

# Genetic Analysis of the Essential Transcription Factor Spn1 in *Saccharomyces cerevisiae*



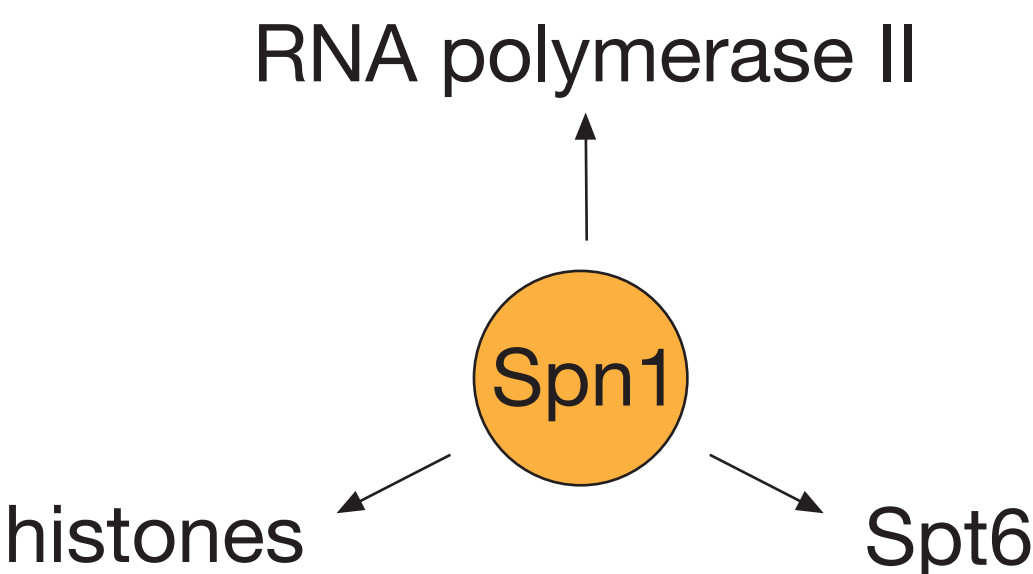
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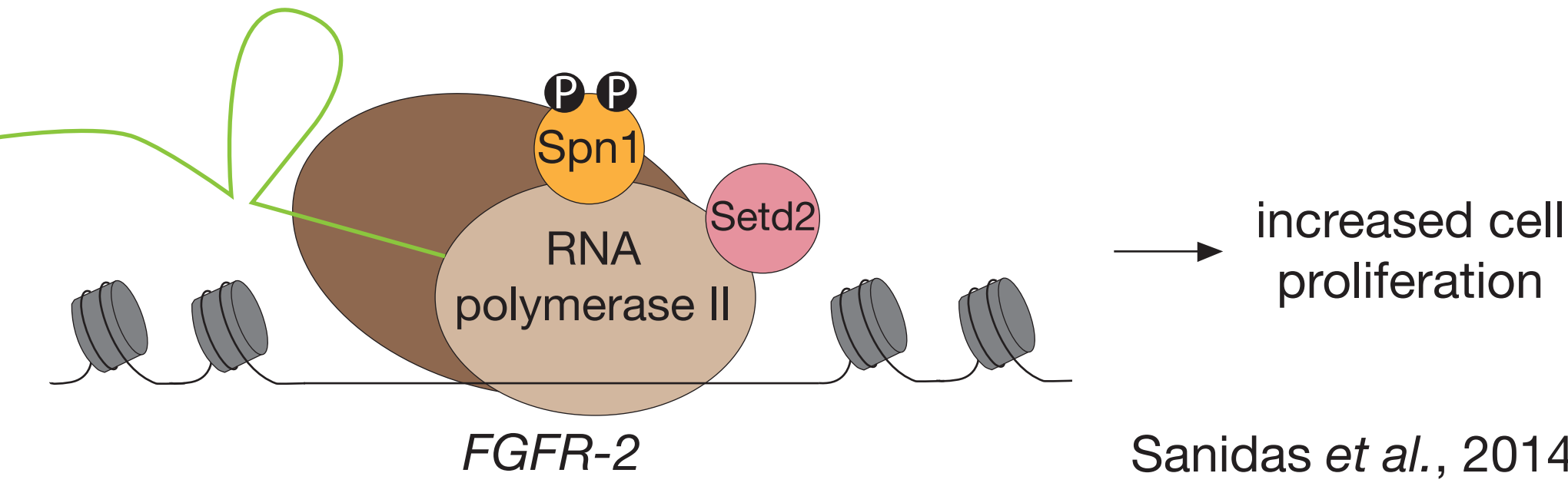
## Research Summary

