

ショウジョウバエと共に28年

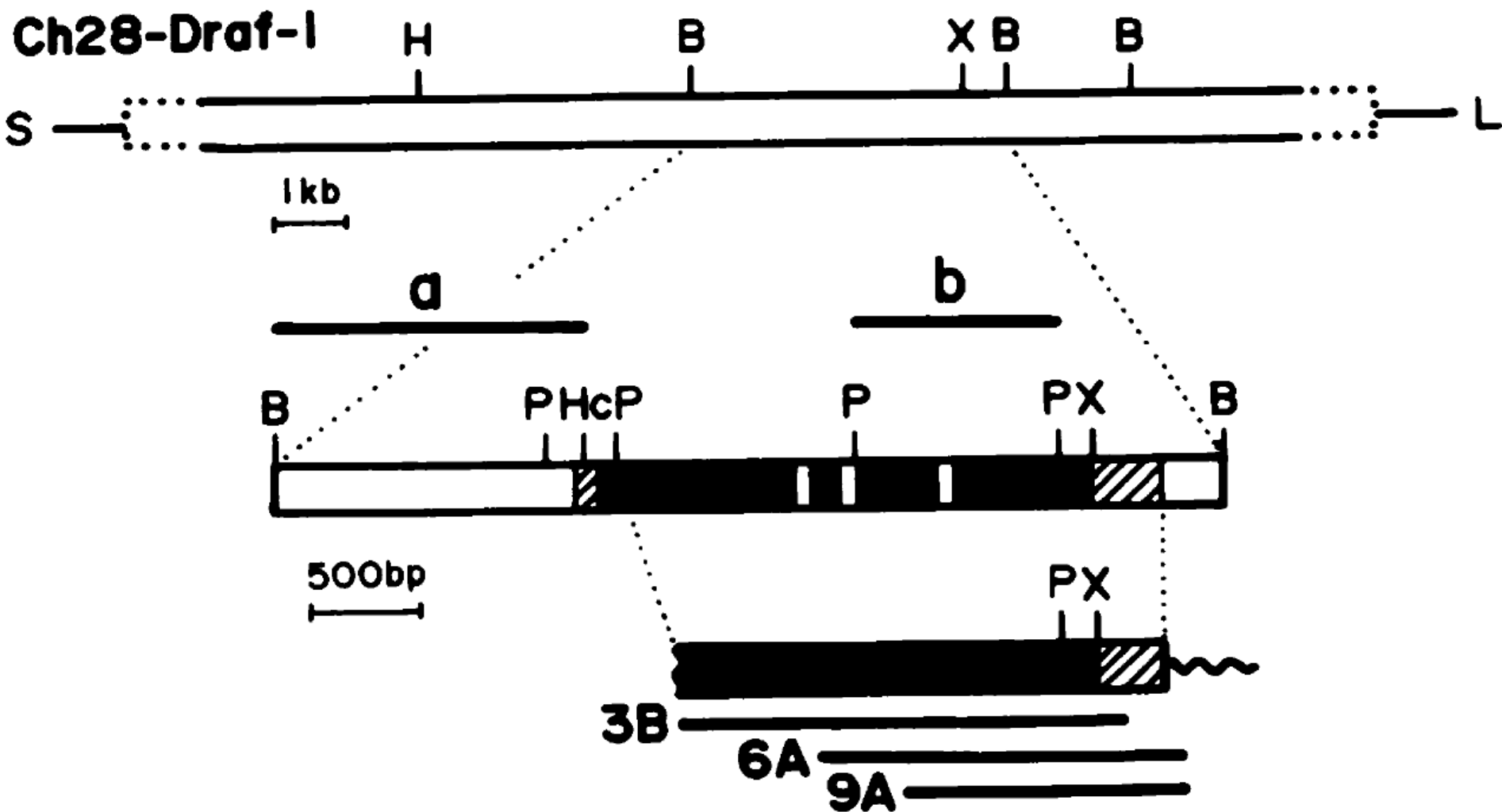


西田 育巧

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

```
NERLNSQDQQ EDSSLVERFK EQPH---YQN QTQILQQQRQ LARVHHGTDL TD-SLGSQPG SQCGTLTRQP KILLRAHLPN QQRTSVEVIS GVRLCDALMK 96
** * * * * *
MEH--IQGAW KTISNGFGFK DAVFDGSSCI SPTIVQQFGY QRRASDDGKL TDPSKTSN-- ----- --TIRVFLPN KQRTVVNVRN GMSLHDCLMK 84

ALKLRQLTPD MCEVSTTHSG ----RHIIPW HTDIGTLHVE EIFVRLLDKF PIRTHIKHQI IRKTFPSLVF CEGCRRLLFT GFYCSQCNFR FHQRCANRVP 192
*** * * * * *
ALKVRGLQPE CCAVFRLLHE HKGKKARLDW NTDAASLIGE ELQVDFLEHV PL---TTHNF ARKTFLLKAF CEICQKFLN GFRCQTCGYK FHEHCSTKVP 181

MLCQFPFMSD YYQLLLAENP DNGVGFPPGRG TAVRFNMSSR SRSRRCSSSG SSSSSKPPSS SSGNHRQGRP PRISQDDRSN SAPNVCINNI RSVTSEVQRS 292
* * * * *
TMCVDWSNIR --QLLLFPNS TIGDSGVPAL PSLTMRRMRE SVSRMPVSSQ HRYSTPHAFT FNTSSPSSEG S-LSQRQRST STPNVHMVST TLPVDSRMIE 278

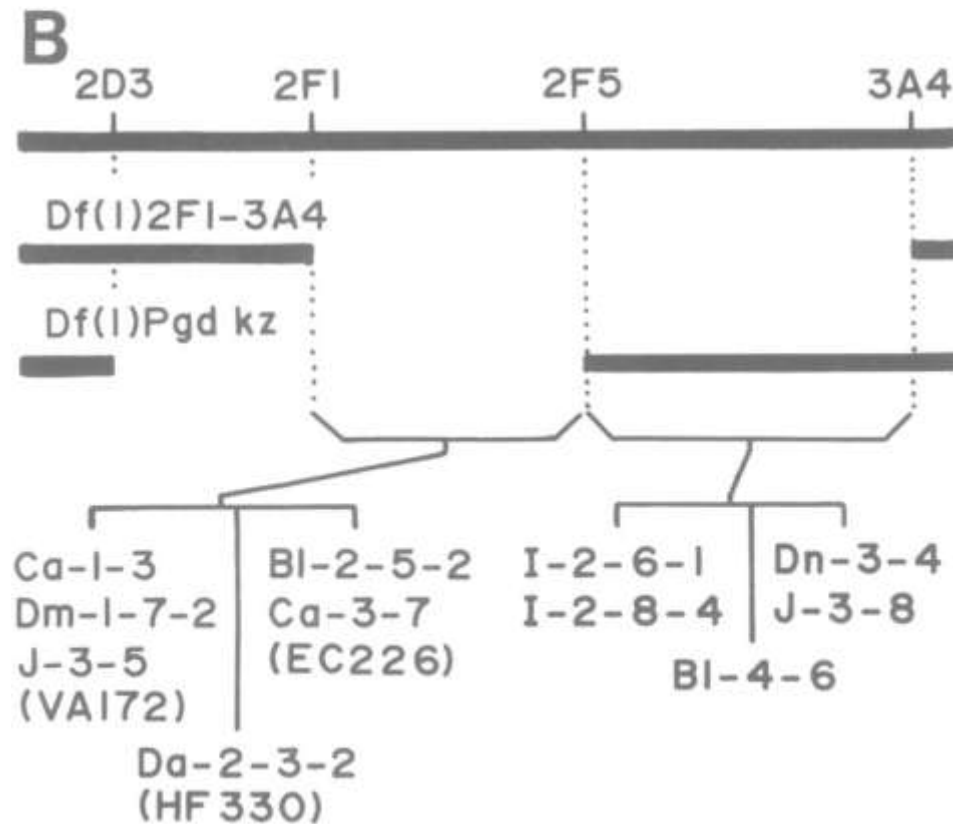
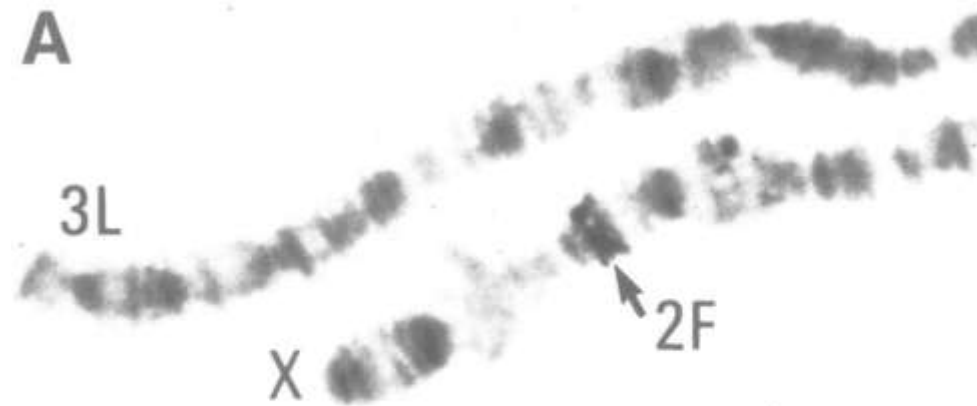
LINQARPPLP HPCTDHSNST QASPTSTLKH -----NRPR AR-SA-DESN KNLLLRDAKS SEENWNILAE EILIGPRIGS GSFQTVYRAH WHGPPAVKTL 384
* * * * *
DAIRSHSESA SPSALSSSPN NLSPTGWSQP KTPVPAQRER APVSGTQEKN KIRPRGQRDS SYY-WEIEAS EVMLSTRIGS GSFQTVYK GK WHGDVAVKIL 377

NVKTPSPAQL QAFKNEVAML KKTRHCNILL FMGCVSKPSL AIVTQWCEGS SLYKHVHVSE TKFKLNTLID IGRQVAQGMD YLHAKNIIHR DLKSNIFLH 484
* * * * *
KVVDPTPEQF QAFRNEVAVL RKTRHVNILL FMGYMTKDNL AIVTQWCEGS SLYKHLHVQE TKFQMFQLID IARQTAQGMD YLHAKNIIHR DMKSNIFLH 477

