Integrate RNA-seq and eCLIP-seq for mining regulation functions of RNA binding proteins

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Alternative Post-transcriptional Regulation in simple form

Alternative splicing, initialization, and termination

from computational perspective

Motivating example using SRSF1

UCSC Genome Browser

Differentially used exon.
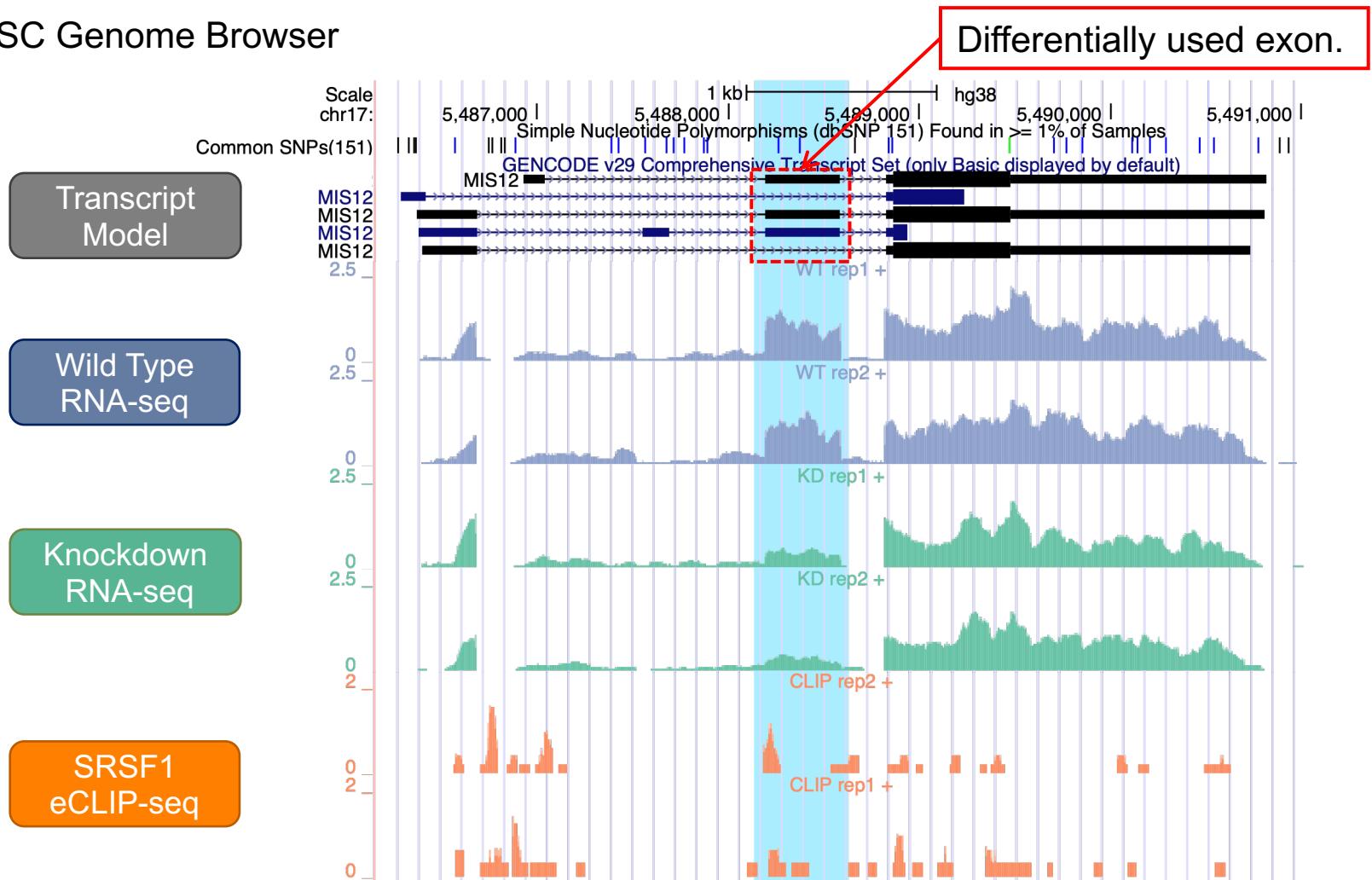
SRSF1 binding to cassette exon promotes inclusion.