- Our study focuses on the essential and conserved protein Spn1/lws1.
- We performed a screen to identify mutations that suppress the inviability of *spn1* null mutants (*spn1Δ*).
- We isolated 106 *spn1Δ* suppressors.
- We performed whole-genome sequencing of 31 of our mutants, and we identified candidate mutations in 19 genes that encode for proteins with functions in transcription and chromatin.
- Single deletions of *RTT109*, *SGF73*, *CHD1*, *SET2*, *RCO1*, and *EAf3* suppress *spn1Δ*.
- We are investigating how loss of the Rtt109 acetyltransferase suppresses inviability of *spn1Δ*.

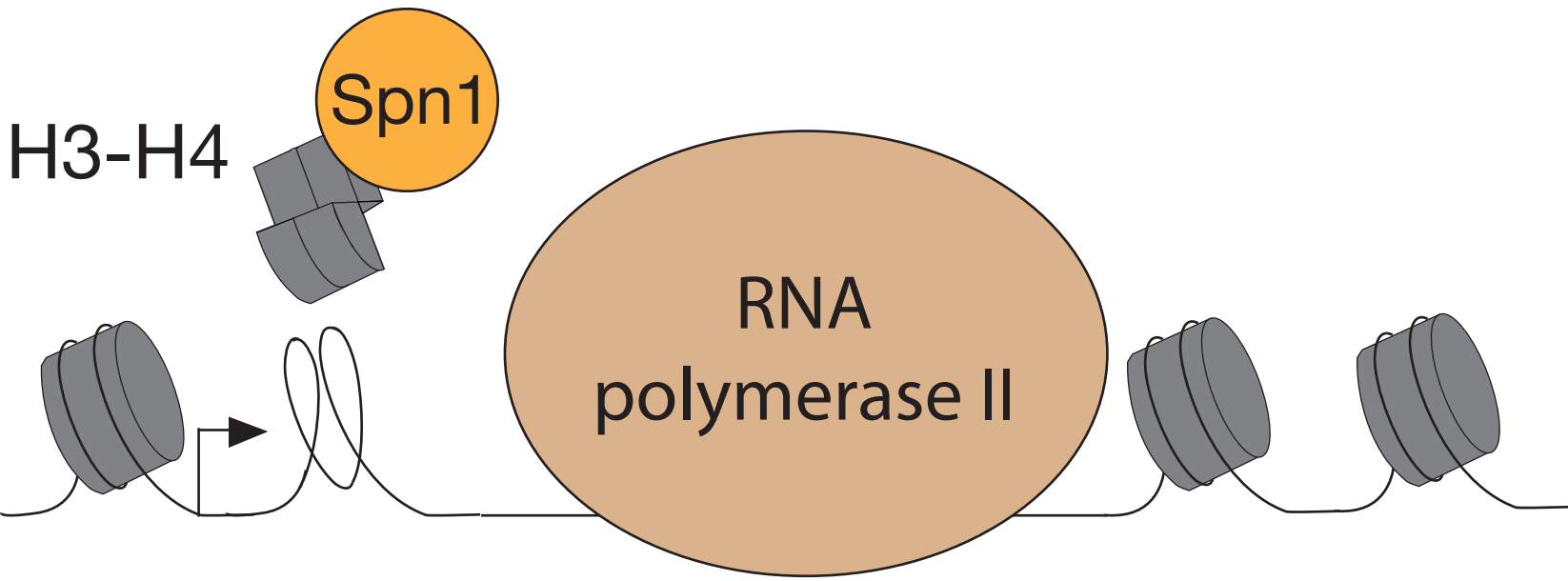
Spn1 is an essential and conserved protein that interacts with transcription factors.