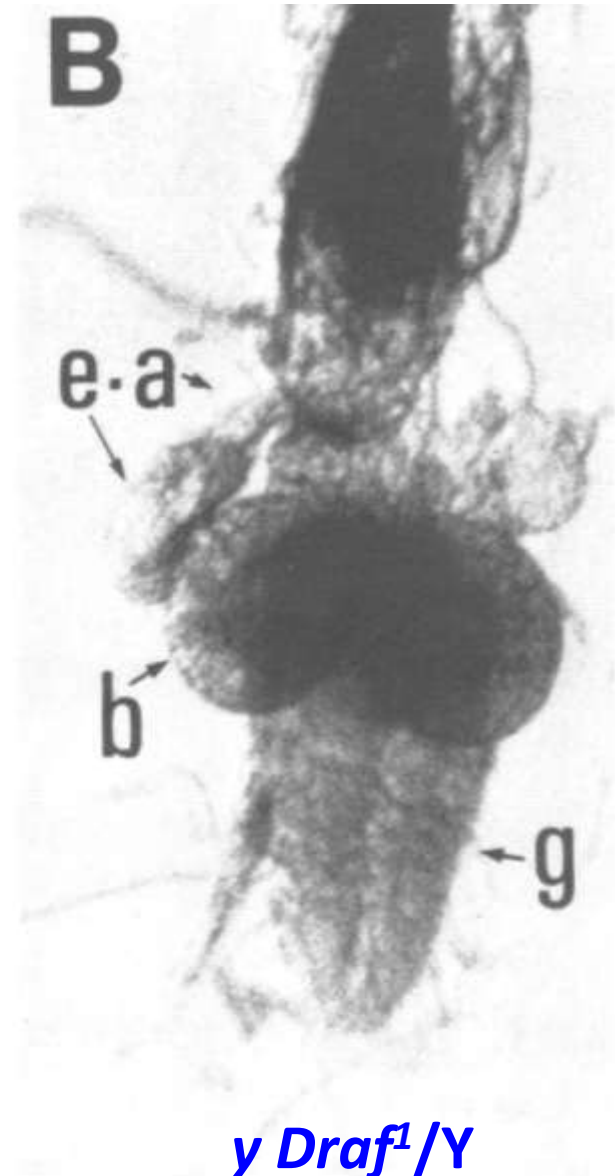
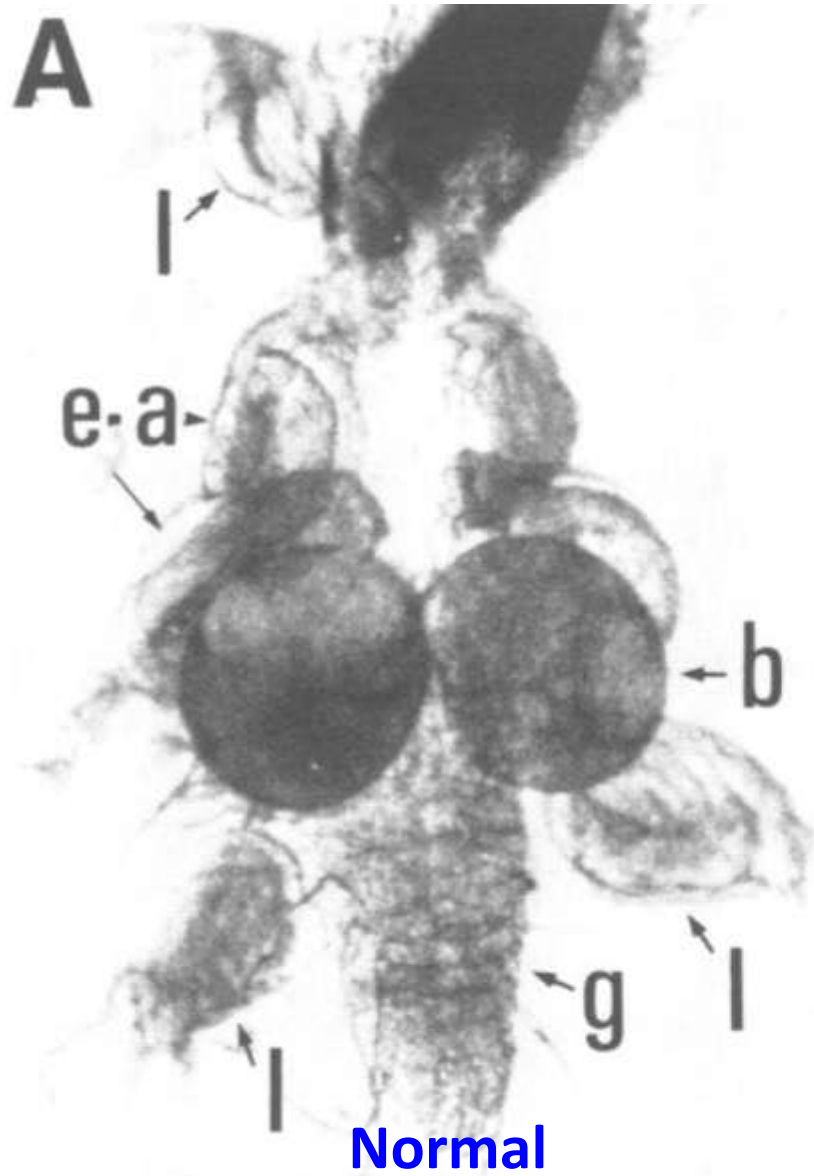
EDLSVKIGDF GLATAKTRWS GEKQANQPTG SILWMAPEVI RMQELNPYSF QSDVYAFGIV MYELLAECPL YGHISNKDQI LFMVGRGLLR PDMSQVRSDA 584
* * * * *
EGLTVKIGDF GLATVKS RWS GSQQVEQPTG SVLWMAPEVI RMQDNNPFSF QSDVYSYGIV LYELMTGELP YSHINNRDQI IFMVGRGYAS PDLKLYKNC 577

RRHRSKRLAED CIKYTPKDRP LFRPLLNMLE NMLRTLPHKI RSASEPNLTQ SQLQNDFFLY -L-PSPKTPV NFNNQFFFGS AGNI.....Draf 666
*** * * * *
PKAMKRLVAD CVKKVKEERP LFPQILSSIE LLQHSLPKIN RTASEPSLHR AAHTEDINAC TLTTSPRLPV -F.....h-c-raf-1 648
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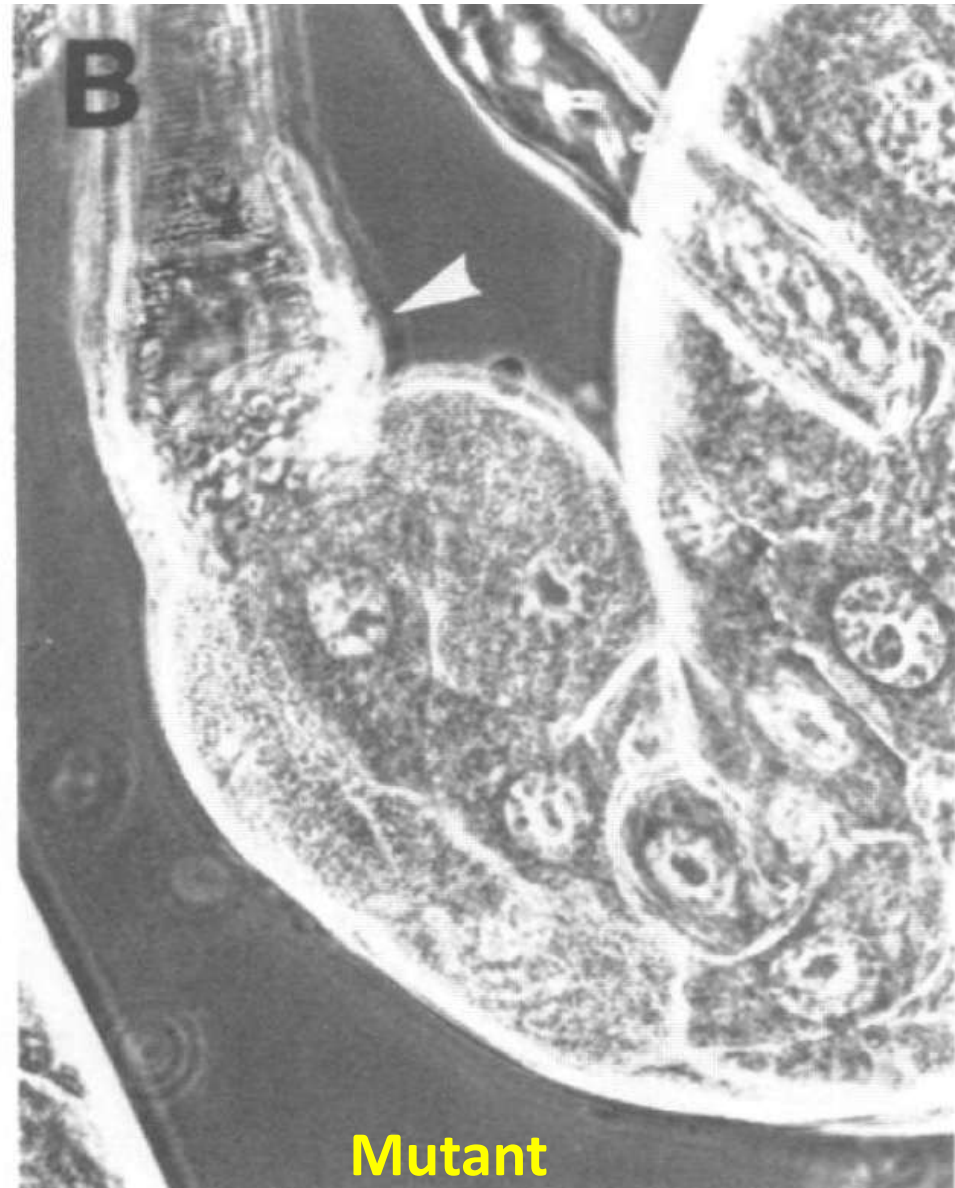
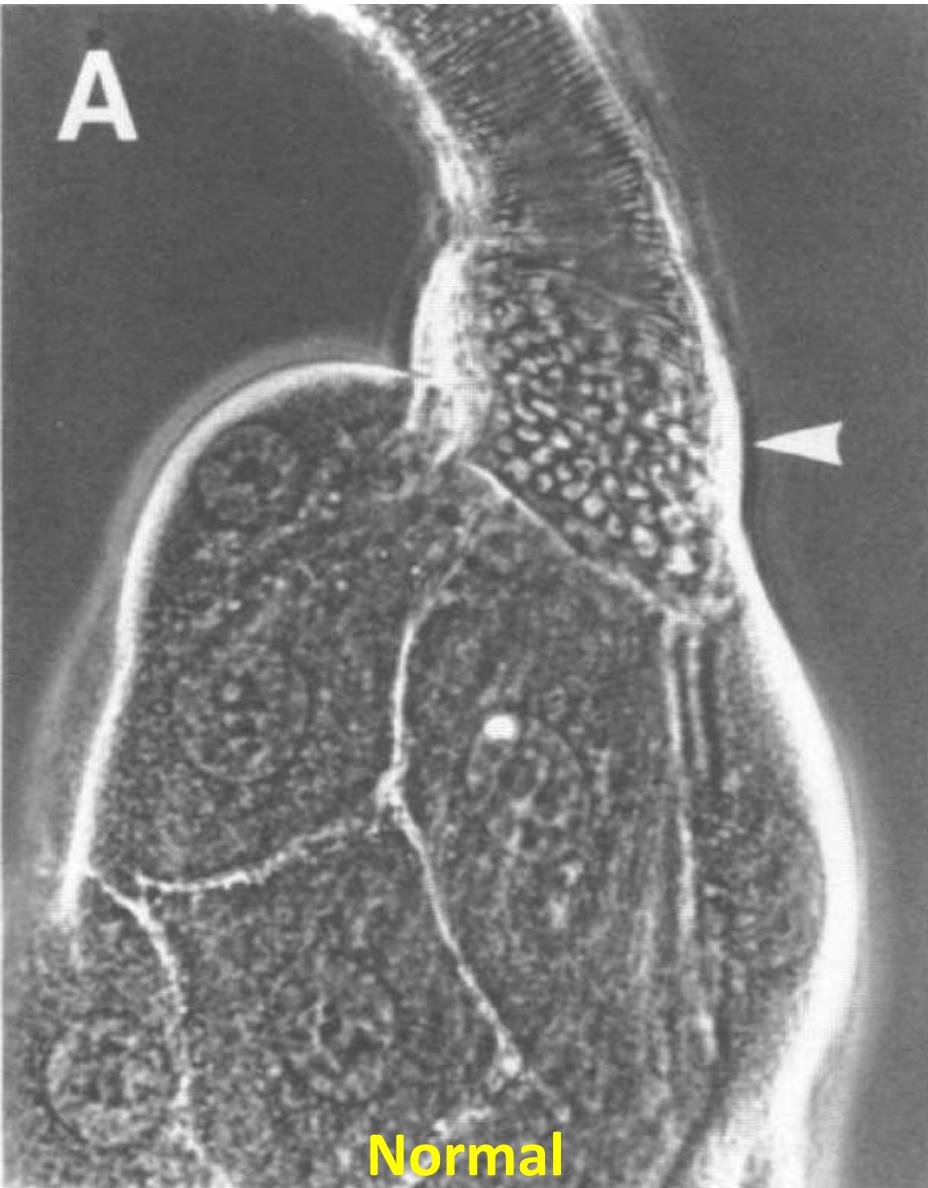
Identification of the *Draf* mutants



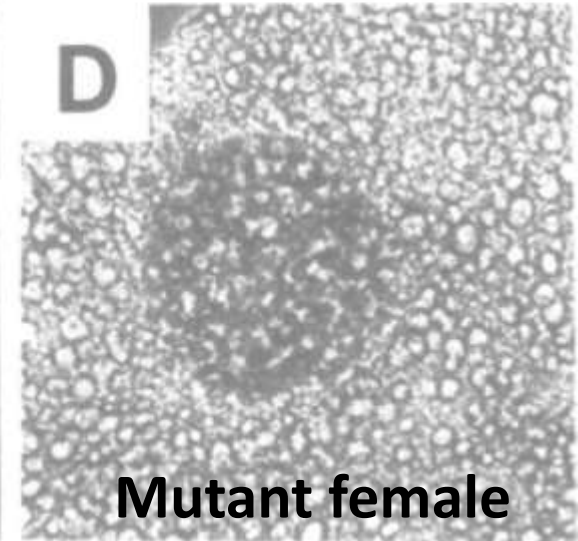
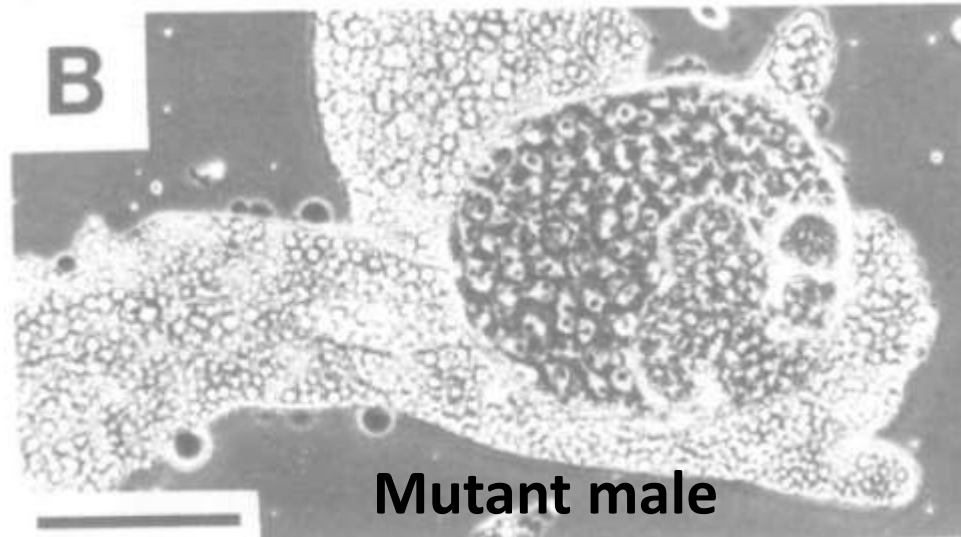
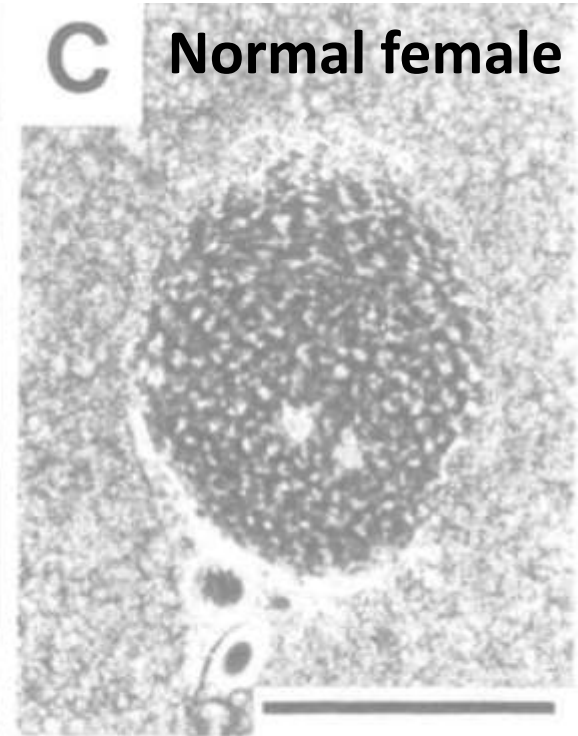
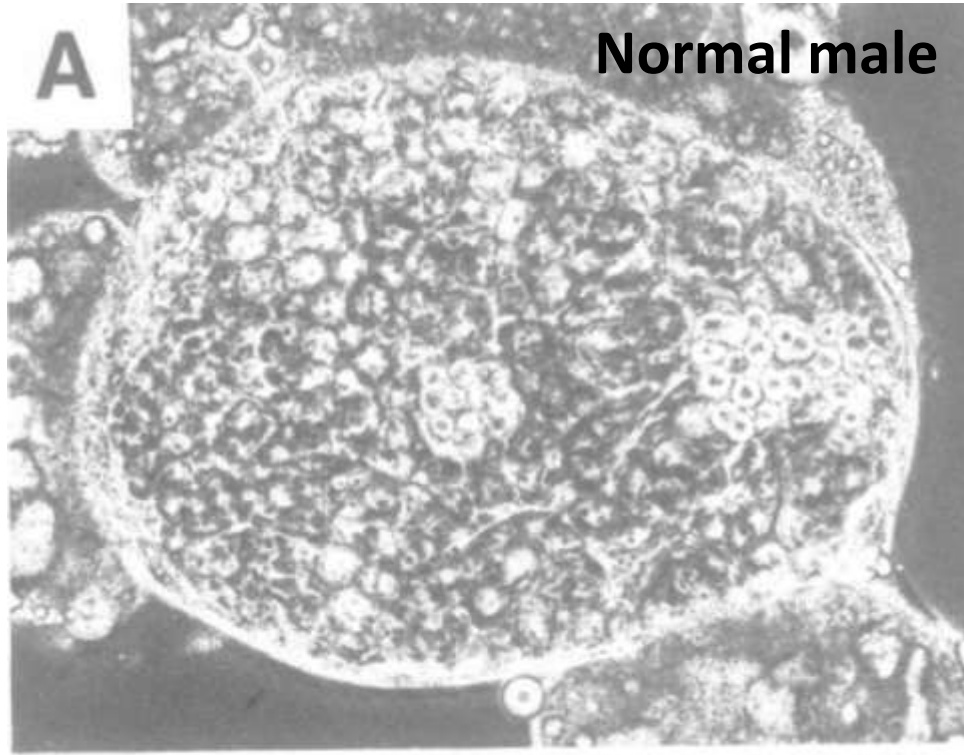
Growth defect of imaginal discs in *Draf*



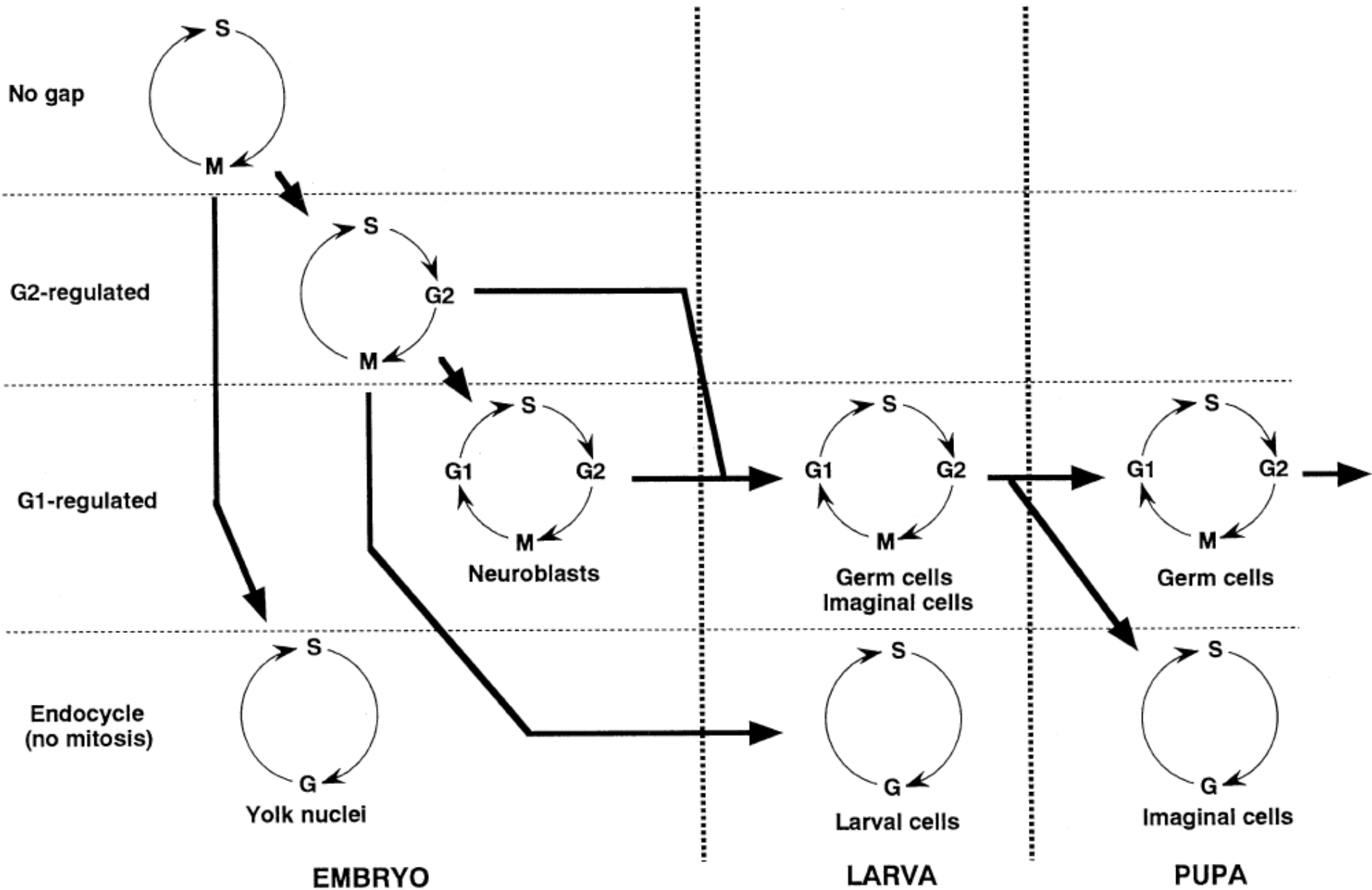
Imaginal salivary gland cells are reduced in *Draf*¹ mutant



Germ cell proliferation is affected in *Draf*¹

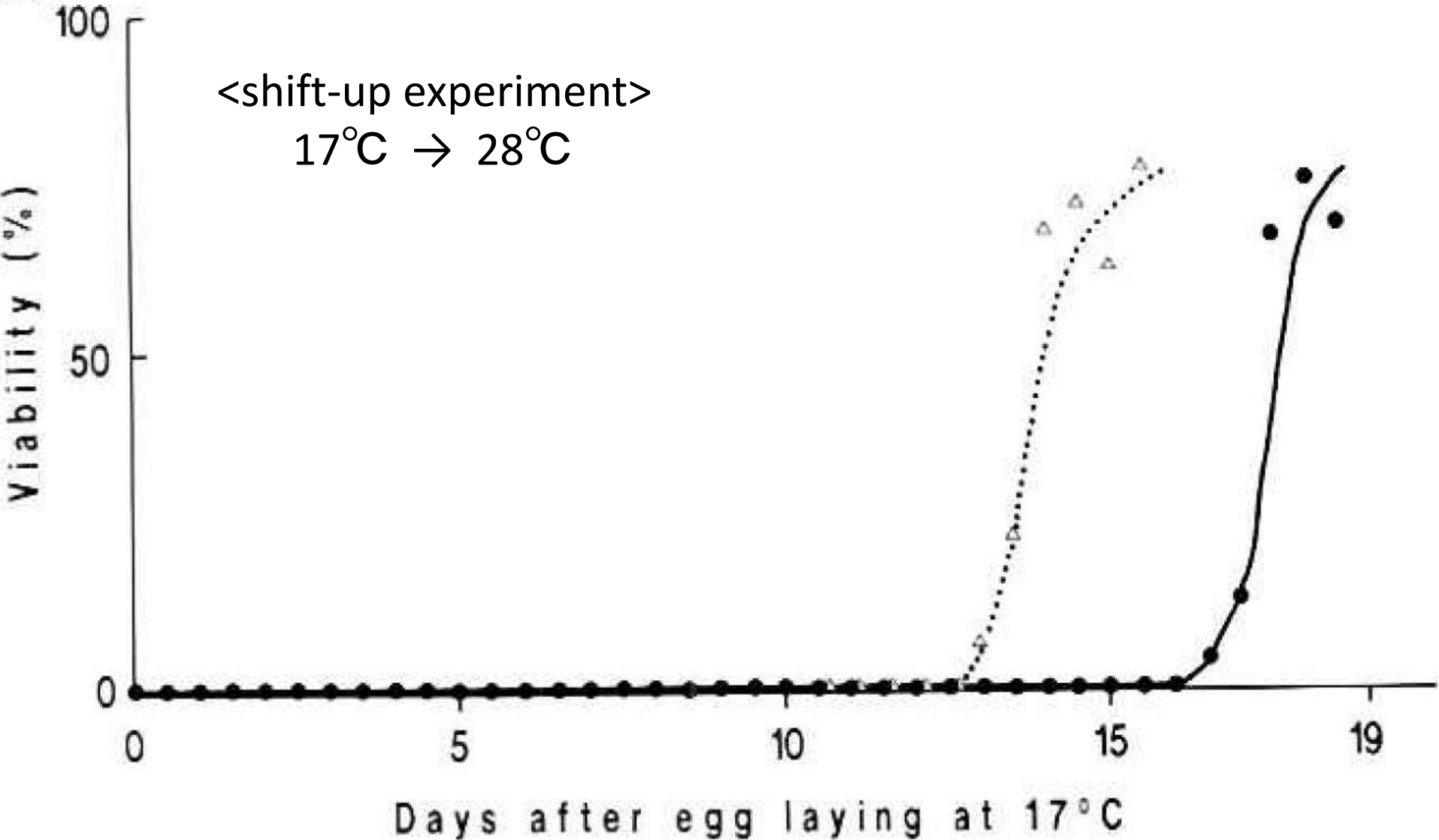


Different cell cycles are programmed during *Drosophila* development

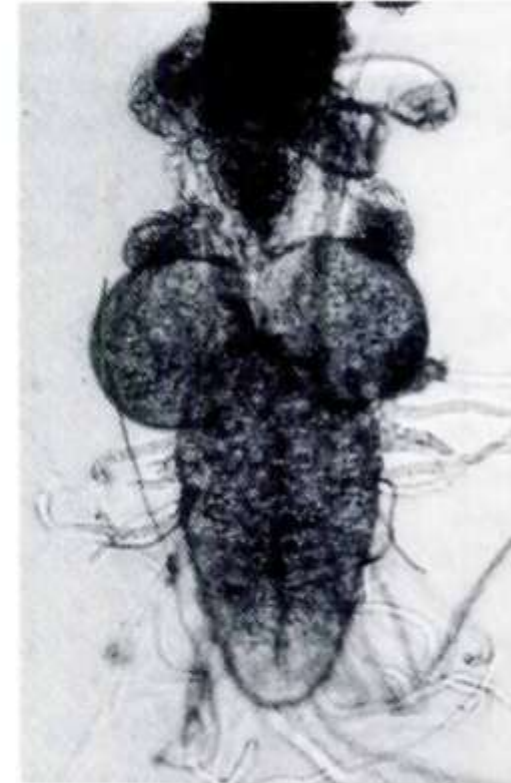
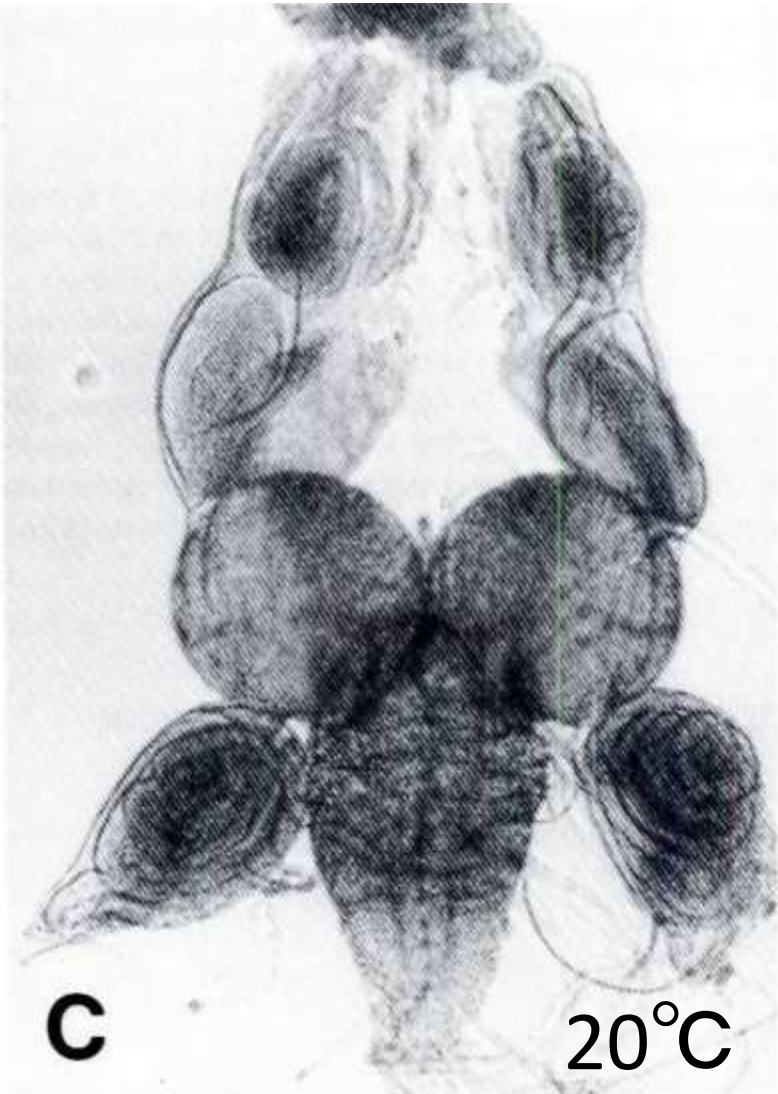


Draf is required throughout development

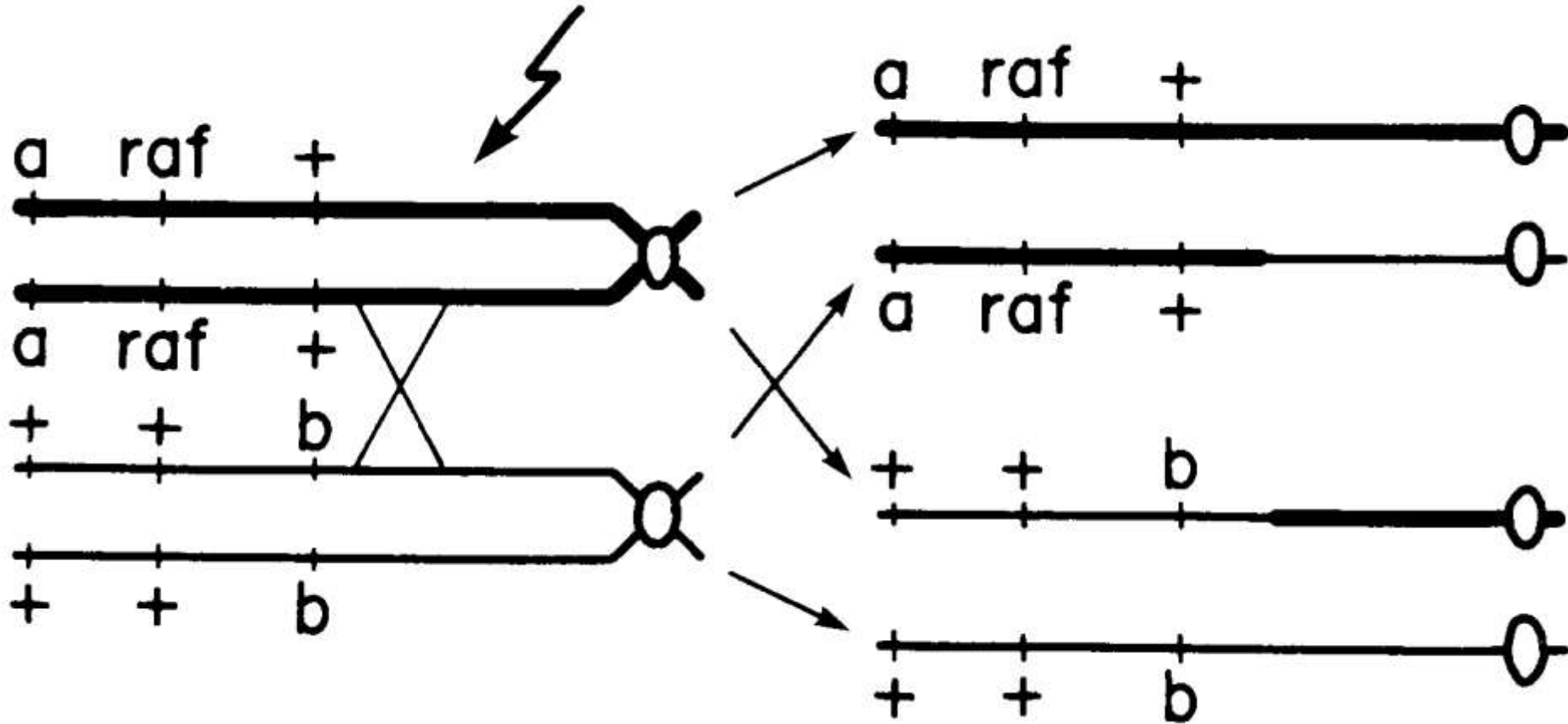
A



