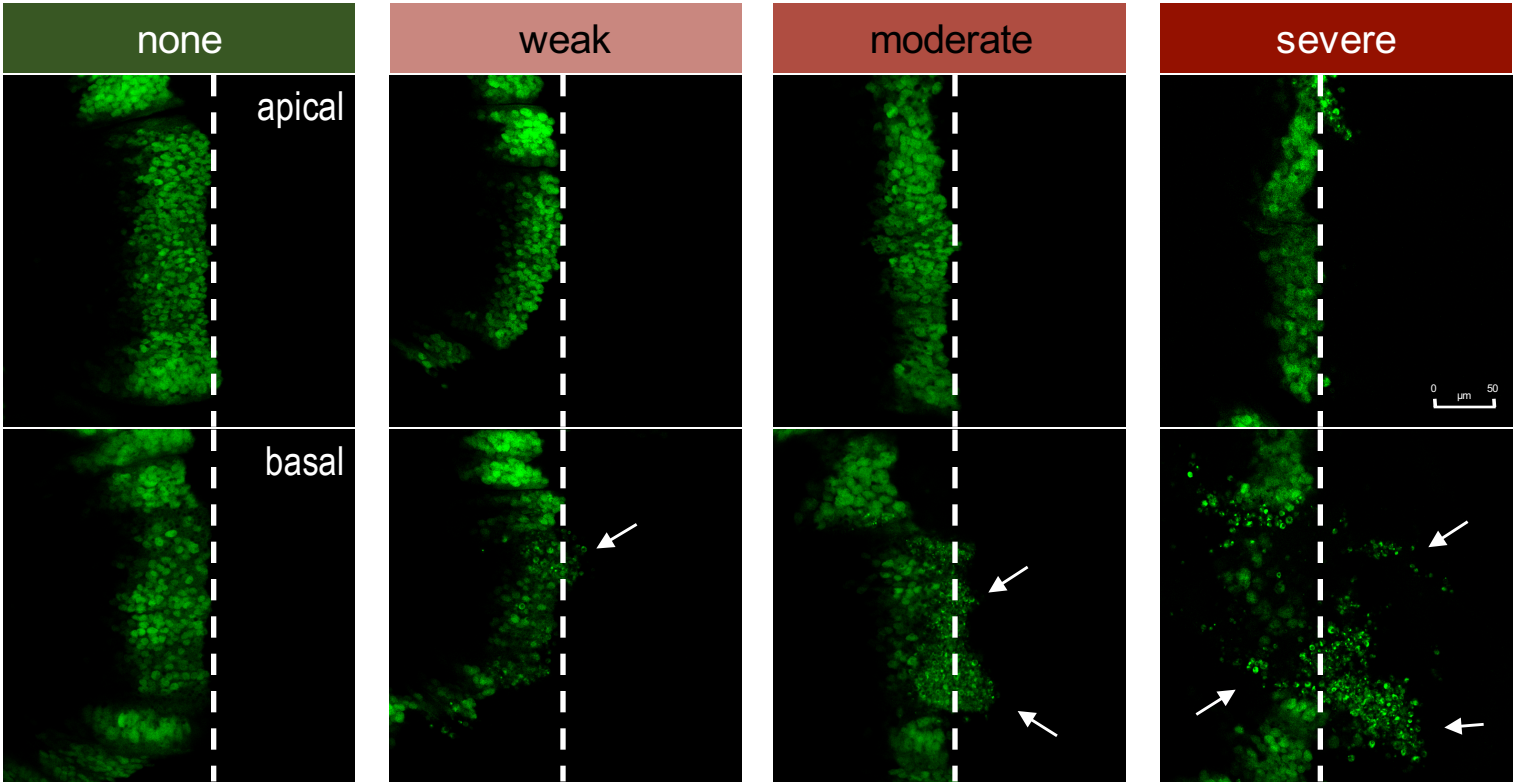