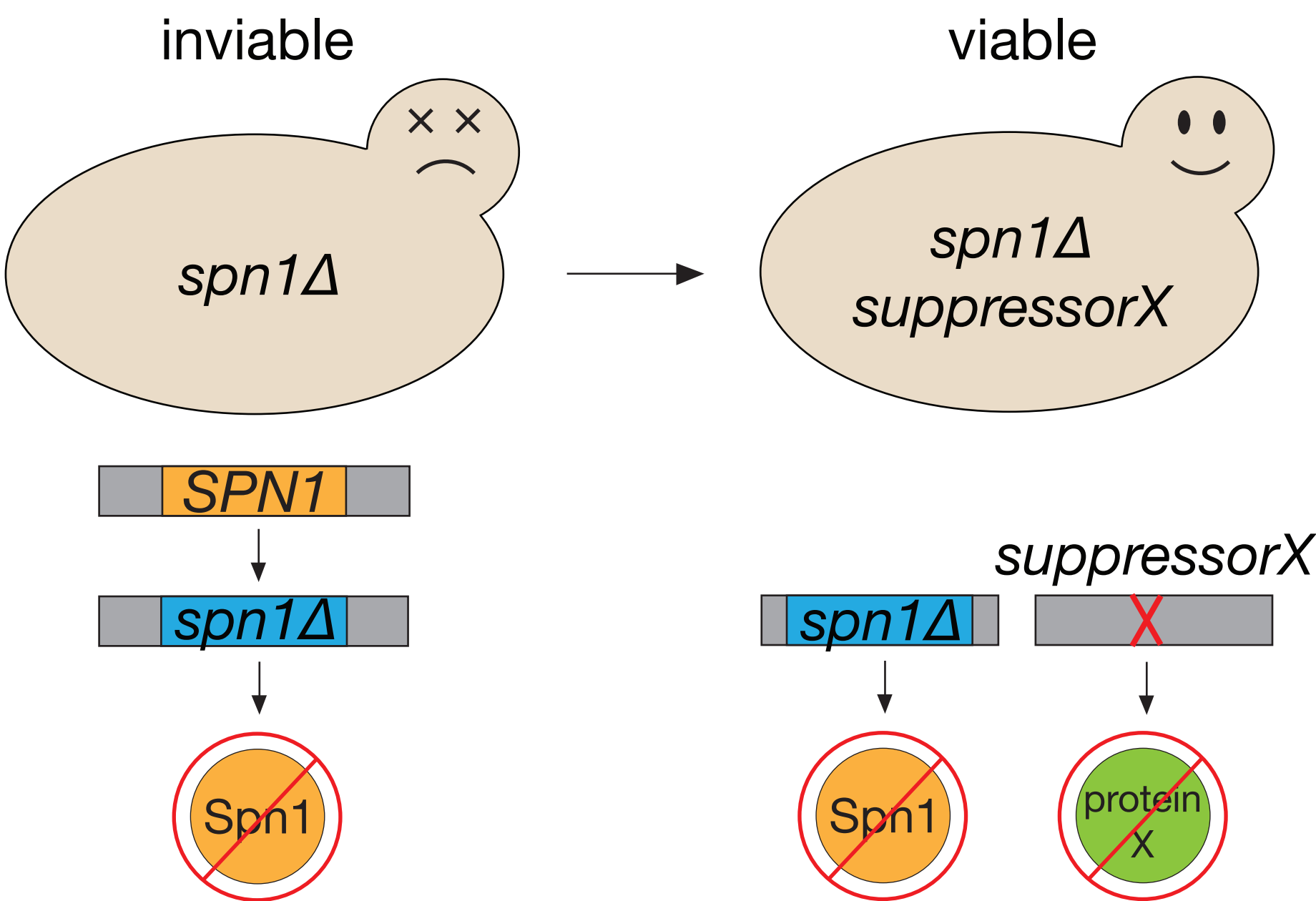
Spn1 has been associated with cancer.