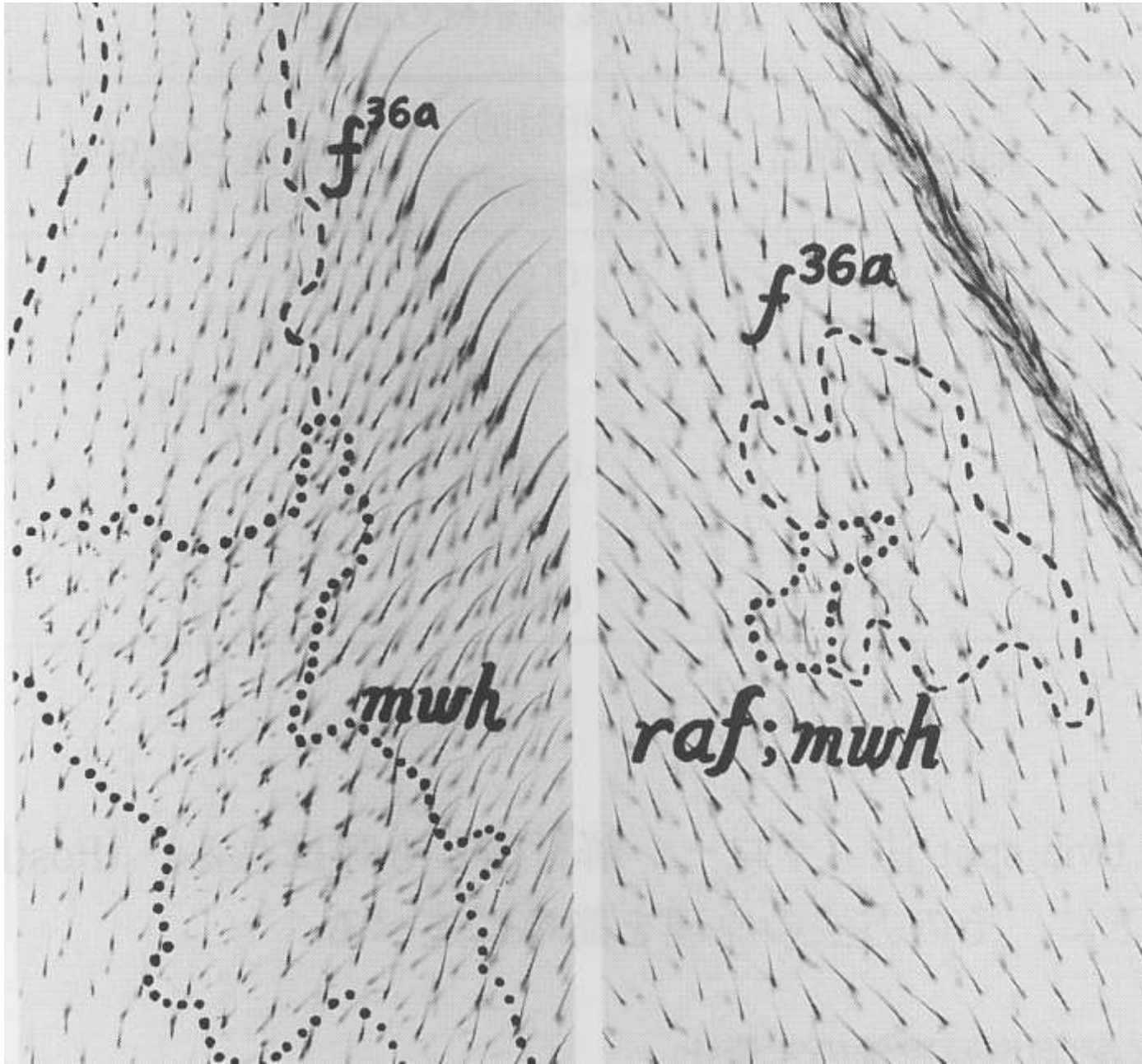
Temperature-sensitivity of imaginal disc growth in *Draf^{E1}*



Twin-spot analysis



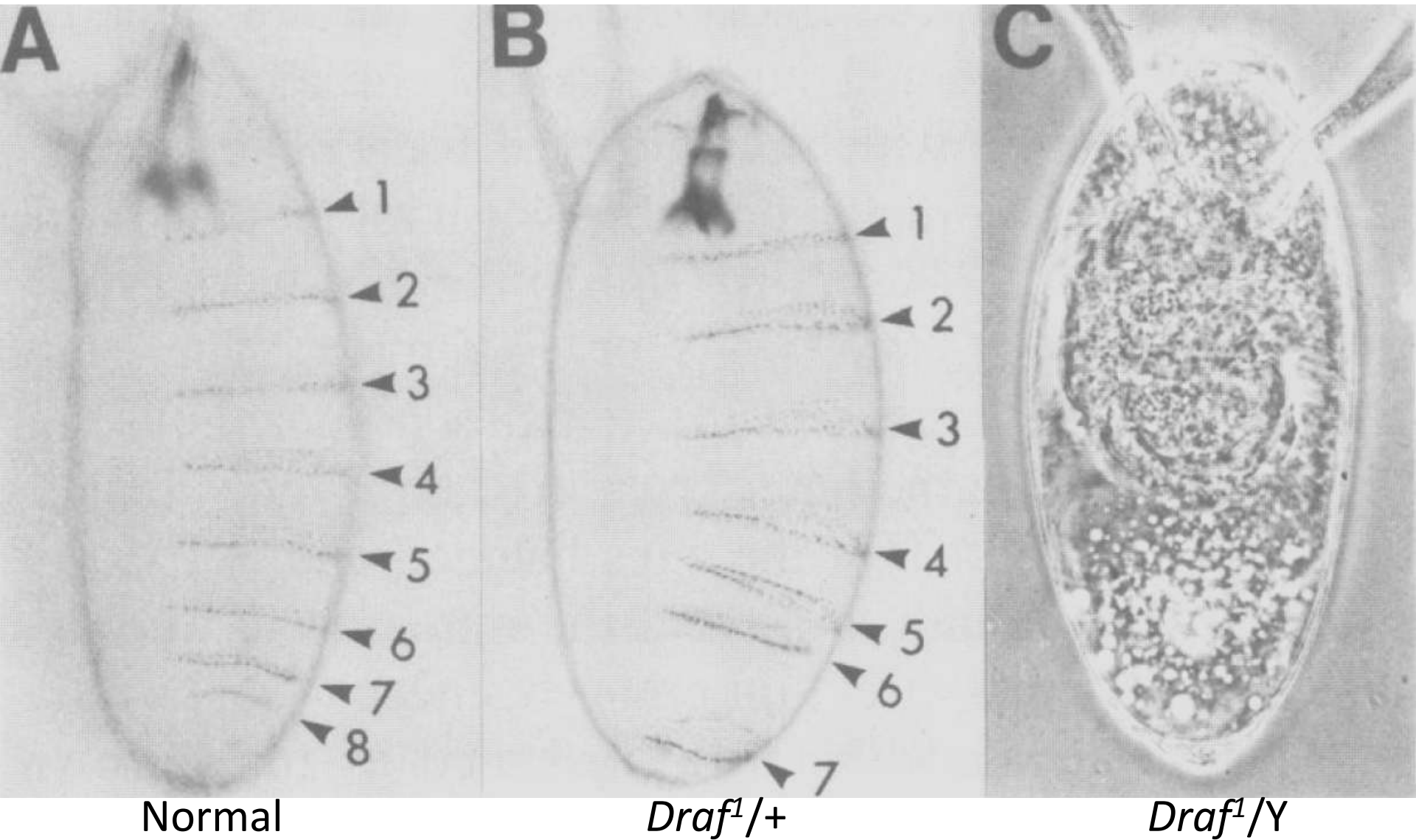
Twin-spots in the wing



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 <i>mwh</i> (A)	Mean No. of doubling <i>f36a</i> (B)	Relative rate (A/B)	Normalized rate
<i>+/M2'; mwh/mwh</i>	25	57	6.63±1.47	7.07±1.51	0.946±0.126	1.00
<i>D-raf</i> ^{E1} / <i>M2'; mwh/mwh</i>	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
<i>D-raf</i> ^{C110} / <i>M2'; mwh/mwh</i>	25	34	5.92±1.20	7.25±1.23	0.817±0.098	0.86
<i>D-raf</i> ^I / <i>M2'; mwh/mwh</i> ^a	25	79	3.41±1.07	5.79±0.99	0.588±0.161	0.62

Draf acts downstream of receptor tyrosine kinases



Screening of Downstream suppressors of Draf (Dsor)

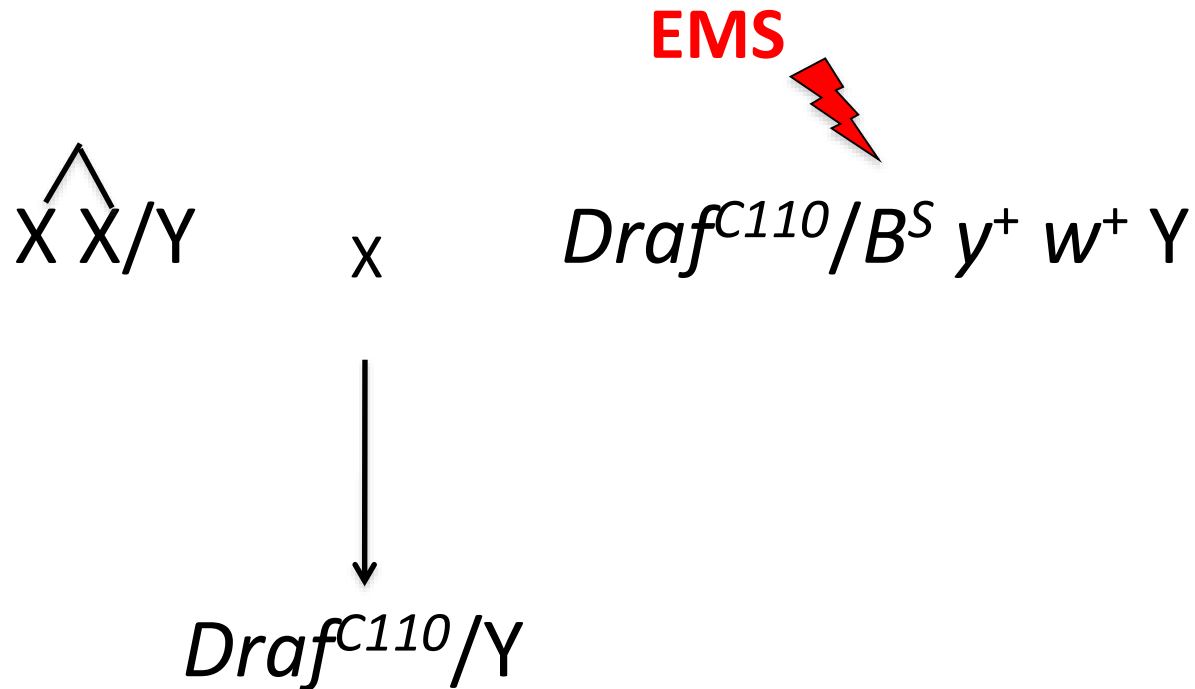


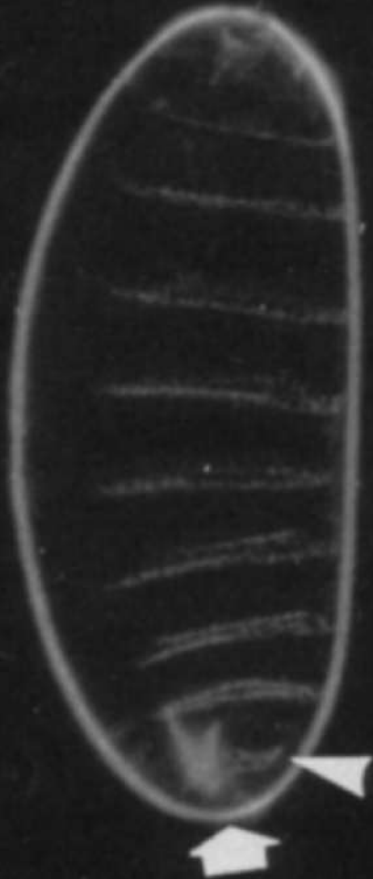
Table 1. Effects of the *D-raf* and *Dsor1* Mutations on the Rate of Proliferation

Genotype	Number of Twin Spots Analyzed	Mean Number of Cell Divisions		Relative Rate (A/B)	Normalized Rate
		<i>mwh</i> (A)	<i>f^{36a}</i> (B)		
+/ <i>M2'</i>	57	6.63 ± 1.47	7.07 ± 1.51	0.946 ± 0.126	1.00
<i>Dsor1^{Su1}</i> / <i>M2'</i>	38	6.37 ± 1.39	6.74 ± 1.29	0.944 ± 0.098	1.00
<i>D-raf¹</i> / <i>M2'</i>	79	3.41 ± 1.07	5.79 ± 0.99	0.588 ± 0.161	0.62
<i>D-raf¹ Dsor1^{Su1}</i> / <i>M2'</i>	74	5.01 ± 1.28	6.34 ± 1.20	0.793 ± 0.133 ^a	0.84