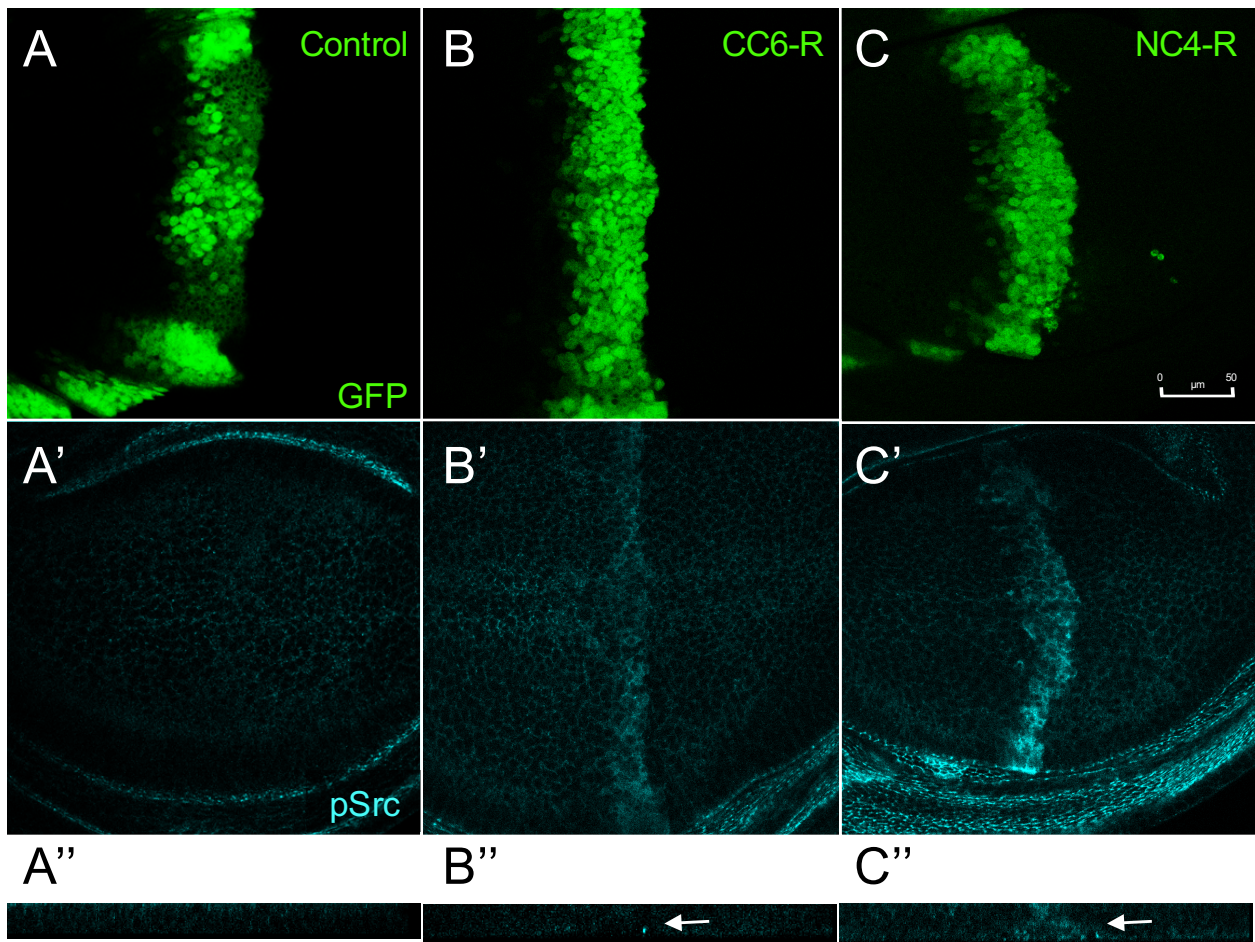


