



# Cyclin G, Transcriptional Control and Developmental Stability

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# Cyclin G, Transcriptional Control and Developmental Stability

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5-10 octobre 2014

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**Collaborations :** Juliette Pouch<sup>2</sup>, Stéphane Le Crom<sup>2</sup>.

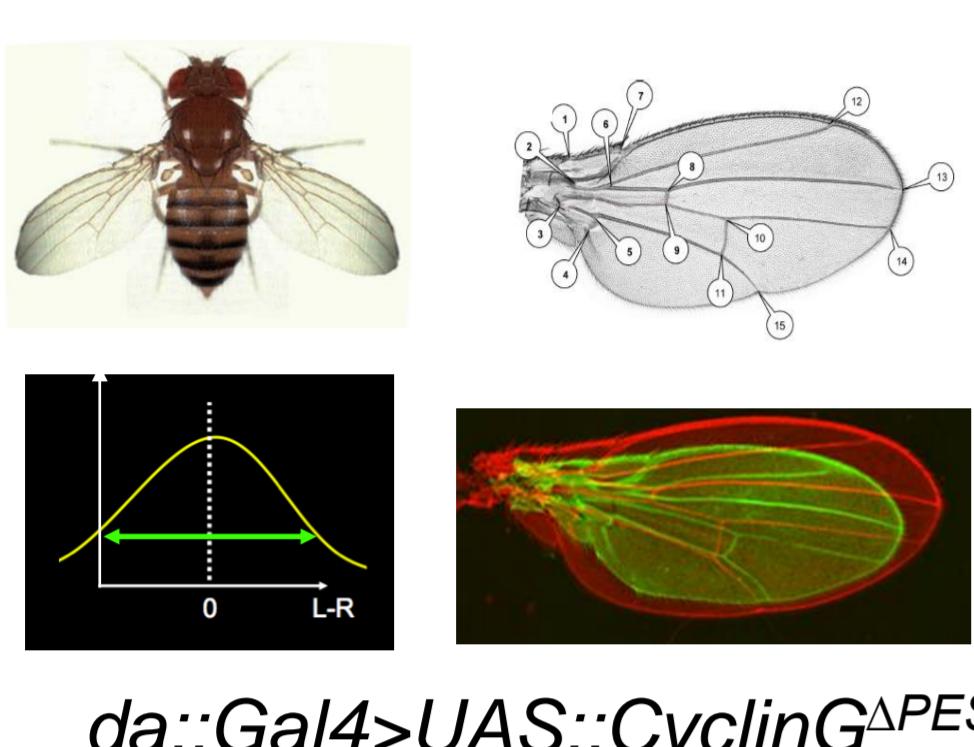
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A central challenge in developmental and evolutionary biology is to understand developmental stability, the process that buffers developmental noise. We recently reported that an individual gene, *Cyclin G* (*CycG*), encoding a cyclin involved in the regulation of transcription and in the cell cycle, plays a central role in developmental stability in *Drosophila* (Debat et al., 2011; Debat and Peronnet, 2013). Indeed, overexpression of *CycG* induces an unprecedented increase in developmental noise. Using *CycG* overexpression as a tool, we aim to investigate the role of *CycG* in transcription and at highlighting gene networks underlying developmental stability. Our data show that Cyclin G interacts with Polycomb and Trithorax factors as well as with components of the spliceosome. Furthermore, several mutations of both Polycomb/Trithorax members and components of the spliceosome increase *CycG*-induced developmental noise. To understand more precisely the role of Cyclin G in transcription and in developmental stability control, we develop two projects : The first one, identify transcriptional targets of cyclin G by RNA-seq and CHIP-seq. the second one, the Cyclin G involvement in alternative splicing.