<i>Dsor1¹</i> / <i>M2'</i>	13	4.82 ± 1.67	8.28 ± 1.77	0.585 ± 0.166	0.62
<i>Dsor1²</i> / <i>M2'</i>	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}*

A

Normal



B

Draf¹/Draf¹



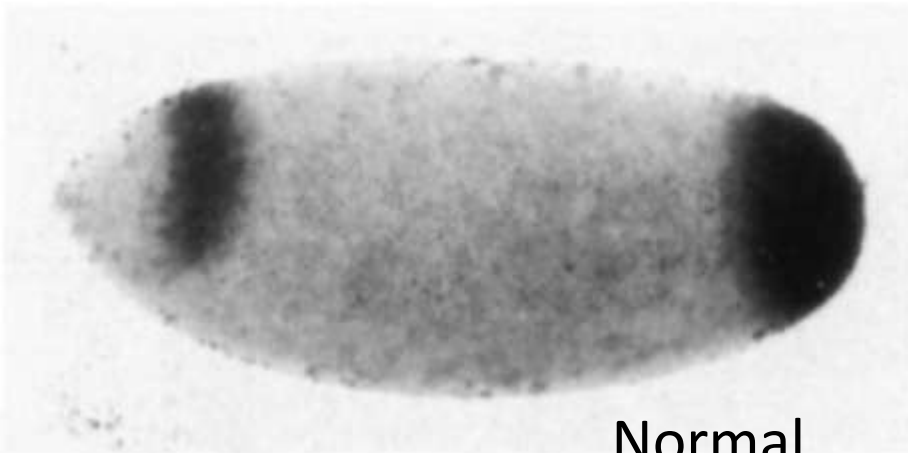
C

Draf¹ Dsor1^{Su1}/Draf¹ Dsor1^{Su1}



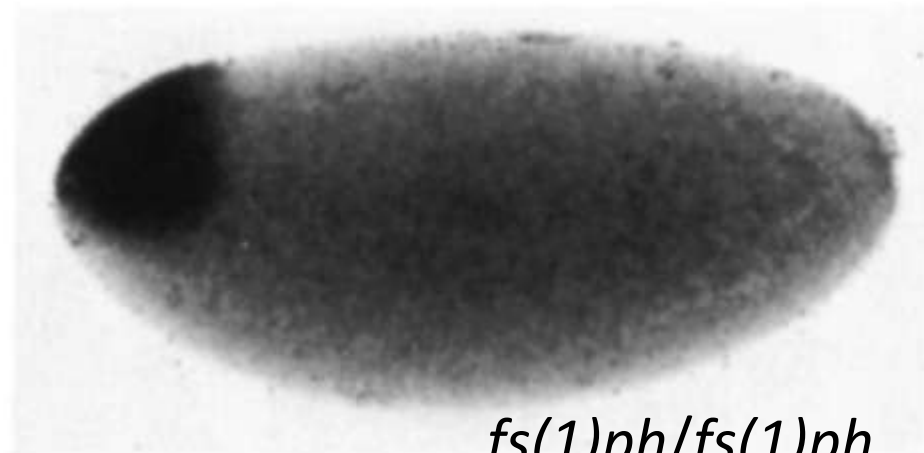
tailless expression patterns

A



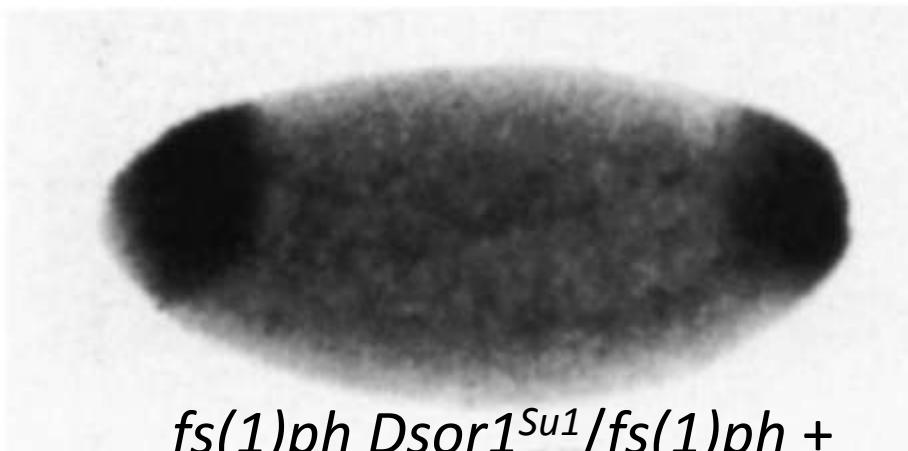
Normal

B



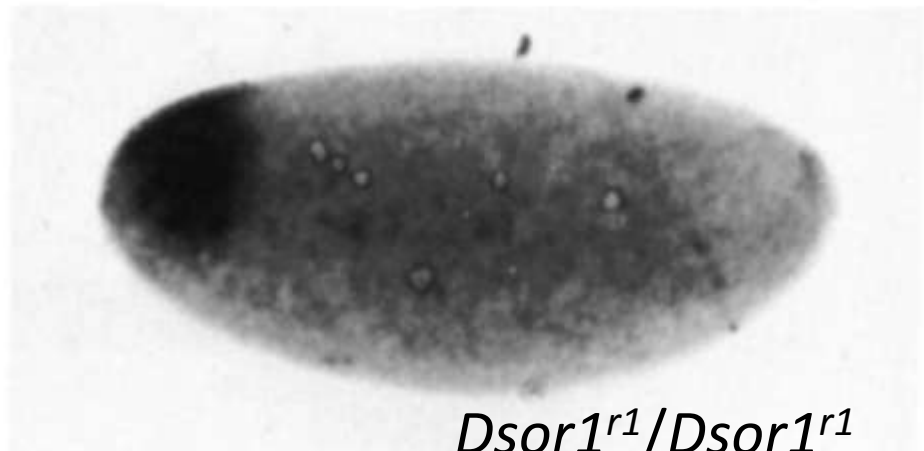
fs(1)ph/fs(1)ph

C



fs(1)ph Dsor1^{Su1}/fs(1)ph +

D



Dsor1^{r1}/Dsor1^{r1}

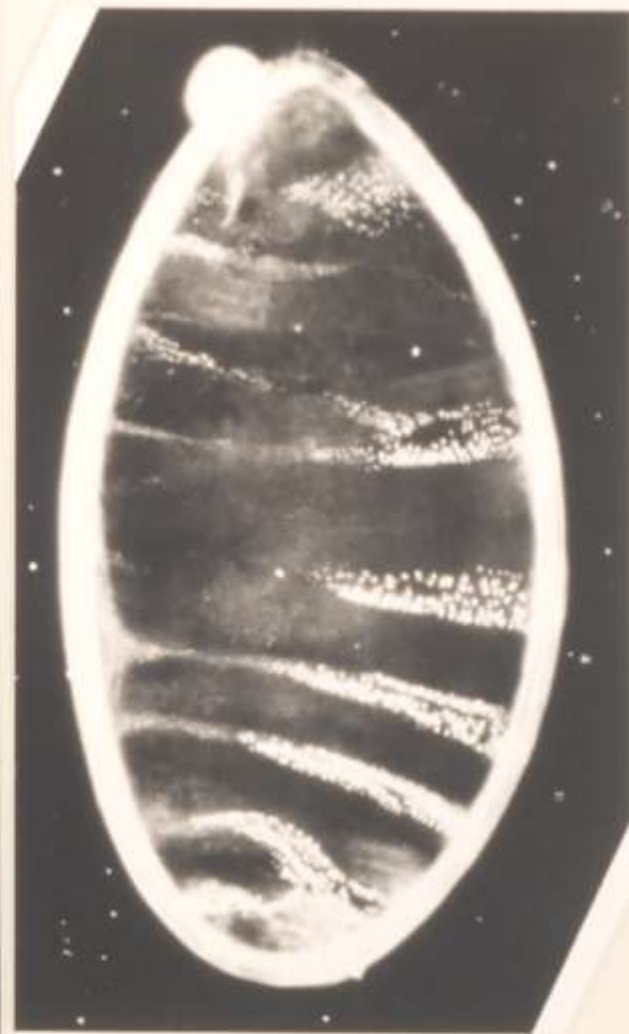
Interaction between *Dsor1^{r1}* and *tor^{RL3}*



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

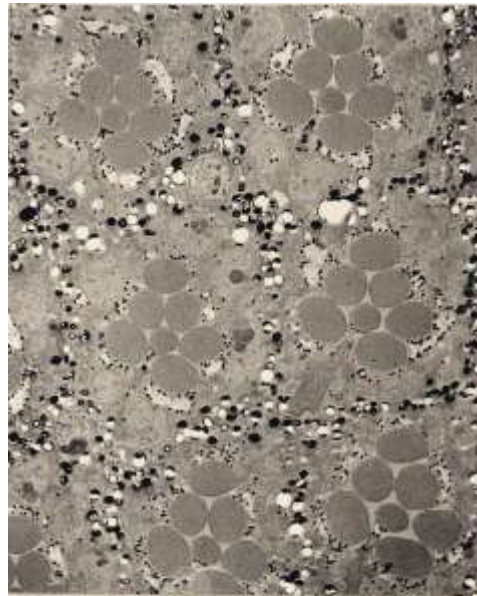


+/+; tor^{RL3}/tor^{RL3}

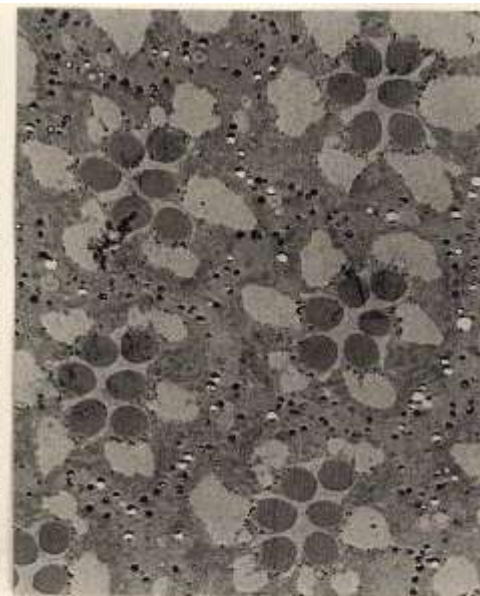


*Dsor1^{r1}/Dsor1^{r1};
tor^{RL3}/tor^{RL3}*

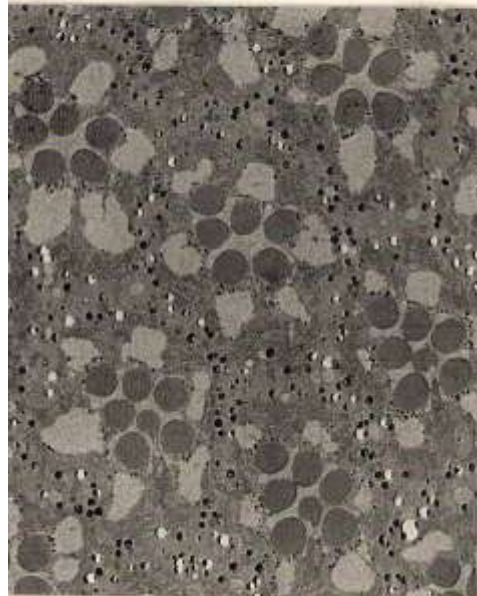
Suppression of *sev* by *Dsor1* and *Sos*



Normal



sev^{E4}/Y

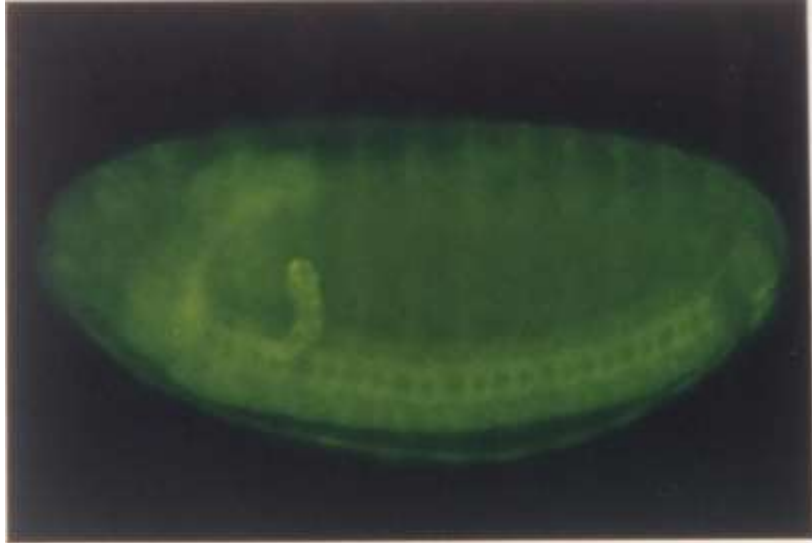


Dsor1^{Su1} sev^{E4}/Y



sev^{E4}/Y; Sos^{JC2}/Sos^{JC2}

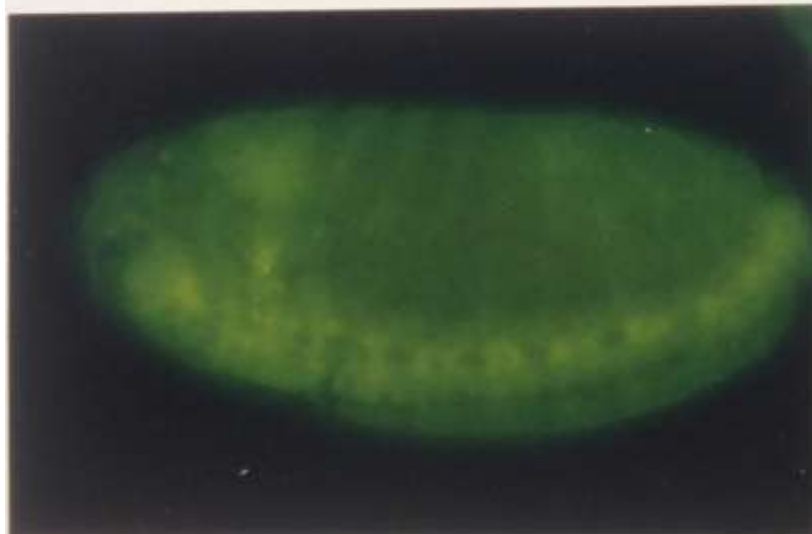
Suppression of *Egfr* by *Dsor1*^{Su1}



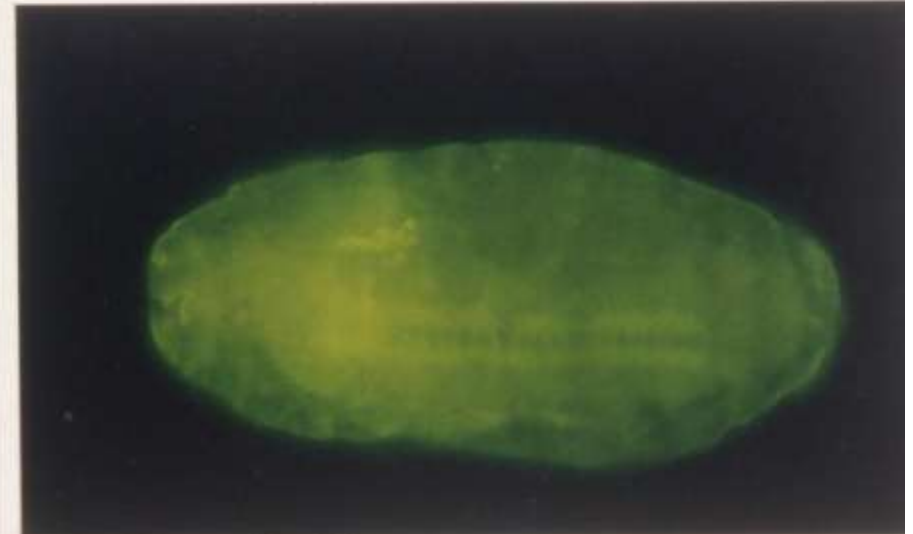
Normal



Egfr^{2w74}/*Egfr*^{2w74}



Dsor1^{Su1}/*+*; *Egfr*^{2w74}/*Egfr*^{2w74}



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



+/+; *SF15/DM7*



Su1 / +; *SF15/DM7*

Dsor1 is homologous to hMAPKK