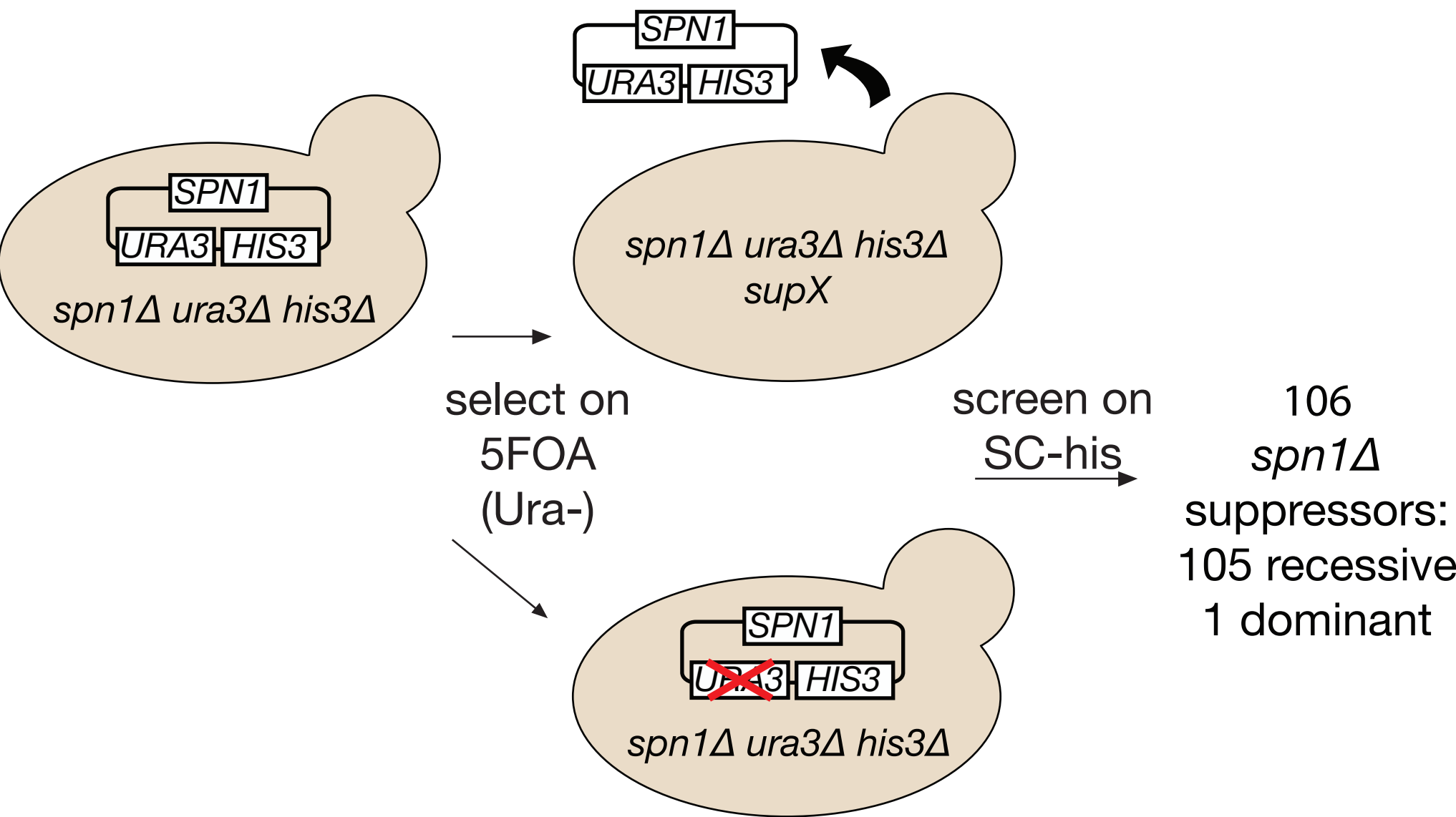
Spn1 has chromatin-associated functions.



Yeast cells that lack Spn1 (*spn1Δ*) are inviable.



We isolated 106 *spn1Δ* suppressors using a selection and screen.



We performed whole-genome sequencing of 31 *spn1Δ* suppressor strains.

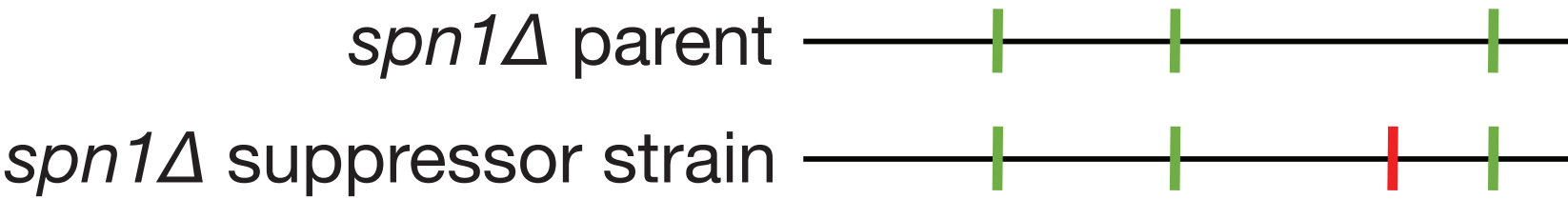


Table 1: 19 candidate genes encoding proteins with roles in transcription and chromatin in which mutations were found