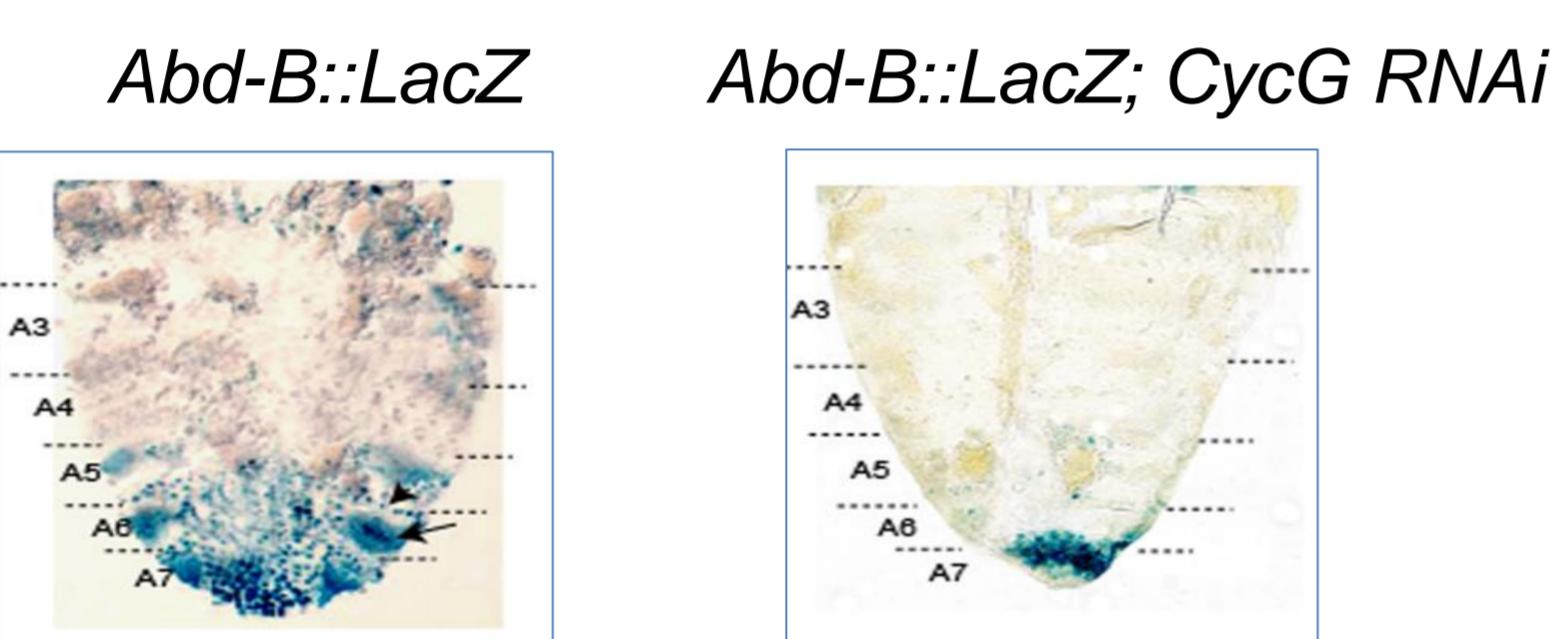
## I - Cyclin G



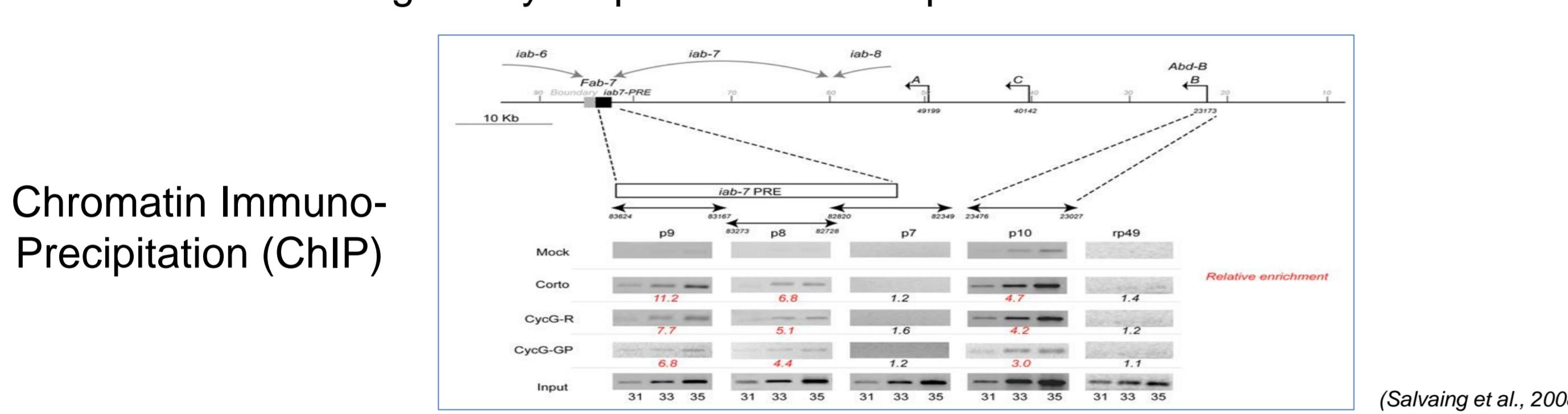
- At low environmental and genetic variations, fluctuating asymmetry is a measure of developmental stability.
- The difference between left and right wing sizes in *da::Gal4>UAS::CyclinG<sup>ΔPEST</sup>* isogenic siblings follows a normal curve centered on zero: this population presents high fluctuating asymmetry (FA).