```
Dsor1 MSKNKLN-LVLPPVNTTEATVAAATVAPTPPFKTPSGTDLLGPKPIDSIDALTETLEGLDMGDTERKRIKMFLSQKEKIGELSDDEDLEKLGE 89
      * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
MEK MPKKKPTPIQLNPAPDGSV-----NGTSSA---ETNLEALQKKLELELELDEQQQRKRLEAFLTQKQKVGELKDDDFEKISE 73

Dsor1 LGSGNGGVVMKVRHHTHLIMARKLIHLEVKPAIKKQILRELKVLHECNFPHIVGFYGFYSDGEISICMEYMDGGSLDLILKRAGRIPE 179
      ** * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
MEK LGAGNGGVVFKVSHKPSGLVMARKLIHLEIKPAIRNQIIRELQVLHECNFPHIVGFYGFYSDGEISICMEHMDGGSLDQVLKAGRIPE 163

Dsor1 SILGRITLAVLKGLSYLRDNHAIHRDVKPSNILVNSSGEIKICDFGVSGQLIDSMANSFVGTRSYMSPERLQGTHYSVQSDIWSLGLSL 269
      *** * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
MEK QILGKVSIAVIKGLTYLREKHKIMHRDVKPSNILVNRSRGEIKLDFGVSGQLIDSMANSFVGTRSYMSPERLQGTHYSVQSDIWSMGLSL 253

Dsor1 VEMAIGMYPIPPPNTATLESIF-----ADNAEESGQPT-----DEPRAMAIFELLDYIVNEPPPKLEHKIFSTEFKDFVDICLK 343
      **** * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
MEK VEMAVGRYPPIPPDAKELELLFGCHVEGDAAETPPRPRTPGRPLSSYGMDSRPPMAIFELLDYIVNEPPPKLPSGVFSLEFQDFVNKCLI 343

Dsor1 KQPDERADLKTLLSHPWIRKAELEEVDISGWVCKTMDL-PPSTPKRNTSPN 393
      * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
MEK KNPAERADLKQLMVHAFIKRSDAEEVDFAGWLCSTIGLNQPSPTPTHAASI 393
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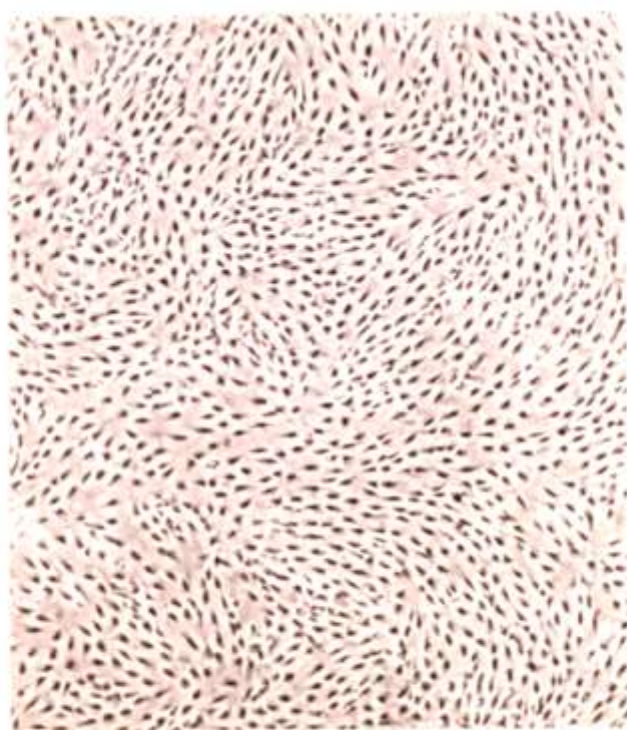
Drosophila MAPKK Mutations

	M (Su6)	K (Su24)	I		
Dm Dsor1	MSKNKLNLY-LPPVNTAATVAAATVAPTPPFKTPSGTDLGKPKTSIDALTTETLEGLDMGDTERRKIKMFLSQEKIGELSDLELKLGLGSGNGGVVM			99	
Mm MEK	MPKKKPTPIQLNPAPDGSAY-----NGTSSA---ETNLEALOKKLELELDEOORKRLEAFLTKOKVYVGGELKDDDFEKISELGAGNGGVVF			83	
Sc MKK1			DR-IETLGI LGEAGGGSVS	236	
Sc MKK2			DE-ITTLGI LGEAGGGSVA	229	
Sc STE7			LQDLVQLGKI GAGNSGTVV	206	
Sc PBS2			DE-LEFLDELGHGNYGNVS	375	
	II	III	IV	V	
			D (Su4)	(Su12) L A (Su6)	
Dm Dsor1	KVRHTHTHLIMARKLIHLEVKPA-IKKOILRELK-VLHECNFPHIVGFYGAIFYSD---GEISICMEYMDGGSLDLI-----LKRAGR-----IPESI			181	
Mm MEK	KVSHKPSGLVMARKLIHLEIKPA-IRNOIIRELO-VLHECNFPHIVGFYGAIFYSD---GEISICMEHMDGGSLDQV-----LKKAGR-----IPEQI			165	
Sc MKK1	KCKLKNKSKI FALKVINTLNTDPEYQKQIFRELQ-FNRSFQSEYIVRYYGMFTDDE-NSSIYIAMEYMGGRSLDAIYKNLLERGGG-----ISEKV			325	
Sc MKK2	KCRLKNGKVKFALKTINTMNTDSEYQKQIFRELQ-FNKSFQSDYIVQYGMFTDEQ-SSSIYIAMEYMGGSLEATYKNLLKRGGR-----ISERV			318	
Sc STE7	KALHVPDSKIVAKKTI PVEQNNSTI INQLVRELSIVKNVKPHENIITFYGAYNQHINNEI I LMEYSDCGSLDKILSVYKRFVQRGTVSSKKTWFNLT			306	
Sc PBS2	KVLHKPTNVIMATKEVRLELDEAKFR-QILMELE-VLHKCNFPHIVDFYGAFFIE---GAVYMCMEYMDGGSLDKIYDESSEIGG-----IDEPQ			460	
	VIA	VIB	VII	VIII	IX
	S (Su1)	(Su18) N N (Su5)		* *	
Dm Dsor1	LGRITLAVLKGLSYLRDNHAI IHRDVKPSN I LVNNS-GEIKICDFGVSGQLIDSMANSFVGT RSYMSPERL-----QGTHYSVQSDIWSLGLSLVEMAIG				275
Mm MEK	LGKYSIAVIGKLTYLREKHKIMHRDVKPSN I LVNSR-GEIKLDFGVSGQLIDSMANSFVGT RSYMSPERL-----QGTHYSVQSDIWSMGLSLYEMAVG				259
Sc MKK1	LGKIAEAVLRGLSYLHE-KKV IHRDIKPN I LLNEN-GQVKLDFGVSGEAVNSLATTFTGT SFYMAPERI-----QGQPYSVTS DVWSLGLTILEVANG				418
Sc MKK2	IGKIAESVLRGLSYLHE-RKV IHRDIKPN I LLNEK-GEIKLDFGVSGEAVNSLAMTFTGT SFYMAPERI-----QGQPYSVTC DVWSLGLTILEVAGG				411
Sc STE7	ISKIAYGVNLGLDHLRYQYK I IHRDIKPSNVL INSK-GQIKLDFGVSGKLLINSIADTFVGT STYMSPERI-----QGNVYSIKGDVWSLGLMI IELVTG				400
Sc PBS2	LAFIANAVIHGLKELKEQHN I IHRDVKPTN I LCSANQGTVKLDFGVSGNLVSLAKTNIGCQSYMAPERIKSLNPD RATYTVQSDIWSLGLSILEMALG				560
			X	XI	
	A (Su7)				
Dm Dsor1	MYPISPPNTATLESIF-----ADNAEESGQPT-----DEPRAMI FELLDYIVNEPPPKEHKI-----FSTEFKDFVDICLKKOPDERADLKT				354
Mm MEK	RYPISPPDAKELELLFGCHVEGDAAETPPRPRTGPRPLSSYGMDSRPPMAI FELLDYIVNEPPPKLPSGV-----FSLEFQDFVNKCLIKNPAERADLQK				354
Sc MKK1	KFPCSSEKMA-----ANIAPFELLMWILT-FTPELKDEPESNI I WSPSFKSFI DYCLKKD SRERPSRQ				481
Sc MKK2	RFPFESDKIT-----QNVAPIELLTMILT-FSPQLKDEPELDI SWSKTFERSFI DYCLKKDARERPSRQ				474
Sc STE7	EFPLGGHND-----TPDGI LDLLQRI VNEPSPRLPKDR----IYSKEMTDFVNRCCI KNERERSSIHE				459
Sc PBS2	RYPYPPE-----TYDNIFSQLSAIVDGP PPRLPSDK-----FSSDAQDFVSLCLQKIPERRPTYAA				616
Dm Dsor1	LLSHPWIRKAELEEVDISGWVCKTMDLP-PSTPKRNTSPN				393
Mm MEK	LMVHAFIKRSDAEEVDFAGWLCSTIGLNQPSTPTHAA SI				393
Sc MKK1	MINHPWI				
Sc MKK2	MLKHPWI				
Sc STE7	LLHHDL I				
Sc PBS2	LTEHPWL				

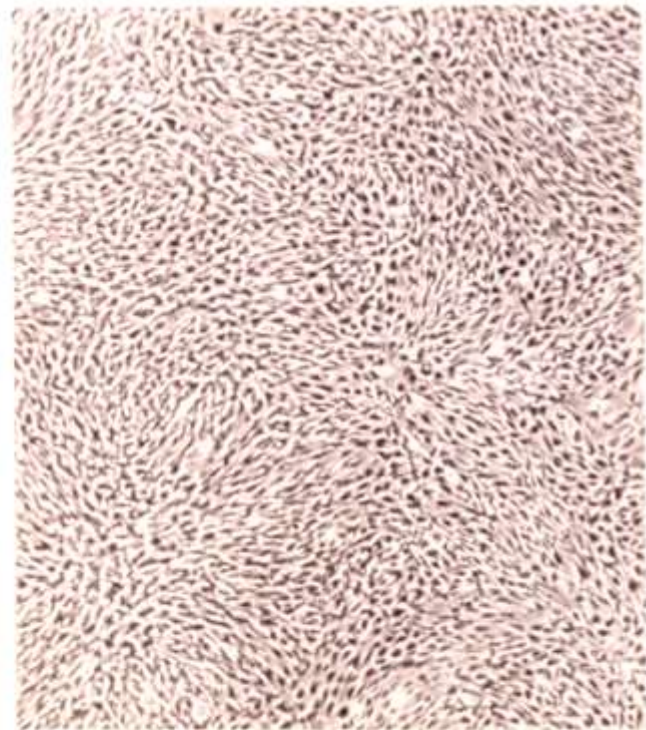
Morphological Change of MEK^{Su1} -transfected Cells



NIH 3T3



MEK



MEK^{Su1}

Downstream suppressors of *Draf* (*Dsor*)

Dsor1 : MAPKK (MEK)

Dsor2a : *rl* (MAPK)