Gene (complex)	Number of mutants found	Protein/complex function	Essential for viability?	Suppression by deletion or mutation
<b>CHD1</b>	11 (all <i>chd1</i> found with other suppressors)	chromatin remodeler	no	weak
<i>SNF2</i> (Swi/Snf)	1	chromatin remodeler	no	
<b>RTT109</b>	4 (2 had same mutation)	acetyltransferase	no	strong
<i>SPT10</i>	3	putative acetyltransferase	no	none
<i>AHC1</i> (ADA)	1	acetyltransferase	no	
<i>SPT16</i> (FACT)	6	histone chaperone	yes	strong
<i>POB3</i> (FACT)	3	histone chaperone	yes	intermediate
<b>SET2</b>	2	methyltransferase	no	weak
<i>JHD2</i>	2	demethylase	no	none
<i>RPH1</i>	1	demethylase	no	none
<b>RCO1</b> (Rpd3S)	4	histone deacetylase	no	intermediate
<b>EAf3</b> (Rpd3S)	4	histone deacetylase	no	weak
<i>ASH1</i> (Rpd3L)	4 (all had same mutation)	deacetylase	no	none
<i>UBP8</i> (SAGA DUB)	1	deubiquitination (catalytic)	no	none
<b>SGF73</b> (SAGA DUB)	1	deubiquitination (structure)	no	very weak
<i>TFG1</i> (TFIIFα subunit)	1	pre-initiation factor	yes	
<i>RPB8</i> (RNAPII)	1	pre-initiation factor	yes	
<i>YTA7</i>	2	chromatin factor	no	none
<i>SIR3</i> (SIR complex)	1	silencing protein	no	