## II - Cyclin G regulates *Abd-B* expression

- ✓ Expression of *Abd-B* in the abdominal epithelium of pupae

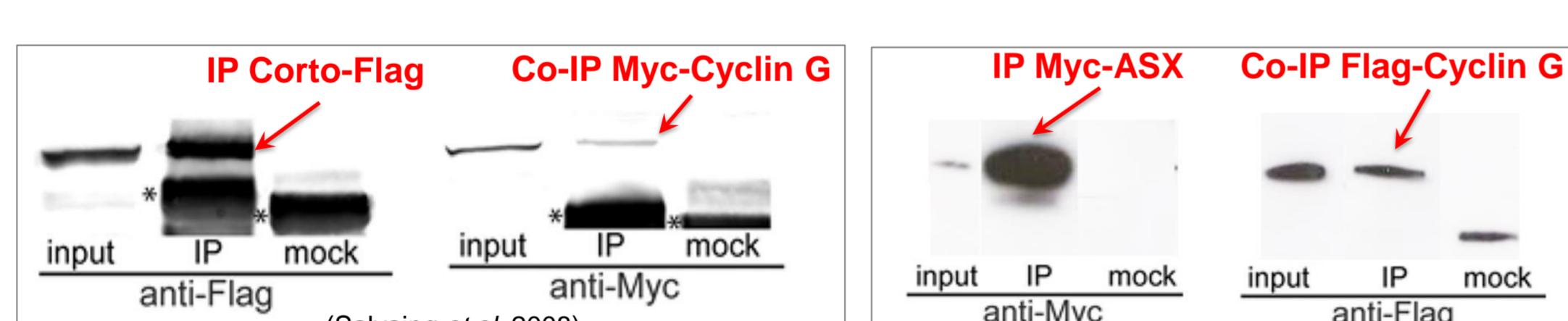


- ✓ Cyclin G binds the cis-regulatory sequences and the promoter of *Abd-B*

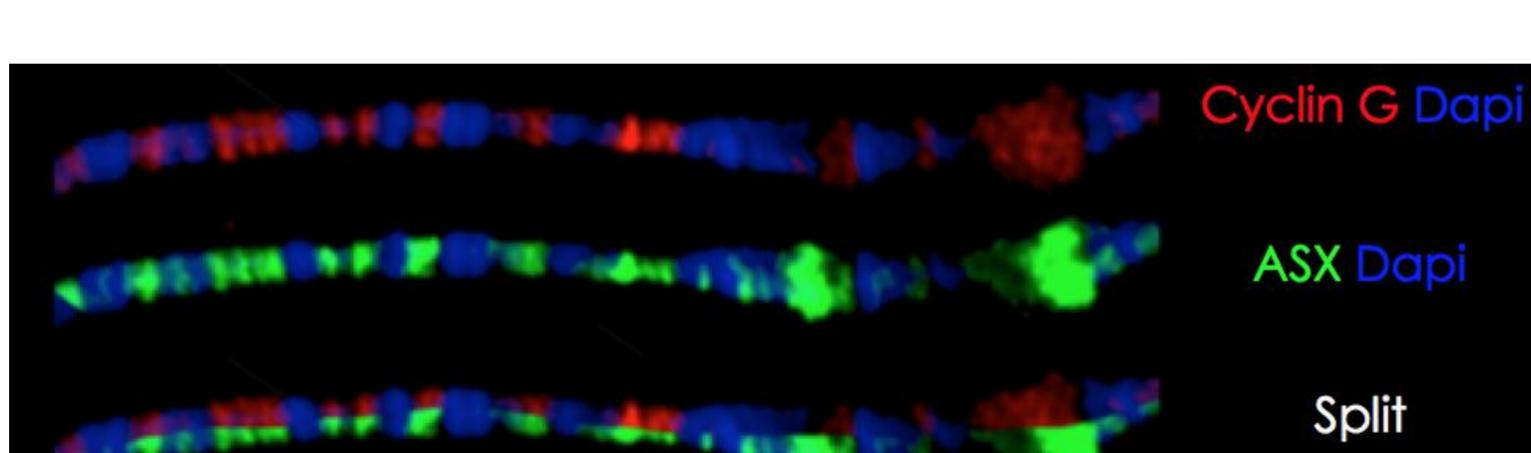