# Alternative Post-transcriptional Regulations
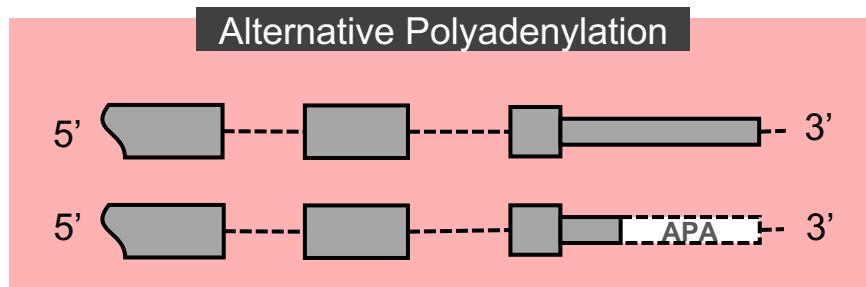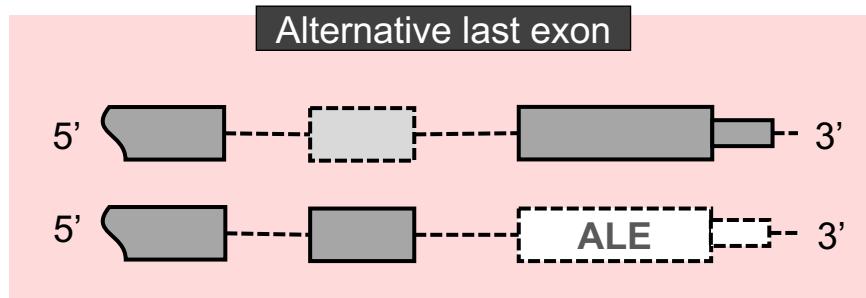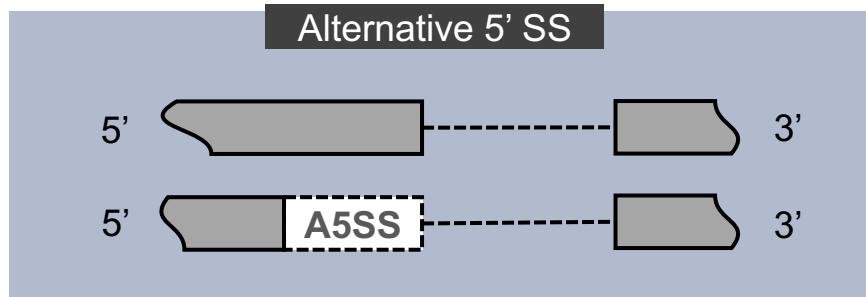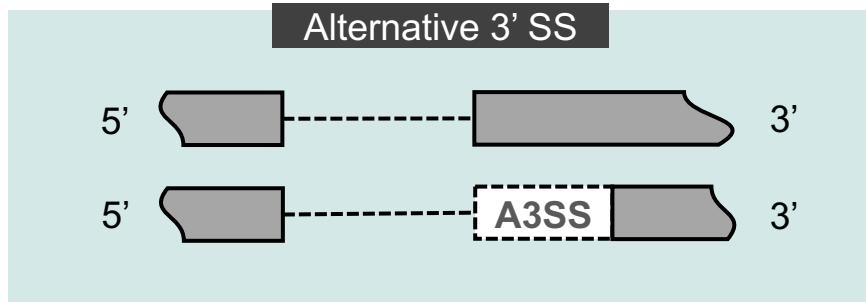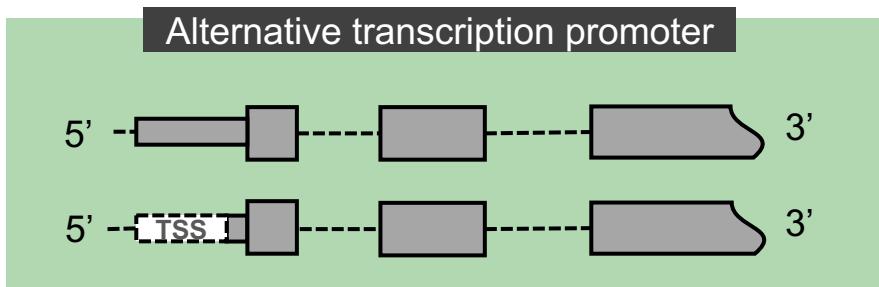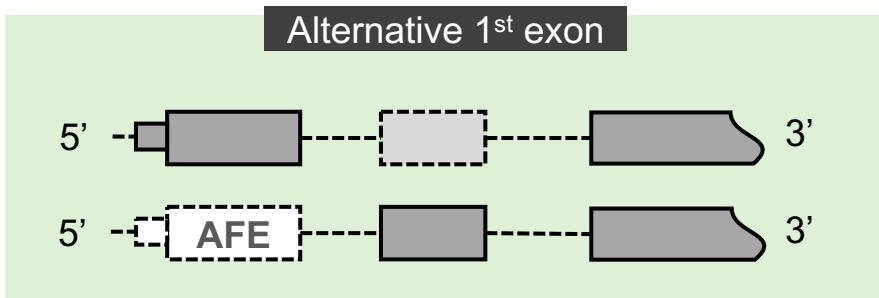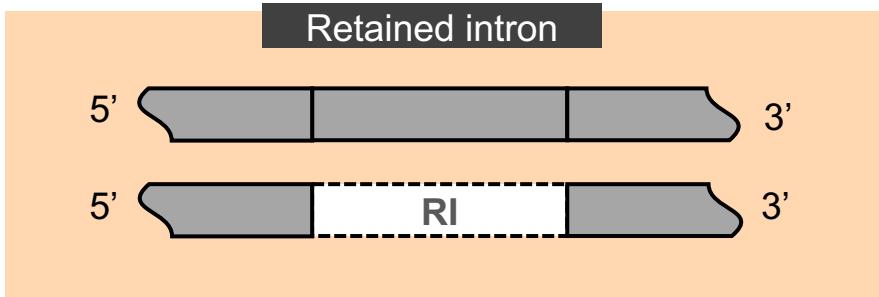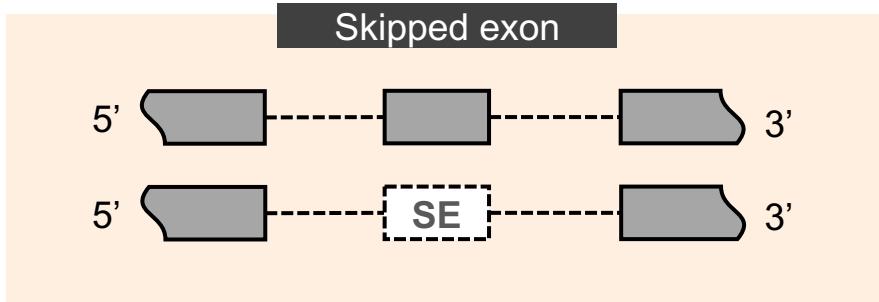
# Look at those events systematically? Use the SURF.

