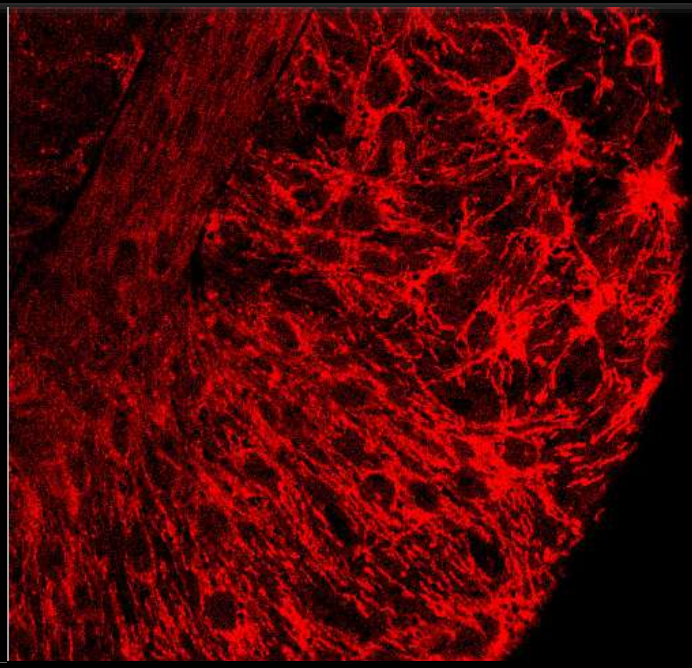
Δ gcc-a::URA
yCPG22-GCC
+glucose
(off)

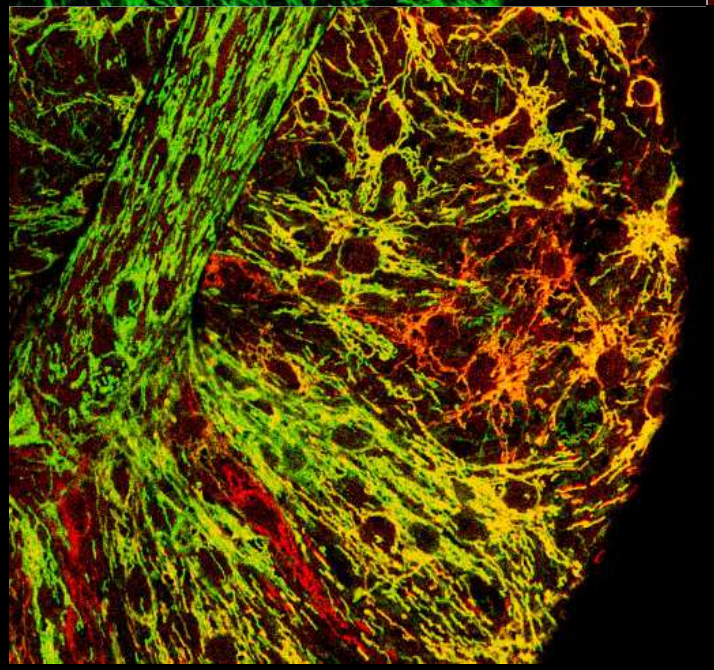
The yeast mitochondrial protein translocator complex