## III - Cyclin G interacts with Polycomb and Trithorax factors

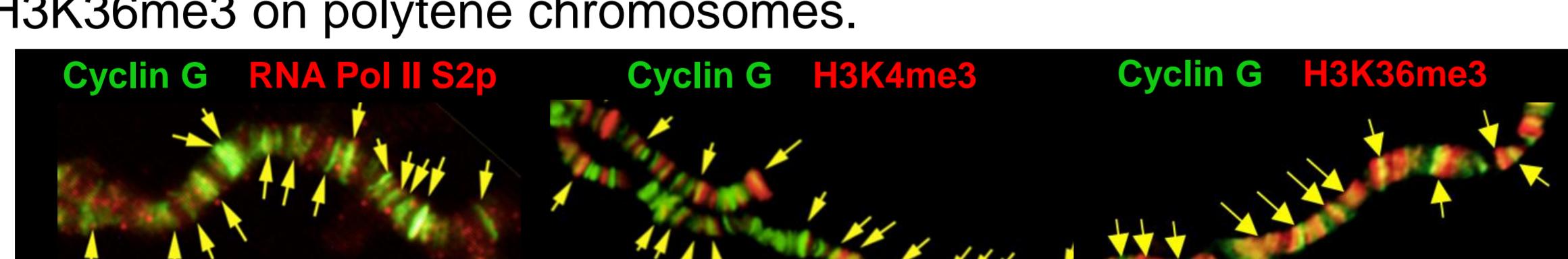
- ✓ Cyclin G directly interacts with two chromatin regulators of the Enhancers of Trithorax and Polycomb family (Corto, ASX).