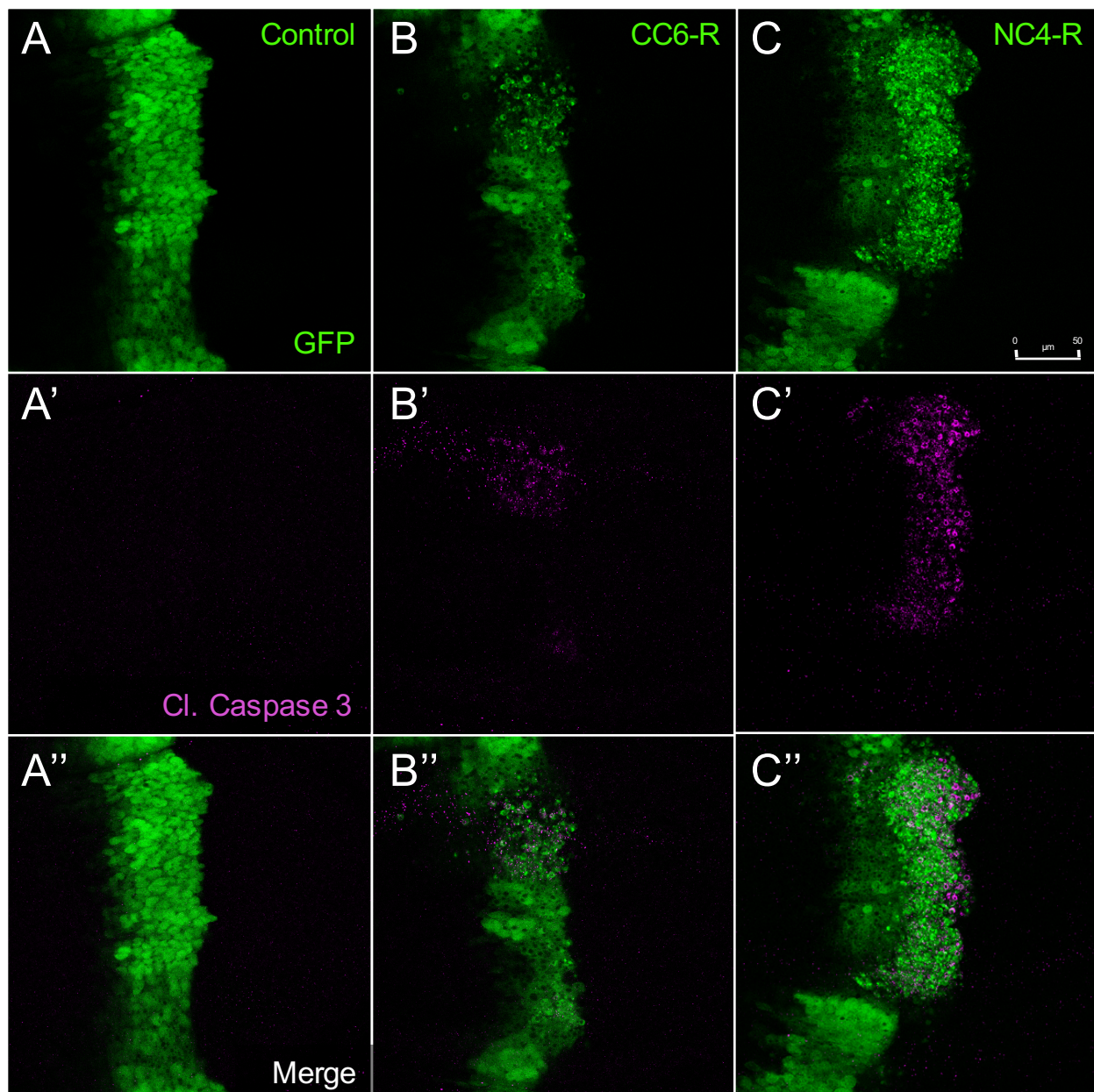
Levinson et al, Supplemental Figure 1



Levinson et al, Supplemental Figure 2



Levinson et al, Supplemental Figure 3



Levinson et al, Supplemental Figure 4



## CCDC6-RET

<i>Drosophila</i> Kinase	Human Ortholog	% Pupariation
Control	-	21%
bsk	JNK	94%
wnk	WNK1	79%
slik	STK10	73%
grp	CHEK1	62%
btk29a	TEC	53%
gek	CDC42BPA	50%

## NCOA4-RET

<i>Drosophila</i> Kinase	Human Ortholog	% Pupariation
Control	-	0%
bsk	JNK	37%
hppy	MAP4K3	23%
sqa	MYLK3	19%
src42A	FRK	19%
wee	WEE1	18%
for	PRKG1	17%
hpo	STK3	15%
takl2	MAP3K7	15%
pvr	VEGFR	11%
shark	SYK	5%
btk29A	TEC	3%

## CCDC6-RET

Drug	% Pupariation	SEM
Control	4%	2%
ponatinib	51%	7%
AD81	38%	2%
regorafenib	17%	5%
gefitinib	17%	4%
vandetinib	12%	1%

## NCOA4-RET

Drug	% Pupariation	SEM
Control	0%	0%
ponatinib	20%	6%
AD81	53%	10%
regorafenib	11%	9%
sorafenib	24%	2%
cabozantinib	10%	2%

## Drug effects on wing invasion

CCDC6-RET					
	<b>none</b>	<b>weak</b>	<b>moderate</b>	<b>severe</b>	<b>p-value</b>
Ctrl	0	10	5	0	
vand.	9	4	0	0	1.20E-04
AD81	13	2	0	0	1.80E-06

NCOA4-RET					
	<b>none</b>	<b>weak</b>	<b>moderate</b>	<b>severe</b>	<b>p-value</b>
Ctrl	0	0	23	2	
vand.	0	0	10	0	1
AD81	11	15	0	0	4.00E-15