We developed the **S**tatistical **U**tilities for **R**BP **F**unctions (SURF)
to learn RBP regulatory functions.

The intuition behind the SURF

- Hypothesis testing

The SURF pipeline

WT RNA-seq

K_1

K_0

KD RNA-seq

K_1

K_0

$$REUC = \frac{K_1}{K_0}$$

REUC

WT 5/19

KD 2/13

Differential Regulation

Regulation effect

inclusion

exclusion

Phenotype

AR event

SE

SURF Dataset

X1 X2 … Xn

5' SE 3'

x_1 x_2 x_3 x_4 x_5 x_6 x_7 x_8

eCLIP-seq

Extract Features

Signal / Count

3

1

2

X1 X2 … X8
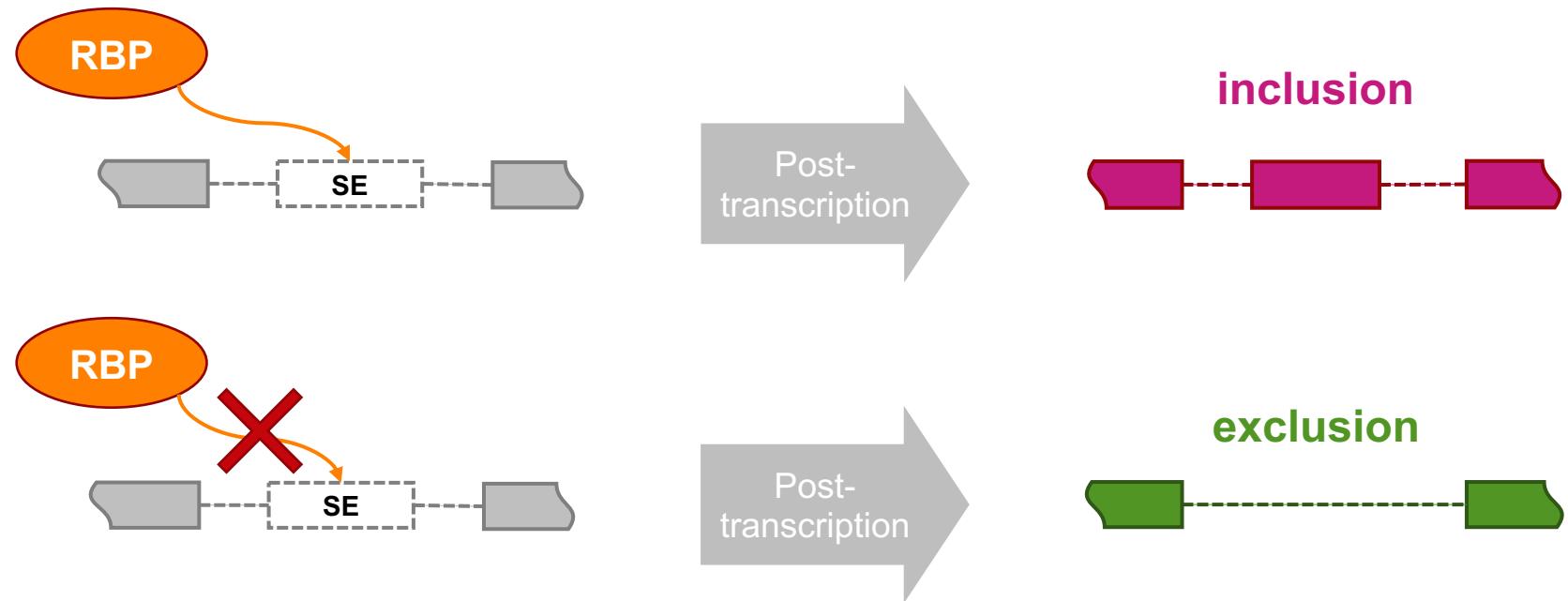
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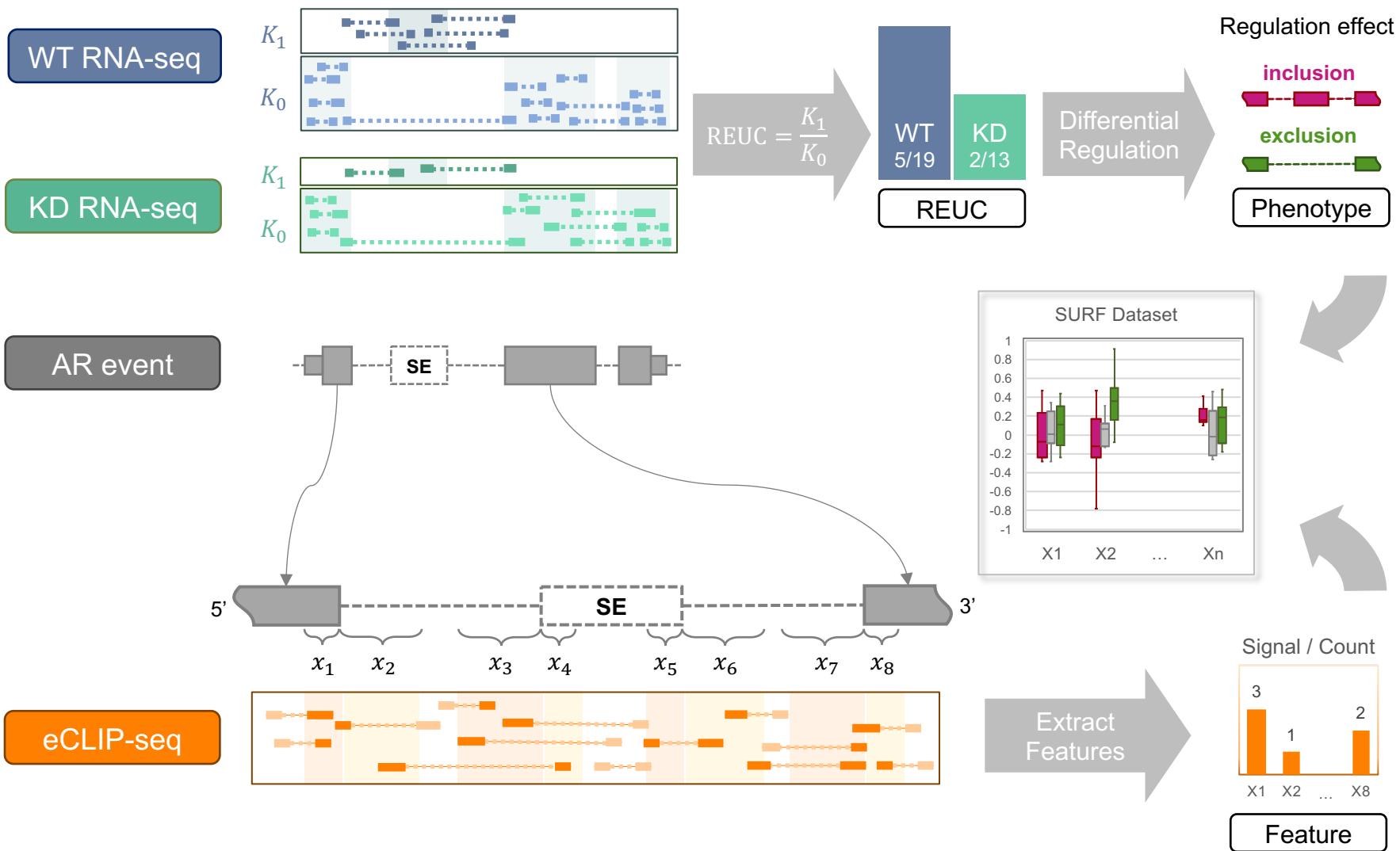
PUM2 regulating functions from the SURF