- ✓ Cyclin G binds polytene chromosomes where it extensively co-localizes with ASX



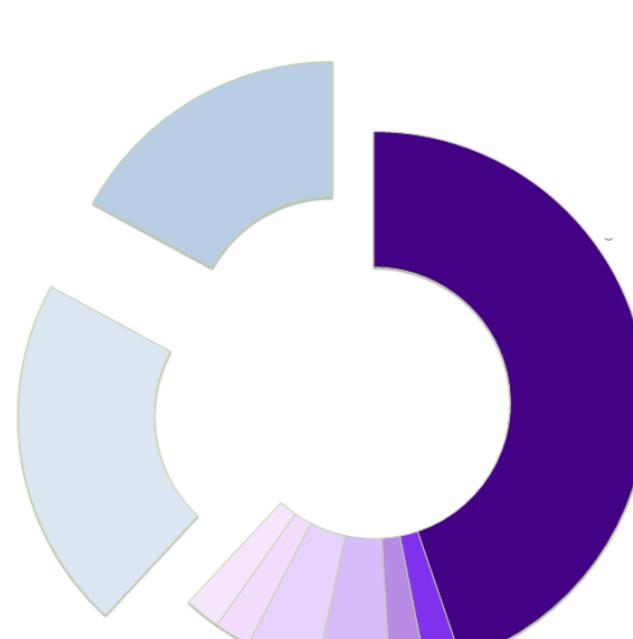
- ✓ Cyclin G co-localizes at many sites with RNA Pol II, and with the active marks H3K4me3 and H3K36me3 on polytene chromosomes.



CyclinG might be involved in transcriptional elongation

## IV - Cyclin G interacts with components of the spliceosome

Direct partners of Cyclin G identified by pull-down and mass spectrometry  
(*Drosophila* Protein Interaction Map; [interfly.med.harvard.edu](http://interfly.med.harvard.edu))



- 39 direct partners
- mRNA splicing
  - mRNA processing
  - rRNA processing
  - oskar mRNA localization
  - Gene silencing by miRNA
  - RNA interference
  - Ribonucleoprotein complex assembly

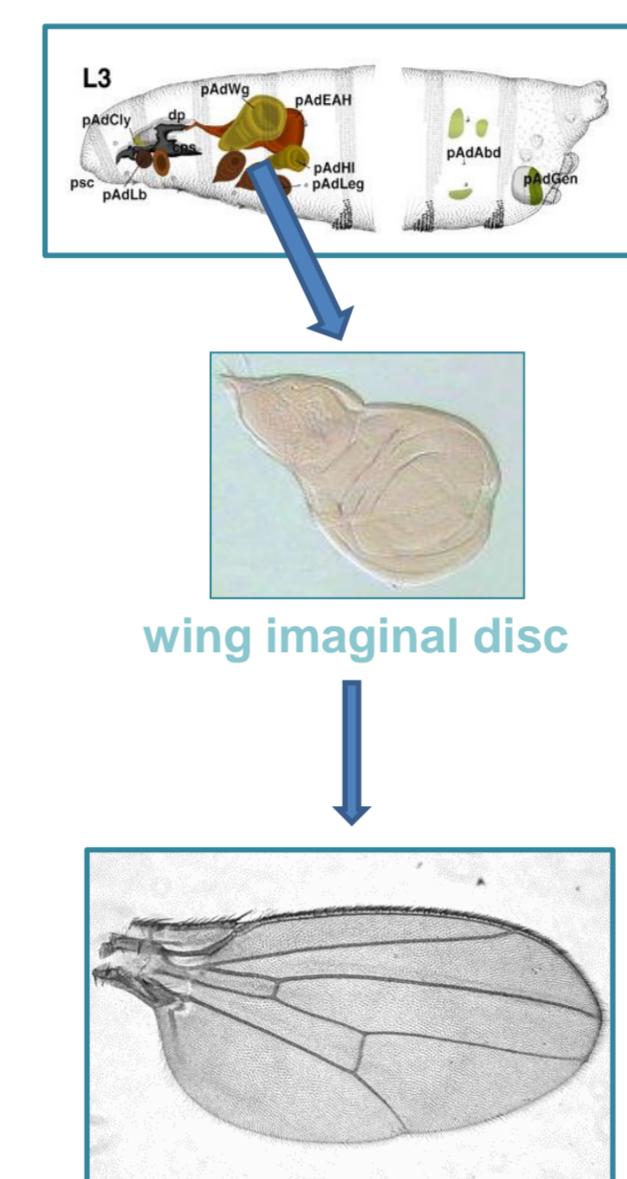
14 of these partners are involved in mRNA splicing, suggesting that Cyclin G might interact with the spliceosome.