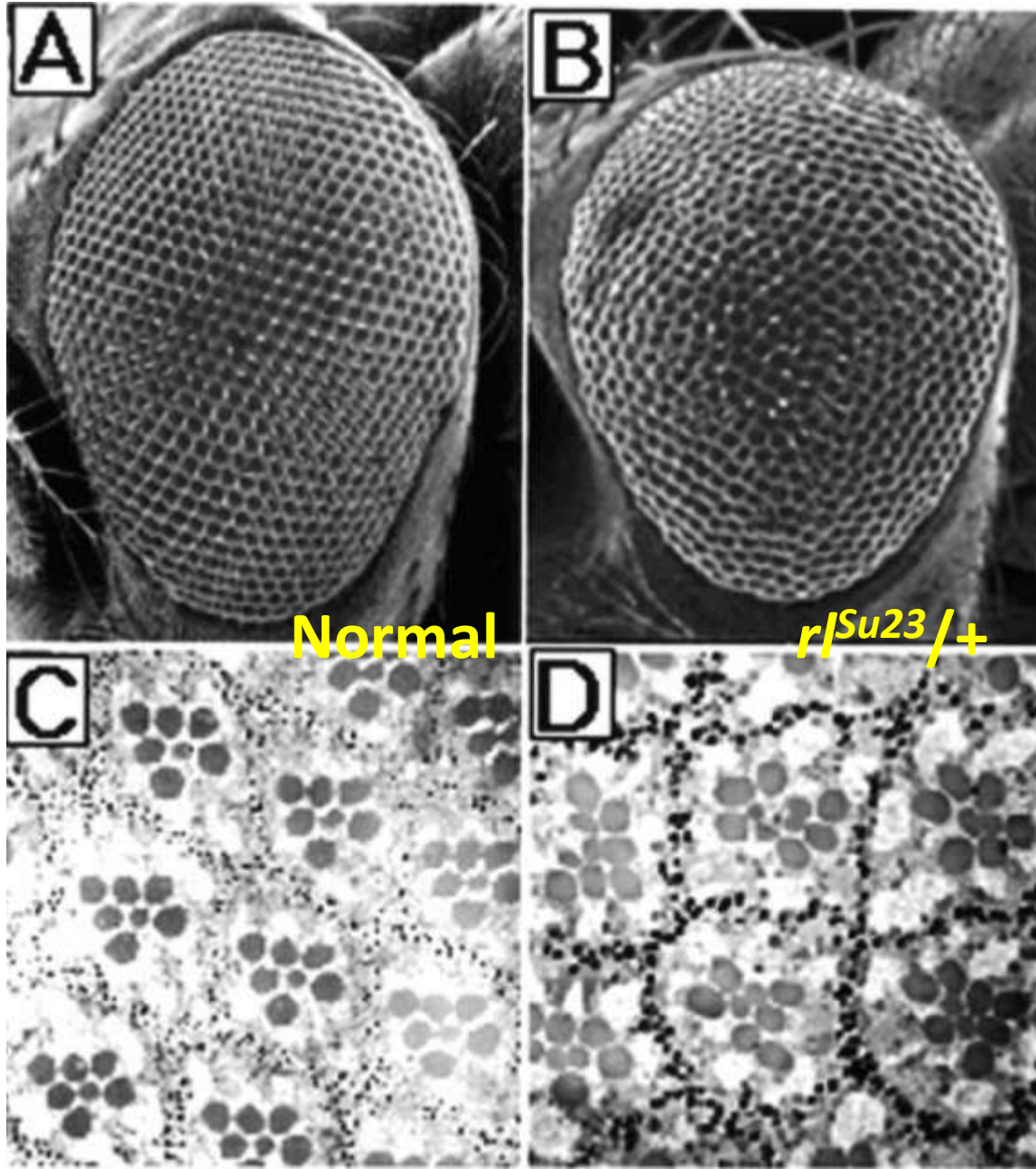
Dsor2b : *Dsrc42A*

Dsor3 : not identified

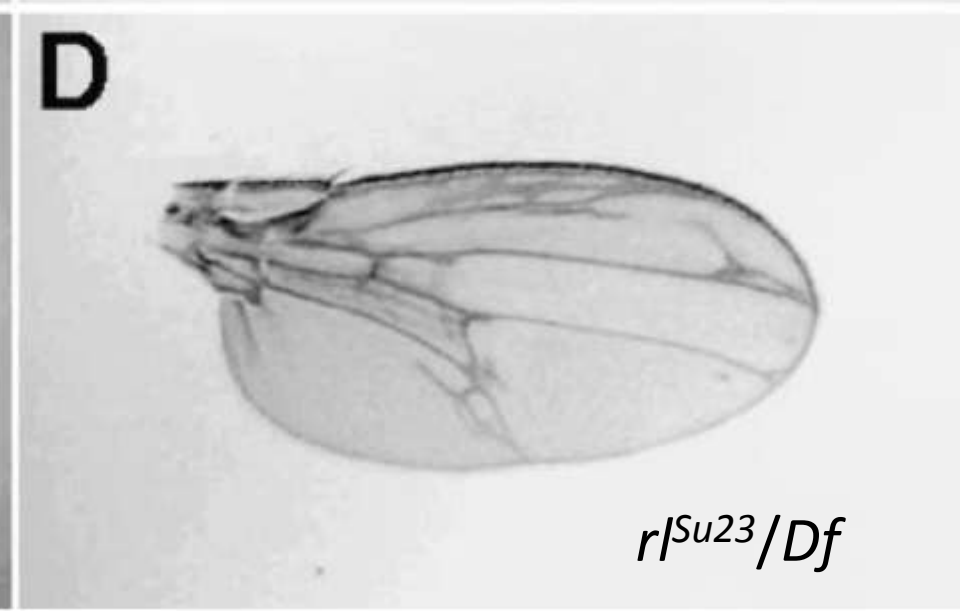
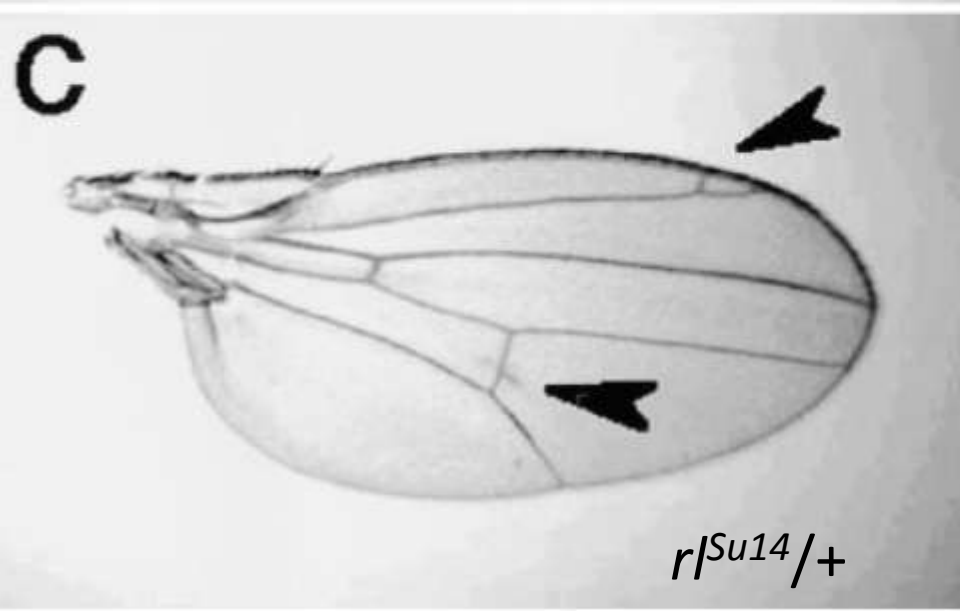
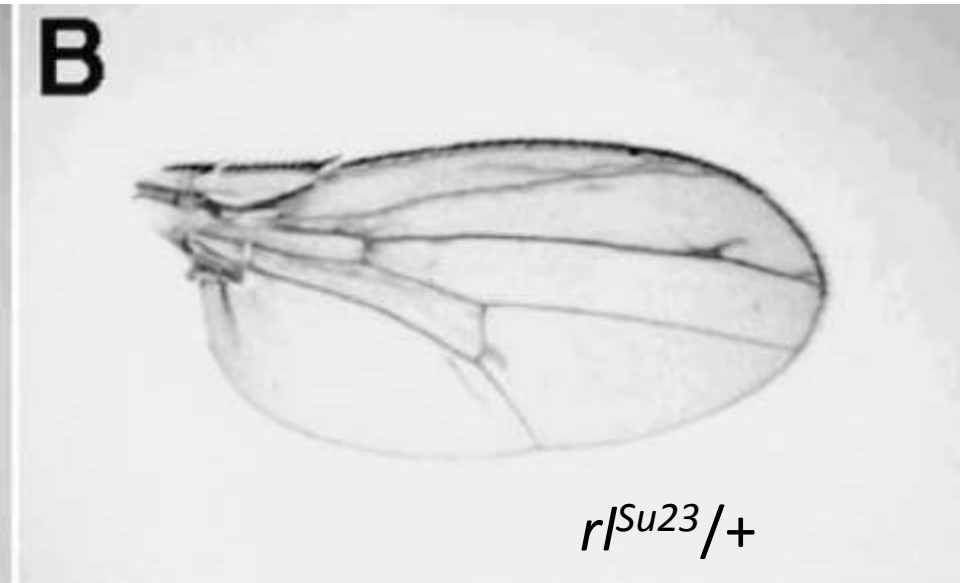
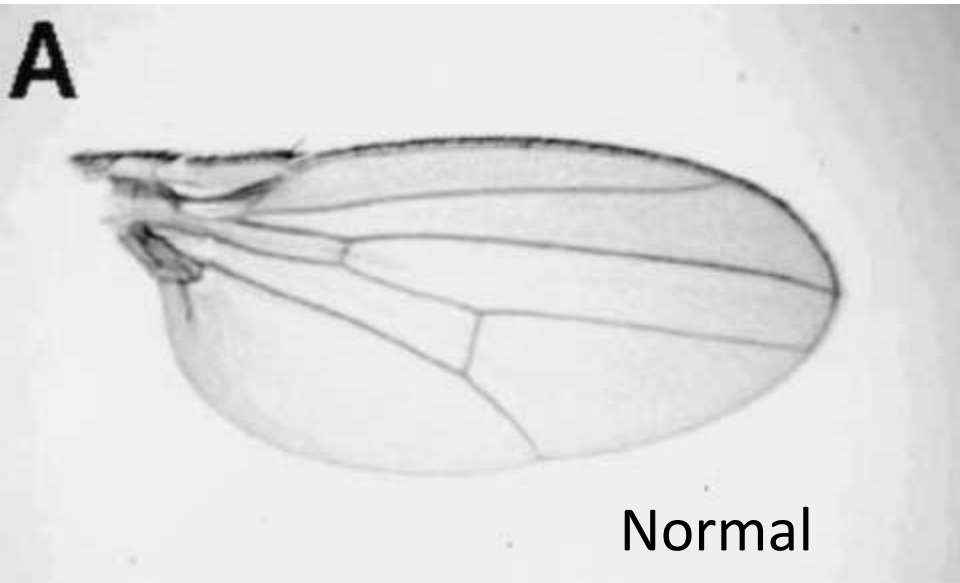
Proliferation defects in loss-of-function mutations of *Dsor1* and *D-raf* and their suppression by a gain-of-function mutation in *rl*

Genotype ^a	No. of twin spots analyzed	Mean no. of doubling		Relative rate (A/B)	Normalized rate
		<i>mwh</i> (A)	<i>r^{36a}</i> (B)		
<i>+ / M2'</i> ; <i>mwh / mwh</i>	24	7.28 ± 1.56	7.87 ± 1.48	0.930 ± 0.141	1.00
<i>+ / M2'</i> ; <i>r^{fu23} / +</i> ; <i>mwh / mwh</i>	13	7.52 ± 0.86	7.87 ± 1.38	0.974 ± 0.138	1.05
<i>D-raf^l / M2'</i> ; <i>mwh / mwh</i>	24	3.37 ± 1.73	5.89 ± 0.60	0.572 ± 0.190	0.62
<i>D-raf^l / M2'</i> ; <i>r^{fu23} / +</i> ; <i>mwh / mwh</i>	13	7.52 ± 0.86	7.87 ± 1.38	0.947 ± 0.138	1.02
<i>Dsor1^{Gp158} / M2'</i> ; <i>mwh / mwh</i>	44	2.06 ± 1.46	6.66 ± 1.22	0.304 ± 0.227	0.33
<i>Dsor1^{Gp158} / M2'</i> ; <i>r^{fu23} / +</i> ; <i>mwh / mwh</i>	14	4.48 ± 1.43	6.91 ± 1.56	0.661 ± 0.193	0.71
<i>Dsor1^{r1} / M2'</i> ; <i>mwh / mwh</i>	13	4.82 ± 1.67	8.28 ± 1.77	0.585 ± 0.166	0.63
<i>Dsor1^{r1} / M2'</i> ; <i>r^{fu23} / +</i> ; <i>mwh / mwh</i>	13	8.65 ± 0.32	8.91 ± 0.33	0.977 ± 0.031	1.05

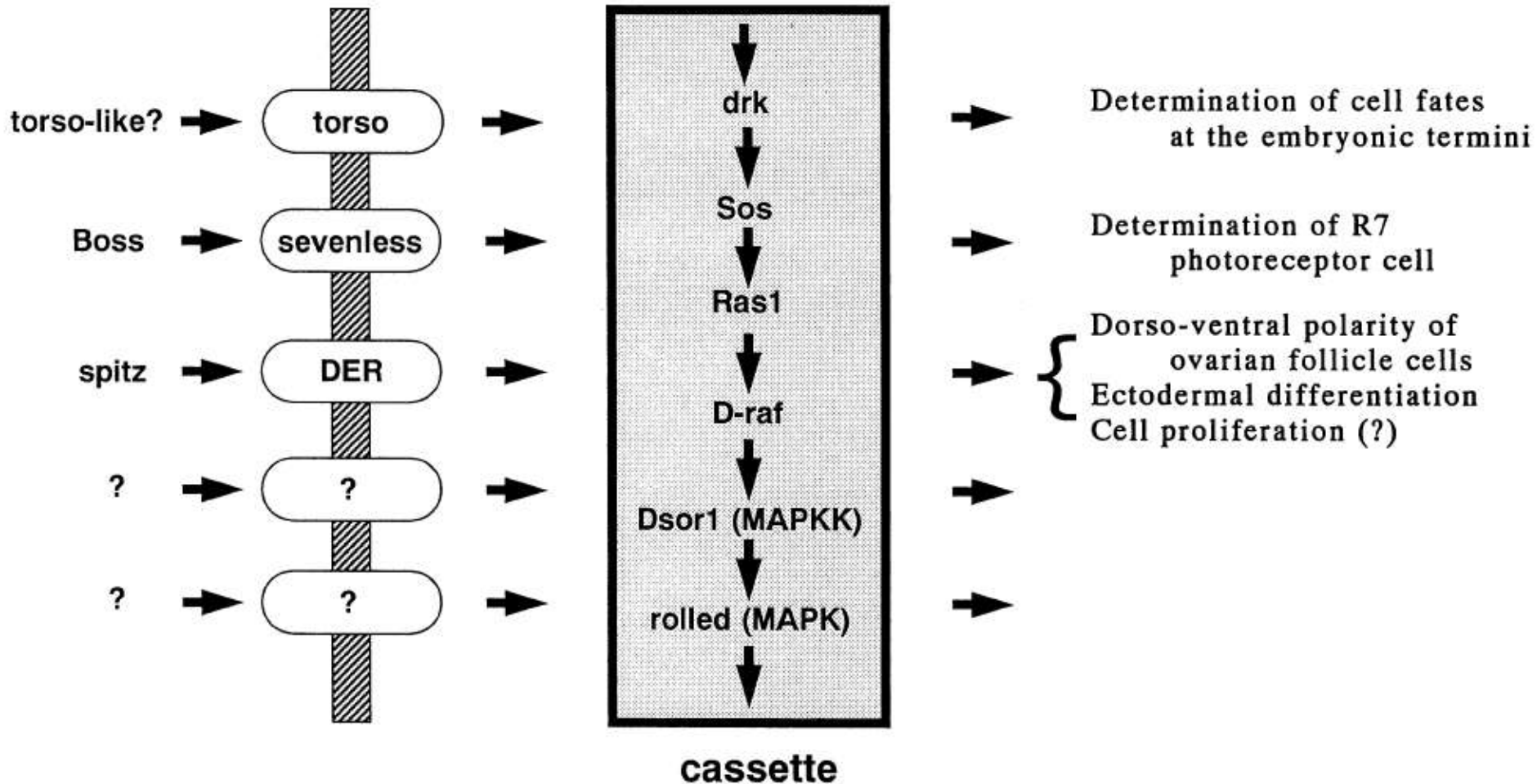
Extra R7 cells in $r/Su23$



Extra wing veins in the r/Su mutants



Signaling cassette of MAPK cascade under multiple receptor tyrosine kinases

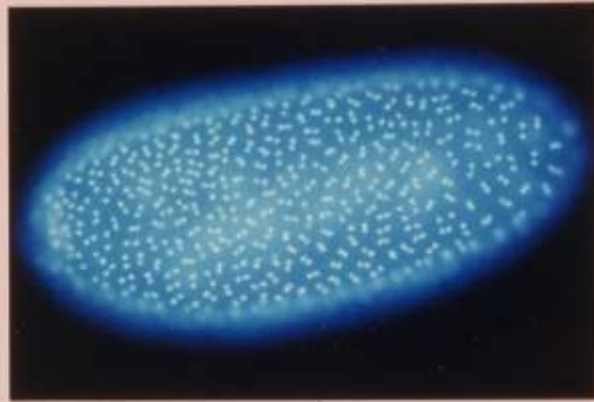


Mutations suppressed by *Dsor1*^{Su1}

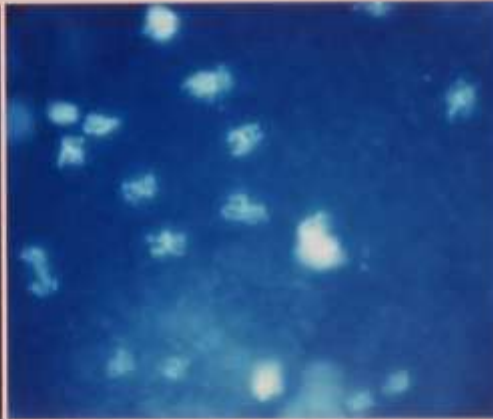
- Gp9 : *sqh* (myosin regulatory light chain)
- Gp99 : *ttm50*
- Gp126: *raptor*
- Hp126: *Dwhn* (*nude* gene homolog)