#	Drug Name	Conc. (uM)	% Pupariation: CCDC6-RET	P value (Mann Whitney)	% Pupariation: NCOA4-RET	P value (Mann Whitney)
	0.1% DMSO		4%		0%	
1	abiraterone acetate	50	1%		0%	
2	Afatinib	200	2%		0%	
3	anastrozole	100	4%		0%	
4	Axitinib	150	0%		0%	
5	bendamustine HCL	200	0%		0%	
6	bortezomib	1	2%		0%	
7	Bosutinib	200	2%		0%	
8	busulflex	200	0%		3%	
9	cabazitaxel	100	4%		0%	
10	Cabozantinib	200	1%		10%	0.0001
11	Capecitabine (xeloda)	200	0%		0%	
12	Carfilzomib	100	0%		0%	
13	Cinacalcet	200	0%		0%	
14	clofarabine	100	0%		0%	
15	crizotinib	50	6%		0%	
16	Dabrafenib	200	1%		0%	
17	dasatinib	10	0%		0%	
18	docetaxel	100	1%		0%	
19	doxorubicin	200	0%		0%	
20	ellence	200	0%		0%	
21	Enzalutamide	100	0%		0%	
22	erlotinib	25	0%		0%	
23	Everolimus	1	0%		0%	
24	exemestane (aromasin)	200	5%		0%	
25	flutamide	200	0%		0%	
26	fulvestrant	200	0%		0%	
27	gefitinib	10	17%	0.0381	0%	
28	gemcitabine	1	0%		0%	
29	imatinib	200	0%		0%	
30	Irinotecan (camptosar)	200	1%		0%	
31	lapatinib	200	0%		0%	
32	Lenalidomide	200	0%		0%	
33	Letrozole	200	0%		0%	
34	nelarabine	200	1%		0%	
35	nilotinib	50	1%		0%	
36	pamidronate	150	3%		0%	
37	Pazopanib	200	0%		0%	
38	pemetrexed DiNA	1	0%		0%	
39	Pomalidomide	200	0%		0%	
40	Ponatinib	200	51%	0.0095	20%	0.0001
41	Rapamycin (sirolimus)	1	0%		0%	
42	Regorafenib	10	17%	0.0381	11%	0.0082
43	sorafenib	200	2%		24%	0.0001
44	Sunitinib malate	100	4%		0%	
45	Tamoxifen (nolvadex)	200	4%		0%	
46	temsirolimus	1	0%		0%	
47	topotecan HCL	1	0%		0%	
48	Trametinib	1	3%		0%	
49	vandetanib	100	12%	0.0238	0%	
50	vemurafenib	200	2%		0%	
51	Vismodegib	1	5%		0%	
52	vorinostat	10	6%		0%	
53	zoledronic acid	14	2%		0%	
54	ibrutinib	100	3%		0%	
55	AD81	100	38%	0.0095	53%	0.0001



# NCOA4-RET Genetic + Drug combinations

% Pupariation

Drug	Conc. (uM)	Kinome LOF Allele											
		Ctrl	bsk	for	btk29A	wee	sqa	shark	hpo	hppy	src42A	takl1	pvr
DMSO	0.20%	0%	7%	3%	0%	0%	0%	0%	0%	2%	0%	0%	0%
ponat.	200	12%	11%	0%	0%	26%	41%	0%	0%	11%	0%	32%	26%
vand.	100	0%	9%	10%	2%	3%	10%	6%	0%	11%	4%	11%	17%
AD81	100	29%	50%	84%	95%	100%	63%	120%	3%	63%	41%	90%	30%
gef.	10	0%	0%	0%	0%	10%	6%	0%	0%	0%	0%	0%	0%
cabo.	200	0%	10%	0%	0%	28%	3%	11%	0%	16%	0%	27%	0%
soraf.	200	0%	63%	61%	30%	111%	100%	79%	53%	69%	34%	67%	25%
rego.	100	10%	81%	47%	39%	68%	95%	-	40%	78%	34%	70%	0%

# CCDC6-RET Genetic + Drug combinations

% Eclosure

Drug	Conc. (uM)	Kinome LOF Allele						
		Ctrl	bsk	btk29A	gek	grp	wnk	slik
DMSO	0.20%	0%	15%	0%	0%	0%	5%	0%
ponat.	200	0%	33%	0%	0%	0%	0%	0%
vand.	100	2%	43%	4%	0%	0%	0%	0%
AD81	100	0%	64%	0%	0%	0%	0%	0%
gef.	10	0%	0%	0%	0%	0%	0%	0%
cabo.	200	0%	36%	6%	0%	0%	0%	0%
soraf.	200	0%	50%	0%	0%	5%	0%	0%
rego.	100	0%	60%	0%	0%	0%	0%	0%

# NCOA4-RET Drug+ Drug combinations

% Pupariation

		Control	ibrutinib (btk29A)	AZD1775 (wee)	HA-100 (sqa)
	Conc. (uM)		50	50	50
0.2% DMSO		0%	0%	0%	0%
AD81	100	40%	78%	107%	113%
sorafenib	200	13%	30%	38%	12%
regorafenib	100	18%	21%	25%	41%

p value (Mann-Whitney)

		Control	ibrutinib (btk29A)	AZD1775 (wee)	HA-100 (sqa)
	Conc. (uM)		50	50	50
0.2% DMSO					
AD81	100		0.0286	0.0216	0.0095
sorafenib	200		0.0524	0.0396	0.5818
regorafenib	100		0.8575	0.3938	0.7859