Is the role of cyclin G in developmental stability related to its role in transcriptional regulation?

Is developmental noise resulting from global disruption of mRNA splicing via CyclinG?

## V - Analysis of *Cyclin G* transcriptional targets (RNA-Seq)

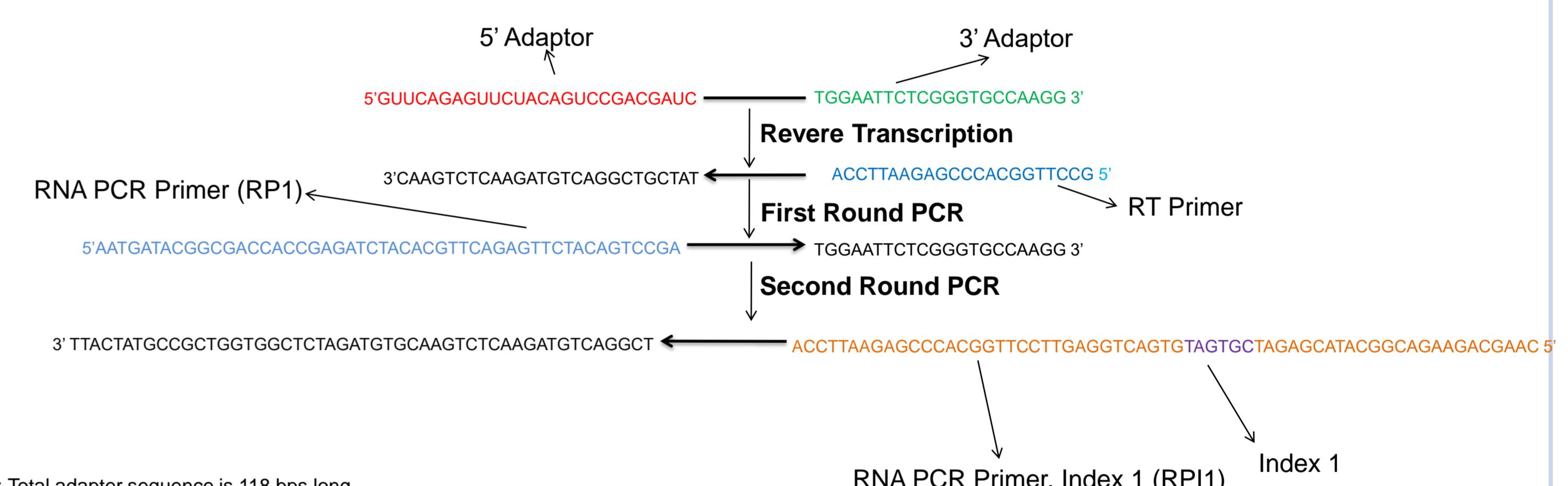
### RNA-seq of wing imaginal discs in which Cyclin G is deregulated



	sd::Gal4>UAS::CyclinG <sup>ΔPEST</sup>	Cyclin G gain of function	X 2
driver scalled	sd::Gal4>wnv	control	X 2
sd::Gal4>RNAiCycG3	RNAi CycG	X 2	
da ::Gal4>UAS::CyclinG <sup>ΔPEST</sup>	Cyclin G gain of function	X 3	
da::Gal4>wnv	control	X 3	

Expression driver	ENS genomic plateforme (S. Le Crom)
sd Gal4	sequencer : Illumina HiSeq 1000 experimental information : PolyA (RT) Single-End read Oriented length reads : 50pb