Maternal effects of the *Gp99* mutation

normal



Gp99



Gp99 Dsor1^{Su1}



Growth defects in the *ttn50* mutants



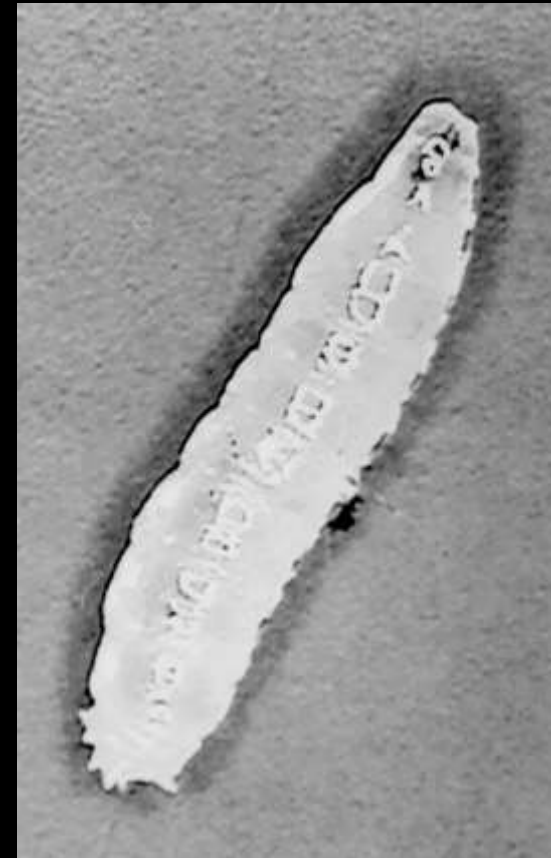
y/Y (normal)



y ttn50^{E1}/Y

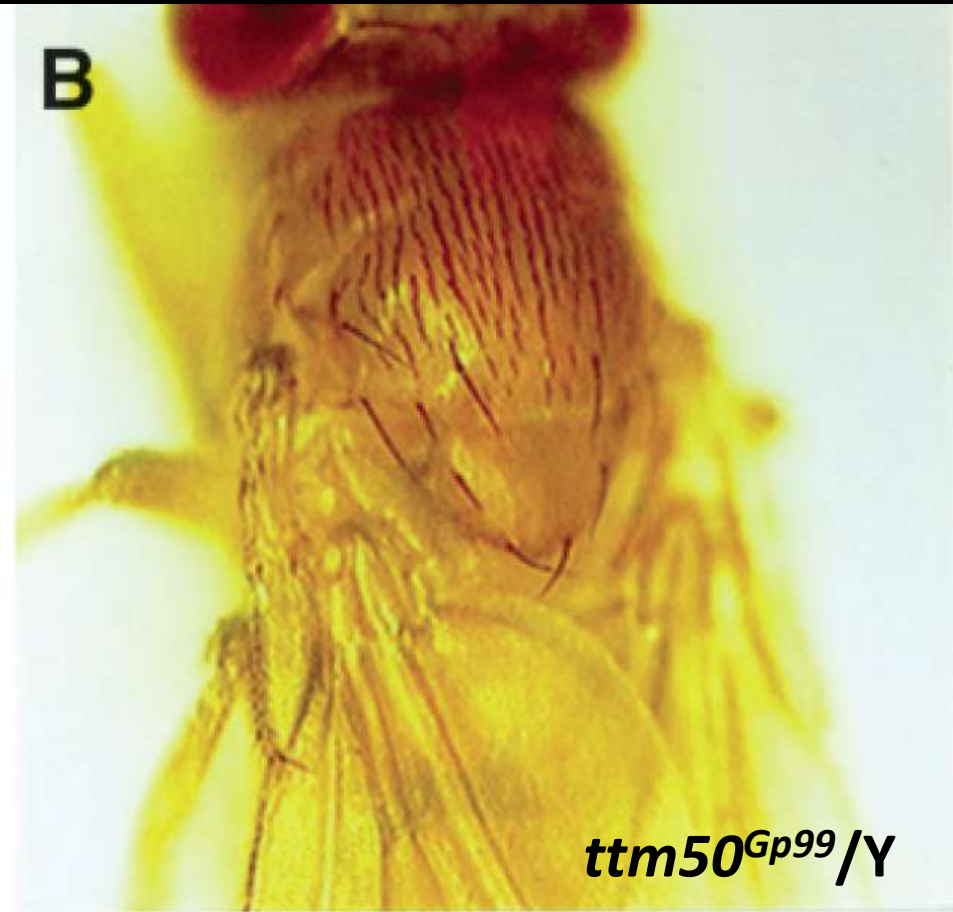
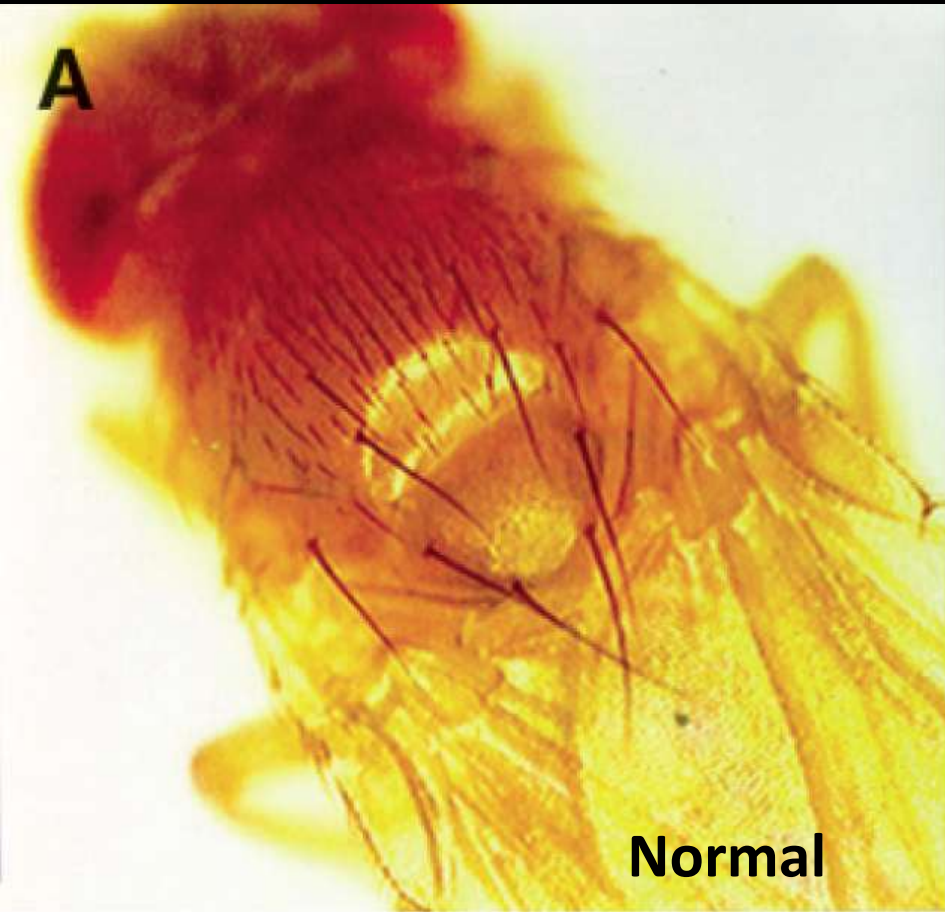


y ttn50^{E2}/Y



y ttn50^{Gp99}/Y

Adult phenotypes of a hypomorph of *ttm50*



Three *Tim50*-like genes in *Drosophila*

B

```
Dm Ttm50  MSMSMA-PATVLQLRGLSTP-RLITHIQHRA LG-NHYHHYHQHYQHQLLHHQQYLR LFTCTALPAAA--PALFSILHTARGYSSTTKQ EAGATGP
Dm Ttm2    MSLI-----AIERVL CGWPKICRKL--IVTSRSLT-SGLRRALVKQPRKGGDVGKPGMELGRCS CFGLRVNL--SNASVVYVGHRRYSTYEK-----
Dm Ttm3    MHKIV-----W-----FGTLNKSIGYIGKKKTC L-LSPEKICLN---SARKTVQRCDKNYSP-----
Hs Tim50   MASALS L GNKCDPFL--RCVLCRGGGALQGRGRGPDDEFESQLSPPGSARRLVRSKRACGNPPDAFGLSRASVHPPLPRV SIGCSSGPGRAKRERVGGAA
Ce T21C9.1 MSLS-KLTQTC--FSRHQAKT FIRLYSSDFKSL LGPPAVANPYADNGRTRFAPIVPINHGNVFASIKLPINETQE AIA--FKSEVEEAPKVEKLEVESPK
Sc Tim50   MLSIL-----RNSVRLNSRALRVVPSAANTLTSVQASRRL----TSYSSFLQKETKDD--

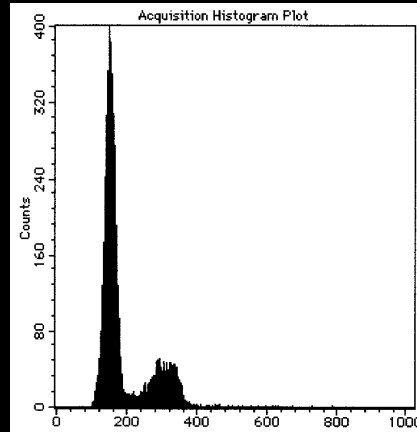
Dm Ttm50   NDAPEV----APNAPLLAKLFP-----QTSPEVDSNAEQERKKREEEEE-KENERSWKRMKLGFAI FGGSAVAAGFWAVYE---FGK
Dm Ttm2    -----TSTQILTKLFP-----QTSEESNDEESRERRKLEEEEEQKELERAFRRMKLGFGLFGIGSMLFSFWAIYF---YGR
Dm Ttm3    -----PKLRRIKNFYT-----YSVVLGSLFSIWMWAIYK---LGK
Hs Tim50   WRQRKM---AASAAVFSRLRSGRLR LGSRLCTRLATPPRRAPDQAAEIGSRGSTKAQGPOQQPGSEGPSYAKKVALWLAGLLGAGGTVSVVYI---FGN
Ce T21C9.1 IEAEKVLSSPPPAPAPTSSAIDELNSLKD SL-EKLESAASKSSSSSGSSDNDSDPGNAEEIEARRKRMERNTRIGAYVL FGGSIIGFISFCFY---YGR
Sc Tim50   -KPKSILTDDML-----FKAGVDVDEKG----QGKNEETS GEGGEDKNEPSSKSEKSRKRQTSTDIKREKYANWFYTFSL SALTGTATYARDWEP

Dm Ttm50   PEVDPNGQPIEDFTHKPLVQQYLQRMWKS IHYYQRMIEPSRAKLLPDPLKPPYVQPRYTLVLEMKDVLVHPDWTYQTGWRFKKRPGVDHFLAECA-KD
Dm Ttm2    PSLDEHGNEVIDEF SCLPQMQLMWR TWKSNVRFQRFKEPSRKKLLPDPLQPPYVQPPYTLVLEIKDVLVHPDWTYETGWRFKKRPGVDVFLKECA-KY
Dm Ttm3    PEEDHRG-PIEDFSQLPWFRQYIMRMWHTLQYYEKMEEPQMARLLPNVWPPPYIQPPYSLVLEIKDVLVHPDWTYQTGWRFKKRPGVDYFLQCCS-RN
Hs Tim50   NPVDENGAKIPDEFDNDPILVQQLRRTYKYFKDYRQMIIEPTSPCLLPDPLQEPYYPYTLVLEL TGVL LHP EWSLATGWRFKKRPGIETLFQQLA-PL
Ce T21C9.1 AQRDEFGNVISDEFSG--SFLAPFYRIANSFKLWRDYVVEPAREQLLPDPLPAPYLQPKYTIIVIELKNILVHPEWYKTYGRFLKRPALDYFLDVIGYPN
Sc Tim50   QESEELKKDIDNGYTL SLMYKRFKARFNSMFTYFQ----EPPFPDLLPPPPPPY-QRPLTLVITLEDFLVHSEWSQKHGWRTAKRPGADYFLGYLS-QY

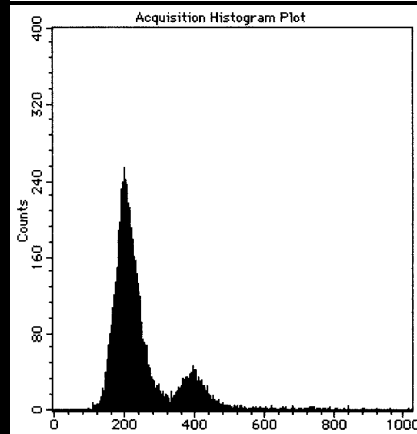
Dm Ttm50   FEIVVFTAEEQGMTVFPILDALDP-NGYIMYRLVRDATHFVDGHHVKNL DNLNRDLKVVVVDWDANATKMHPDNTFGLARWHGNDDDGQLLDLIAFLKII
Dm Ttm2    FEIVVYTAEQGVTFPLVDALDP-NGCIMYRLVRDSTHF DGGHHVKNL DNLNRDLKRVVVDWDRNSTKFHPSNSFSIPRWSGNNDTTLFELTSFLSVL
Dm Ttm3    FEIVIYTS EQMTAFPLLDALDP-YGYIKYRLVRGATDLVEGQHTKNLDYLNDRDL SRVIVVDCDPYTTPLHPDNSLVLTKWLGNDDDVQLFDLTAFLQLI
Hs Tim50   YEIVIFTSETGMTAFPLIDSVD P-HGFISYRLFRDATRYMDGHHVKDISCLNRDPARVVVDCKKEAFRLQPYNGVALRPWDGNSDDRVL L DLSAFLKTI
Ce T21C9.1 FEVVIYSSSEMMTAAPVVSDFDP-QQRIMYK LFRDCTKYMNGHHVKDLSKLNDRDLSKVIIYIDF DAKSQGLNPENMLRVPEWKGNMDDTSLVDLAE LKTI
Sc Tim50   YEIVL FSSNYMYSKIAEKLDP IHAFVSYNL FKEHCYKDGVHIKDL SKLNDRDLSKVIIIDTPNSYKLPENAIPEPWNGEADDK-LVRLIPFLEYL

Dm Ttm50   AQNVDDVREVLHYYRQFDDPINQFRENQRKLA EQ-----MLEAERIEQSKTKPM-----VKQWSRNILGR
Dm Ttm2    GTSEIDDVREVLQYYNQFSDSLSQFRENQRKLGEL-----MHAEEVEKTSKSRPV-----VKNWTRGFINH
Dm Ttm3    AEHQVNDVREVLRYRQFEDPMEQFKDNQRRLQE Q-----SQESIQNLP TSER-----QWNLTLLGRSLRGSSIK
Hs Tim50   ALNGVEDVRTVLEHYALEDDPLAAFKQRQSRL EQE-----EQQLAELSKSNK-----QNLFLGSLTSRLWPRSKQP
Ce T21C9.1 HLSDAEDVRPMLQYYSQYDDPAKEFRRAVYLSQ Q-----EEQKKQPPDSSM-----LKRYSGRLFGSRRHVNA
Sc Tim50   ATQQTkdvrPILNSFEDKKNLAE EFDHRVKKLKD K--( 47 aa )--IEEKEKIRIQEQMGQTFTLKDYVEGNLPSPEEQMKIQLE
```

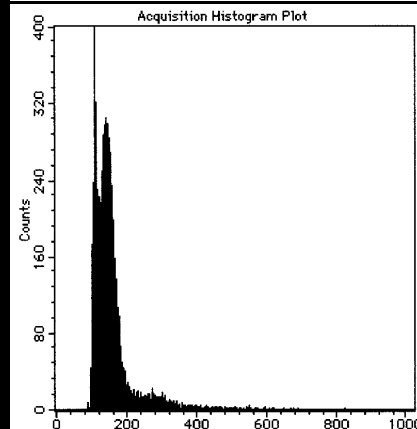
G1 arrest in Δgcc disruptant



15D (WT)