Mitochondrial localization of Ttm50





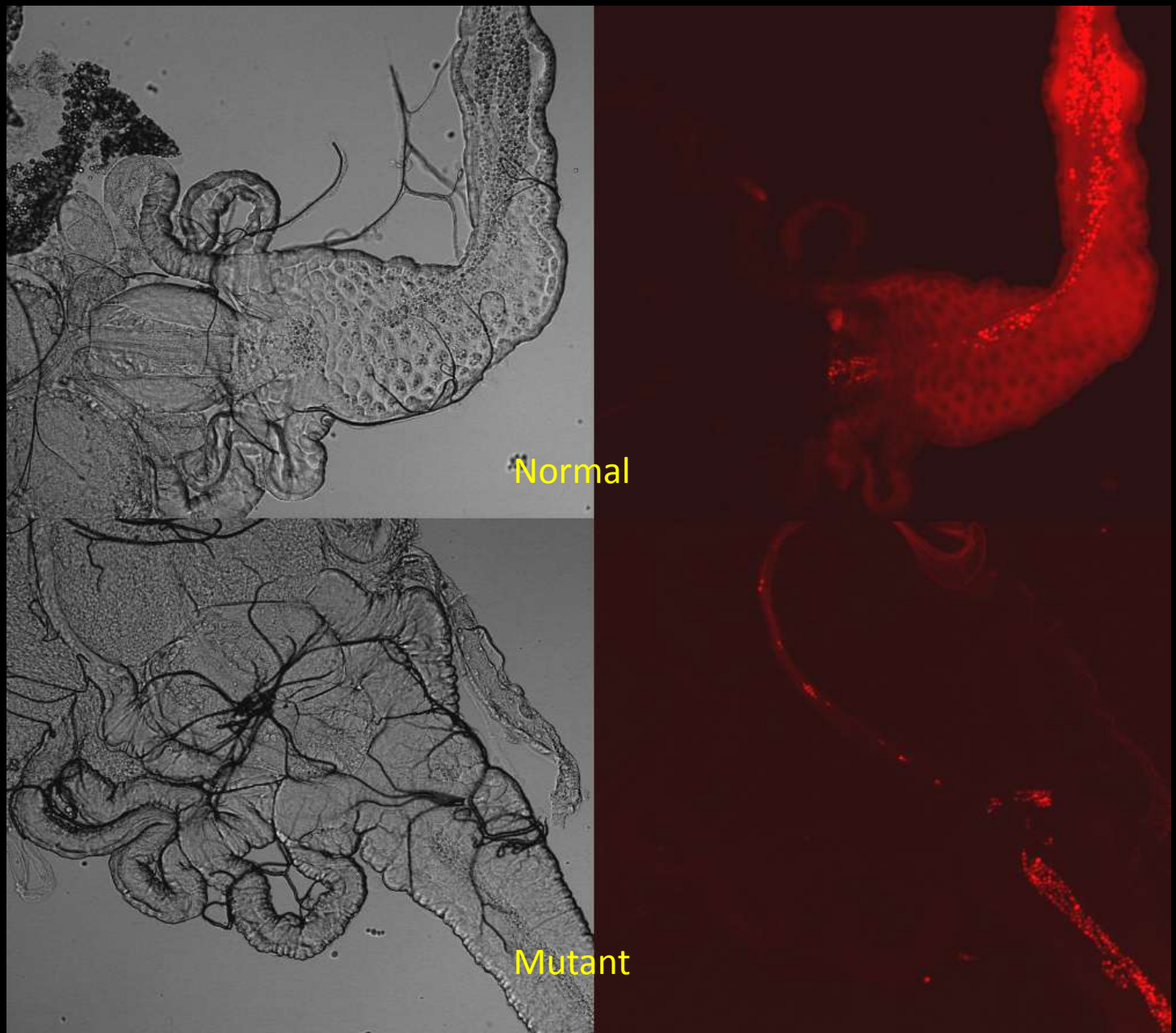


Stain:

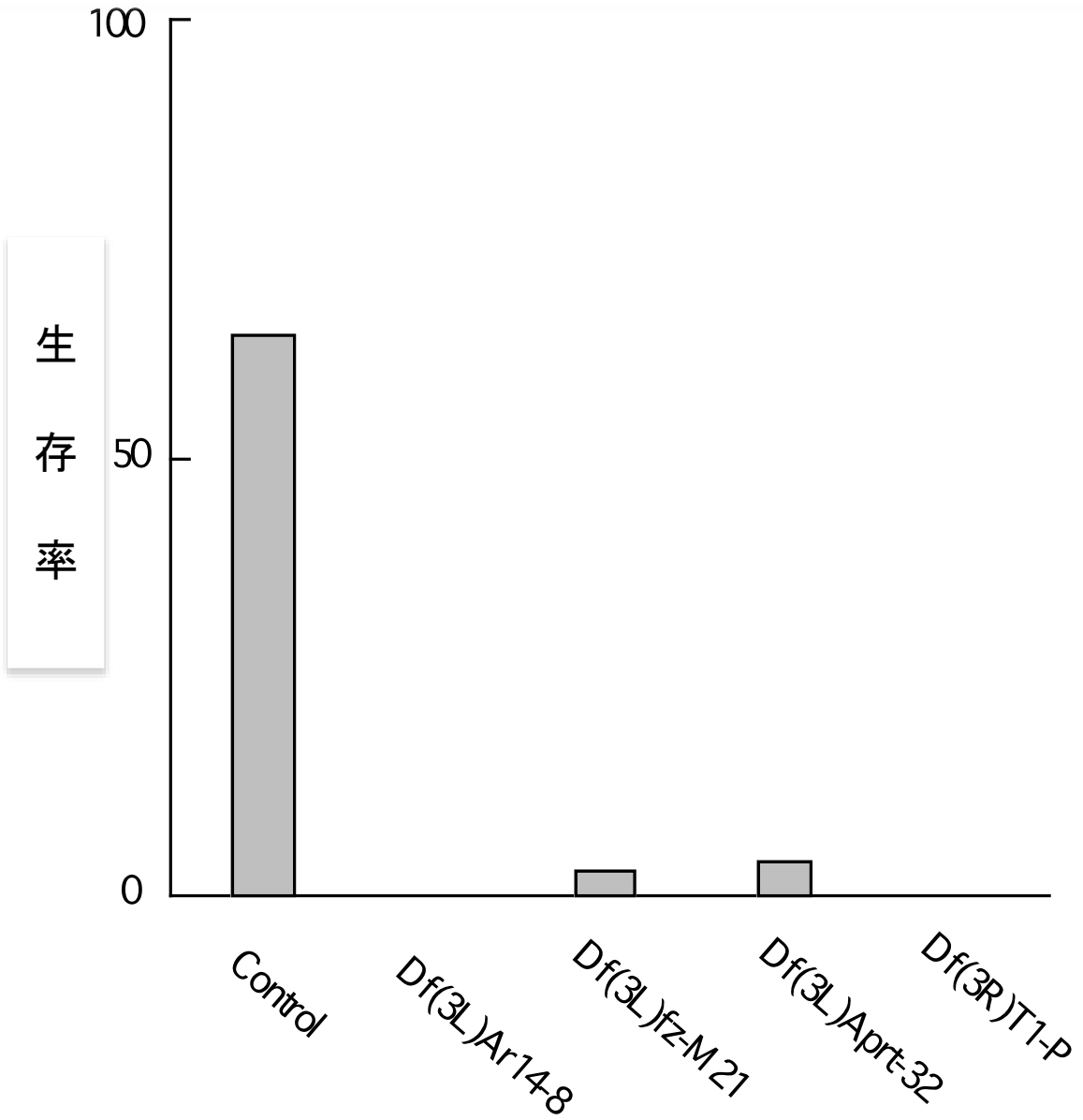
Ttm50-HA

Mitotracker red

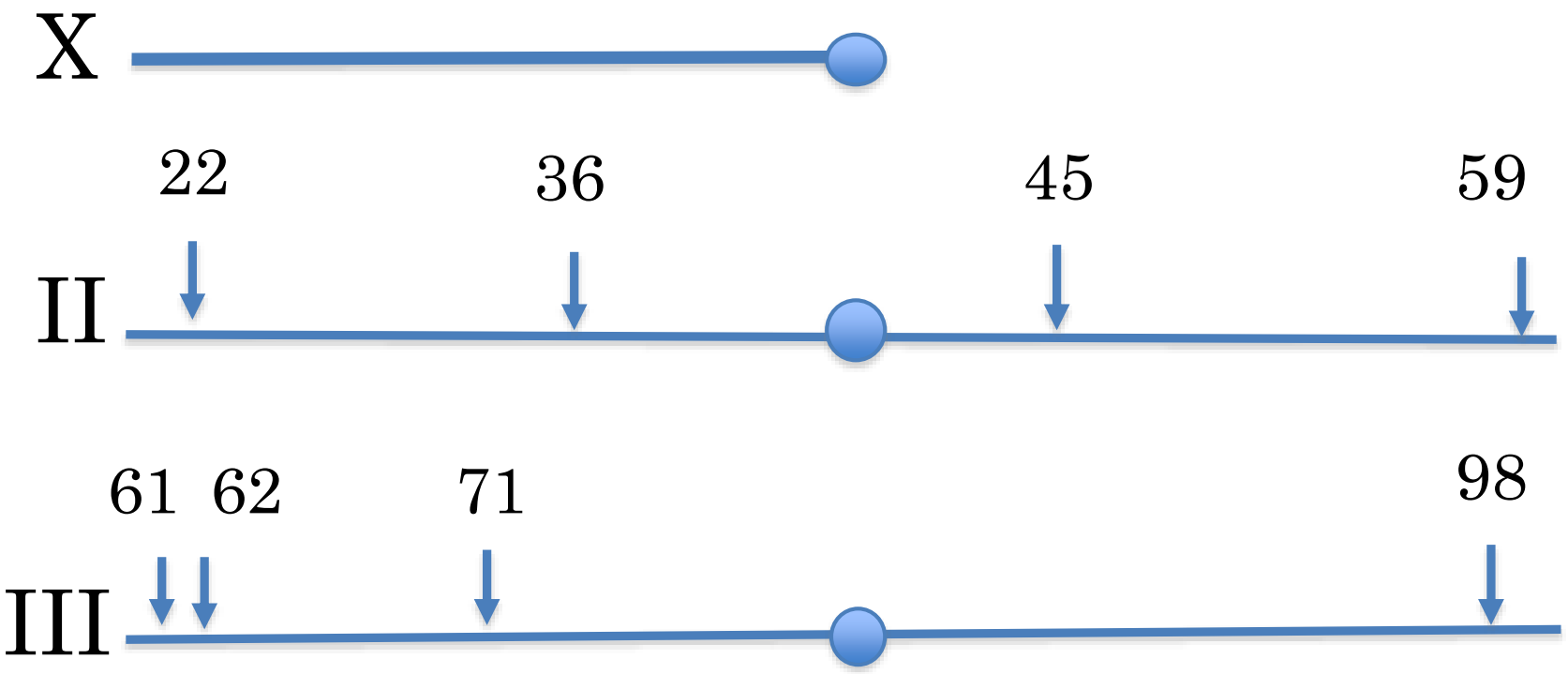
Mitochondrial membrane potential (MMP) in the anterior midgut was reduced in *ttm50* null mutants



3rd chromosomal enhancers of *ttm50*^{Gp99}



ttm50^{Gp99} enhancing deficiencies



Candidate genes

1. Mitochondrial protein translocators
2. Mitochondrial proteins (cargos)
3. AMPK – TOR system
4. Cell cycle genes
5. Gut function
6. Metabolism
7. mRNA production
8. Protein synthesis
9. Signal transduction
10. Unknown pathway

Candidate genes

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2. Mitochondrial proteins (cargos)
X 3. AMPK – TOR system
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8. Protein synthesis
9. Signal transduction
10. Unknown pathway

*ch*ronologically *in*appropriate *mo*rphogenesis (*chinmo*)

- 2L, 22A5-22B1, late larval lethal
- Evolutionary conserved BTB-Zn finger transcriptional repressor
- Target of JAK/STAT signaling pathway
- Inhibit differentiation and maintain stem cell renewal

共同研究者

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林　永美、秦　真美、水野政巳、館野　実、杉村　勇、田中良晴、
小貫智也、後藤智和、吉田新一郎、伊達秀之、三浦真理子、
佐野頼方、三井真司、森藤　曉、加藤順子、本多孝行、
大綱英生、山崎泰豊、壱岐一也、筒井響子、古川義己、
山田道明、西村真由子、松岡真弥、遠藤玄崇、山本　剛、
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