Figure 1: Confirmed non-essential *spn1Δ* suppressors

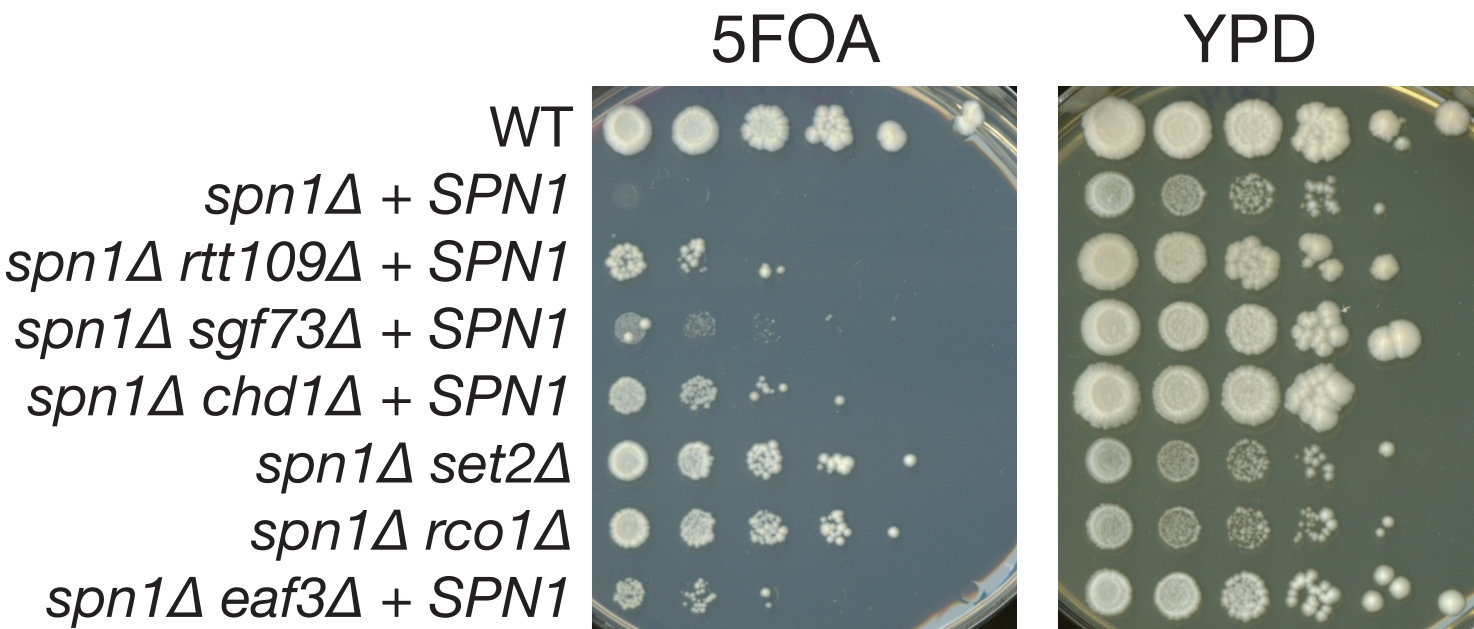


Table 2: Half of the suppressor strains contain mutations in two or more transcription- and chromatin-associated genes

Suppressor strain	Candidate genes
31	<i>POB3</i>
32	<i>CHD1</i> , <i>UBP8</i>
34	<i>YTA7</i> , <i>CHD1</i>
50	<i>CHD1</i> , <i>JHD2</i>
6	<i>SPT16</i> , <i>CHD1</i>
17 (dominant)	<i>SPT16</i>
18	<i>CHD1</i> , <i>SET2</i>
19	<i>SPT16</i> , <i>CHD1</i>
20	<i>RCO1</i>
22	<b>RTT109</b>
83	<i>RCO1</i>
84	<i>CHD1</i> , <i>SPT16</i>
85	<b>RTT109</b>
88	<i>YTA7</i> , <i>SNF2</i> , <i>CHD1</i>
92	<i>EAf3</i>

Table continued	
93	<b>RTT109</b>
96	<i>SPT16</i> , <i>CHD1</i>
100	<b>RTT109</b>
105	<i>SGF73</i>
110	<i>CHD1</i> , <i>ASH1</i>
113	<i>SPT10</i> , <i>ASH1</i> , <i>EAf3</i>
116	<i>TFG1</i>
122	<i>AHC1</i> , <i>SPT10</i> , <i>RPB8</i>
123	<i>CHD1</i> , <i>POB3</i> , <i>ASH1</i>
125	<i>ASH1</i> , <i>JHD2</i> , <i>SPT10</i>
L1	<i>RCO1</i>
L2	<i>SPT16</i>
L3	<i>POB3</i>
L4	<i>SET2</i> , <i>RPH1</i>
L5	<i>EAf3</i>
L6	<i>EAf3</i> , <i>SCH9</i> , <i>SIR3</i>

We want to investigate how loss of Rtt109 suppresses inviability of *spn1Δ*.