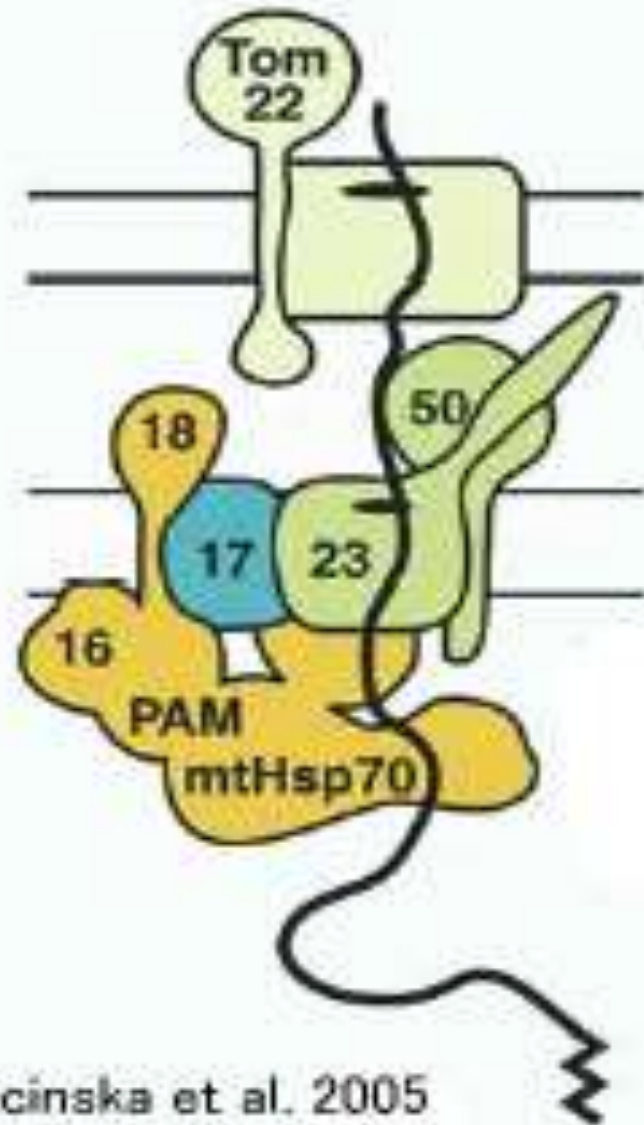


$\Delta gcc-a::URA$
 $yCPG22-GCC$
+ galactose
(on)



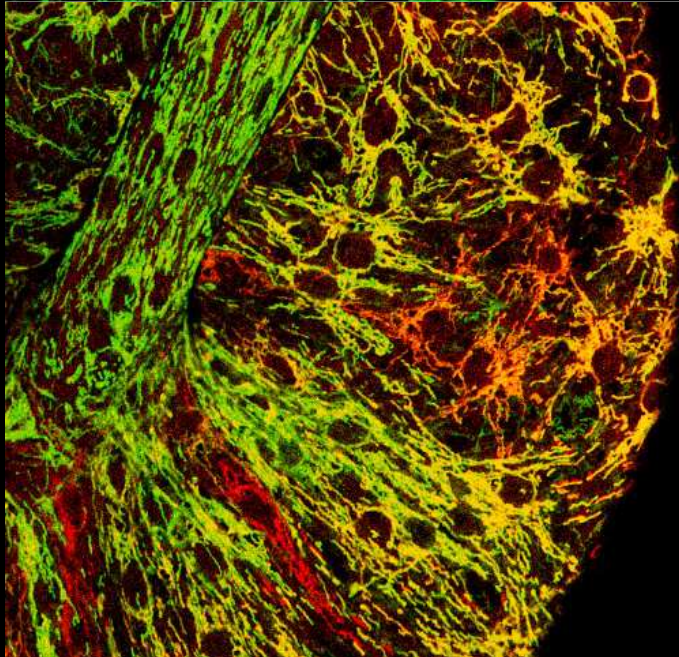
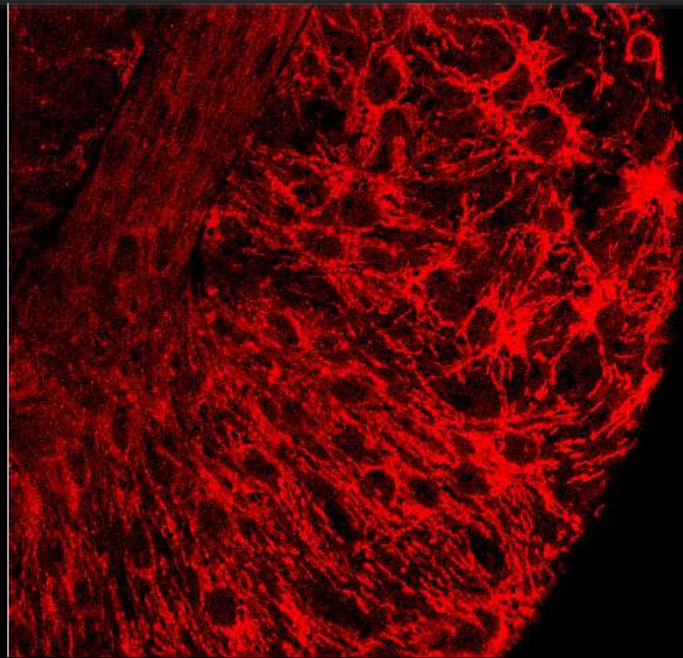
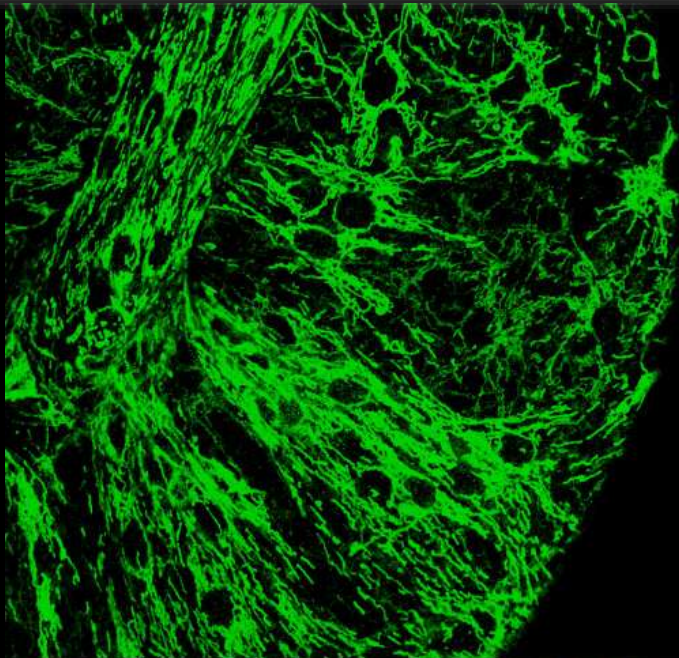
$\Delta gcc-a::URA$
 $yCPG22-GCC$
+ glucose
(off)

The yeast mitochondrial protein translocator complex



Chacinska et al. 2005

Mitochondrial localization of Ttm50

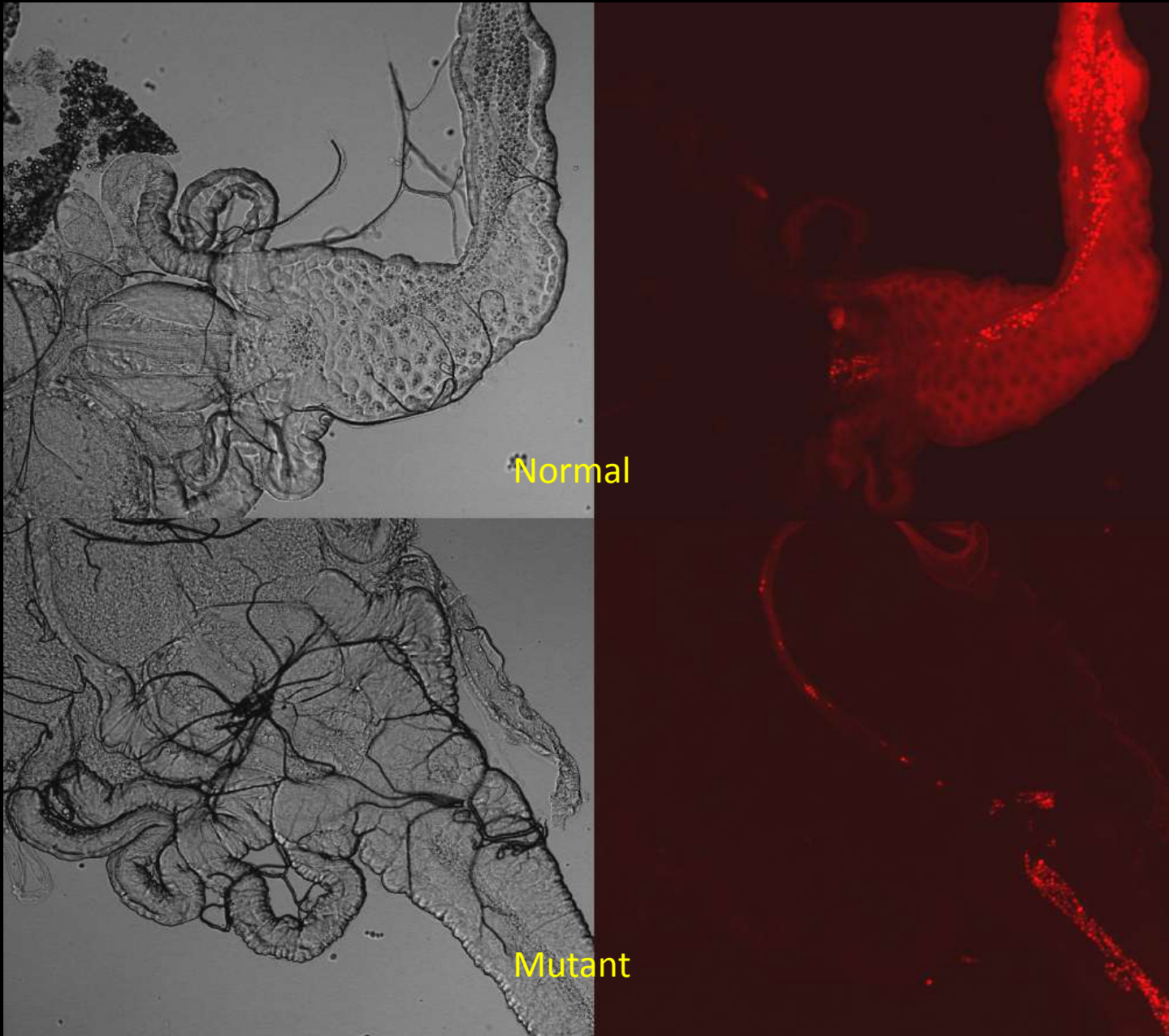


Stain:

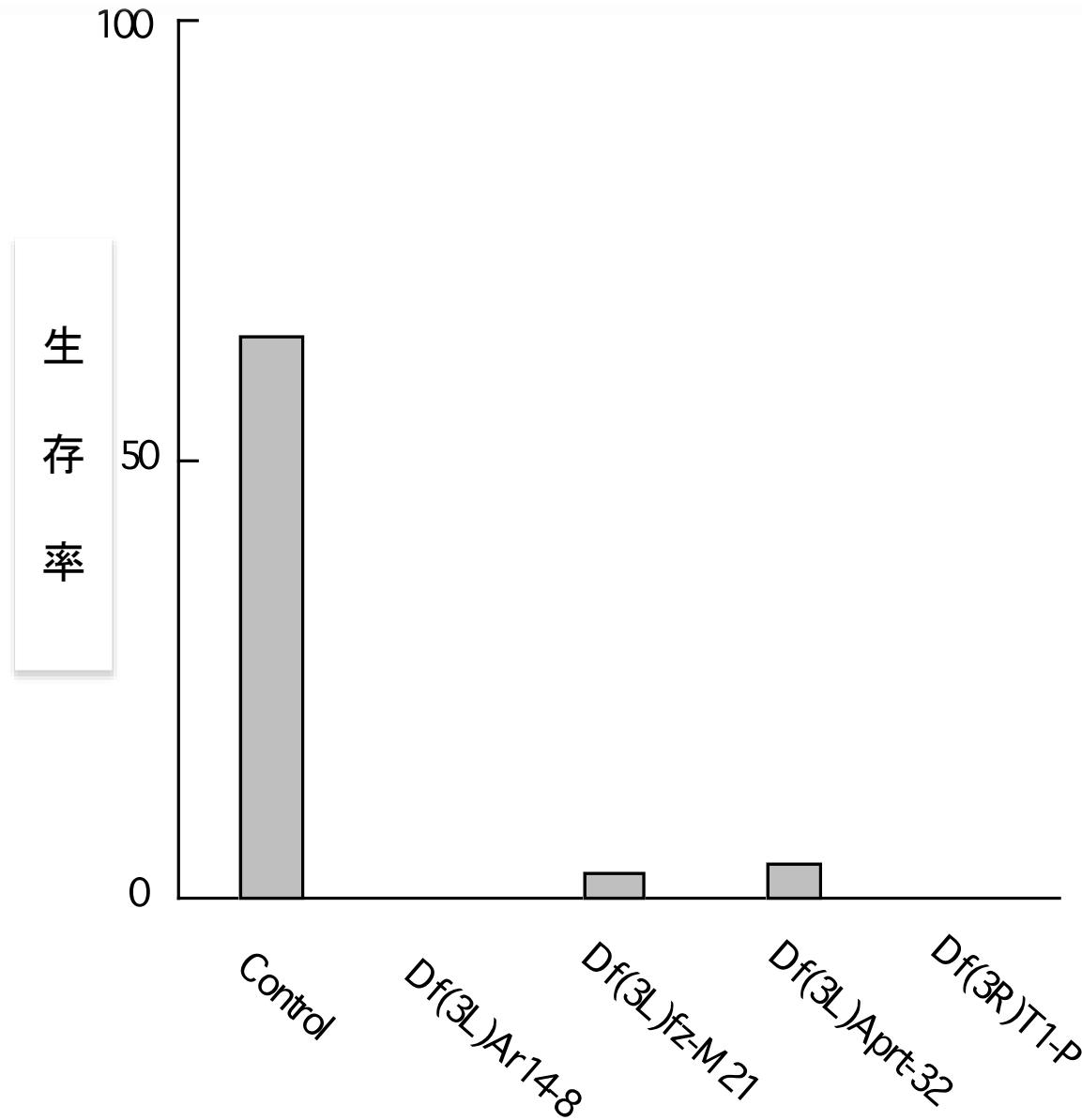
Ttm50-HA

Mitotracker red

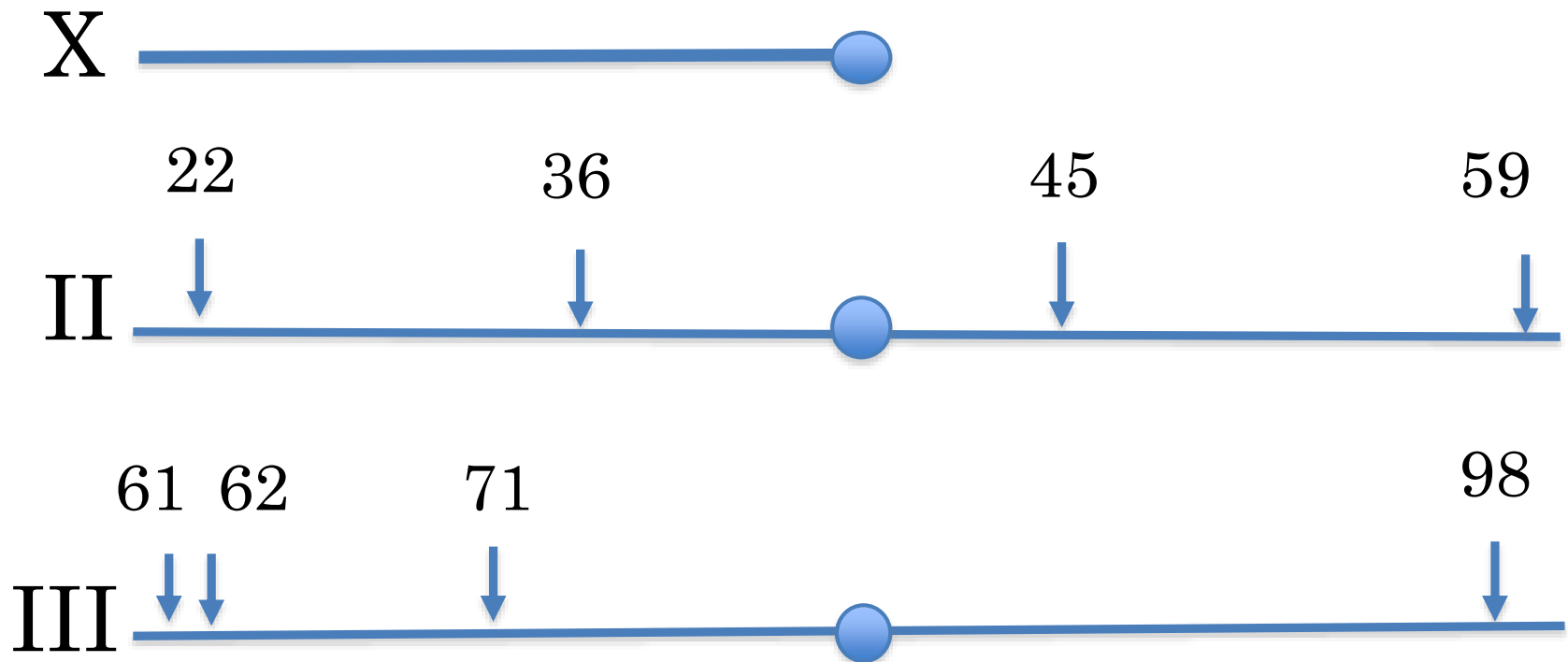
Mitochondrial membrane potential (MMP) in the anterior midgut was reduced in *ttm50* null mutants



3rd chromosomal enhancers of *ttn50*^{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

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

chronologically inappropriate morphogenesis (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

井上喜博、杉山 伸、八木克将、安達 卓、劉 美愛、津田玲生、
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、壺岐一也、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、
苗村季美子、佃 亮、劉 自広、原 直史、神戸中智章、
水野智亮、水野友彦、太田宜秀、小山裕明、岡田駿吾、
榎木亜美、柴田哲志、李 虹、木村優子、漆山誠一、浜中 毅