### Adaptor illustration for Truseq small RNA Sample Prep



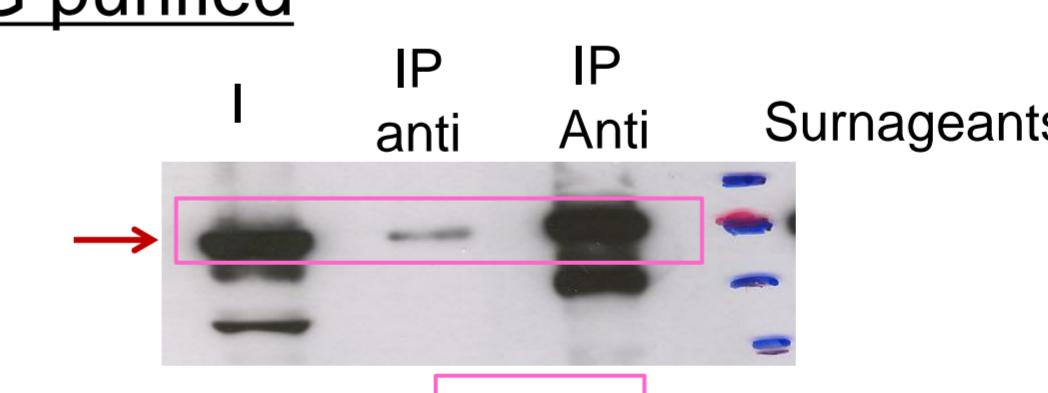
Notes : Total adapter sequence is 118 bps long

Sample name	Description	Reads	Filtered reads	Alignments	Unmap reads	Reads with multiple alignments	Reads with unique alignment	Reads used for expression
2013_033	sd::Gal4>RCG76-1	41874452	38087401	50706148	2371828	25237494	23096826	22373671
2013_034	sd::Gal4>RCG76-2	40533326	37679265	46907856	2625762	18457182	25824912	25067211
2013_035	sd::Gal4>RNAiCycG3-1	41860928	38169640	47506876	2796805	18674472	26035599	25185942
2013_036	sd::Gal4>RNAiCycG3-2	3831593	34388807	42047835	2564506	1518056	24165273	23387562
2013_037	sd::Gal4>wnv-1	41584205	37182626	46006156	2656414	17647060	25702682	24811053
2013_038	sd::Gal4>wnv-2	32087565	29456407	36187167	2120232	13461520	20605415	19965563
2013_039	da::RCG76-1	31215180	29044092	32118945	2318058	6149706	23651181	23046534
2013_040	da::RCG76-2	36051720	33712754	45308733	2116858	23191958	1999917	19308628
2013_041	da::RCG76-3	37581632	34042979	40807620	2531374	13529282	24746964	23965786
2013_032	da::Gal4>wnv-1	41841815	37569578	45248737	3210933	15358318	26679486	25837134
2013_0343	da::Gal4>wnv-2	45170847	40869061	43438167	5138212	34815256	33961840	24284741
2013_0344	da::Gal4>wnv-3	36799853	34016644	41249793	2498754	14466298		23536471

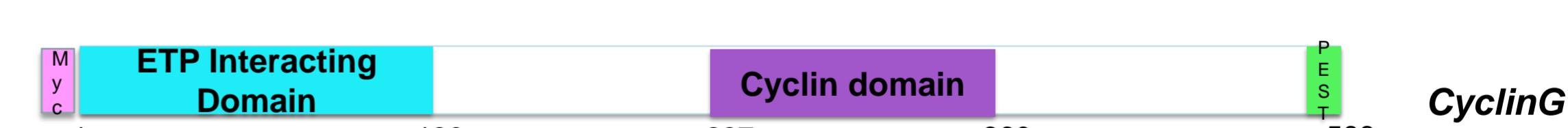
## VI - Analysis of *Cyclin G* transcriptional targets (CHIP-Seq)

- ✓ Determine genome-wide binding sites of Cyclin G (Chip-Seq)

### Anti-CycG purified



### Anti-Myc tag antibody- Chip Grade



- ✓ Identification of its direct transcriptional targets by correlation with RNA-seq

## projects

- ✓ Analyze alternative transcripts in *CycG* overexpressing flies.
- ✓ Test the role of genes belonging to the identified sub-network in developmental stability.

## References

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