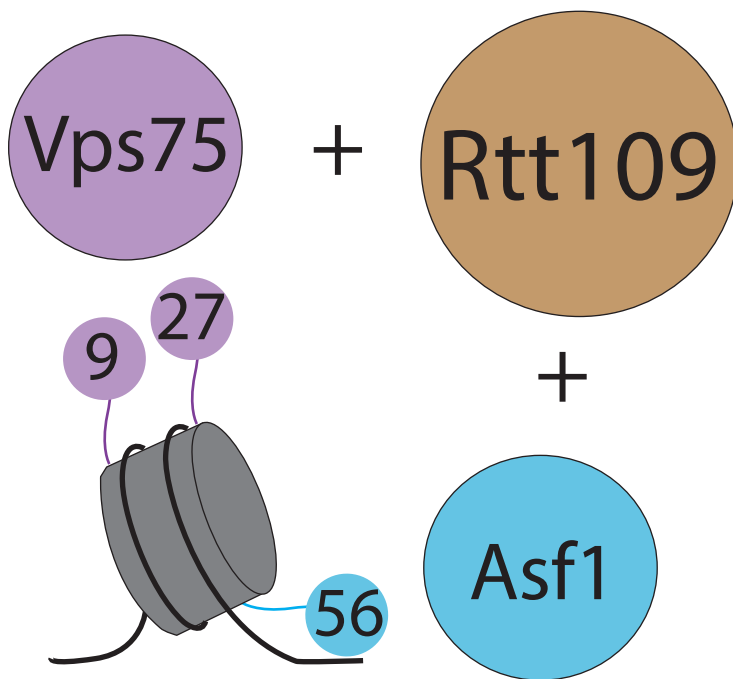
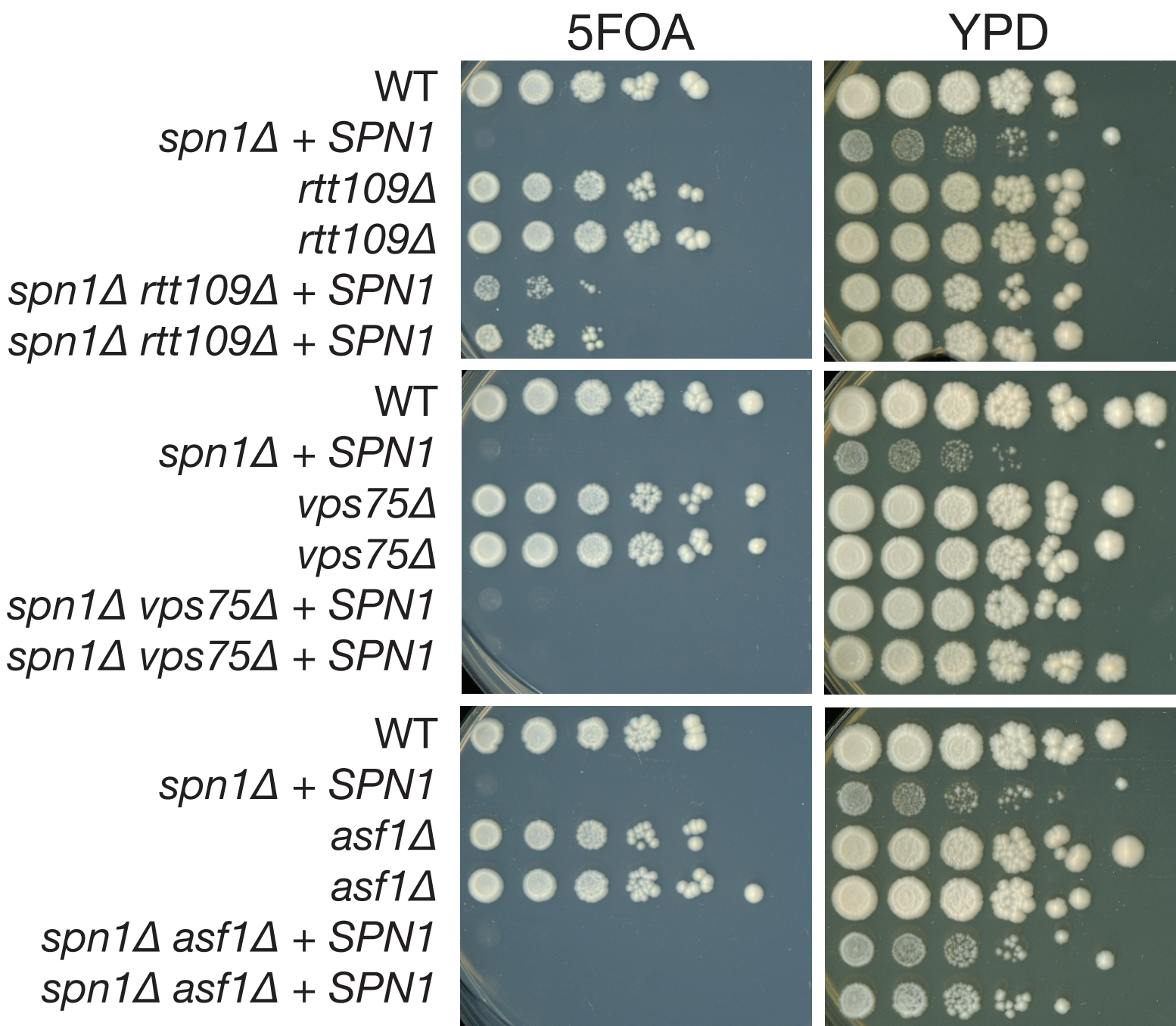


Figure 2: *spn1Δ* is not suppressed by loss of Vps75 or Asf1



## Future directions

- Determine if loss of H3K56 acetylation caused by *H3K56R* or *H3K56Q* mutations suppresses *spn1Δ*
- Assay the levels of the acetylation marks performed by Rtt109 in the *spn1Δ* suppressor strains
- Assay *spn1Δ* suppression by loss of Rtt109 in combination with mutations that alter FACT

## Acknowledgements

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