- Promotes exclusion of APA, binding to the body or upstream
- Promotes inclusion of SE, binding to exonic regions
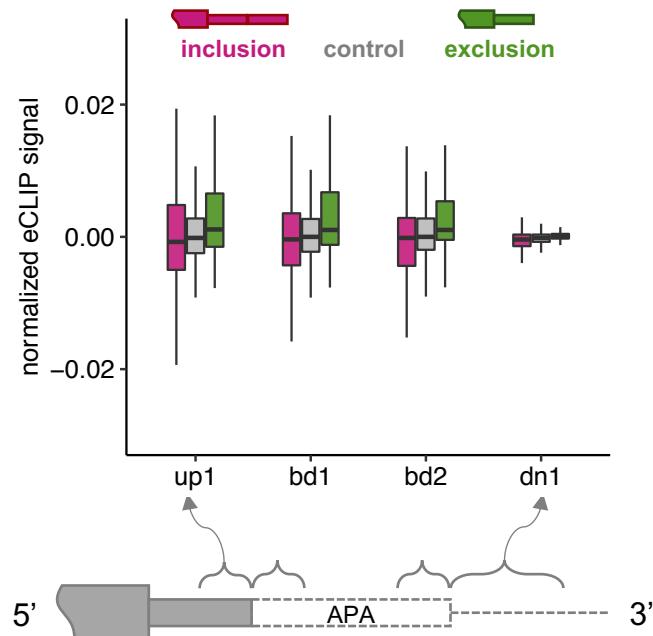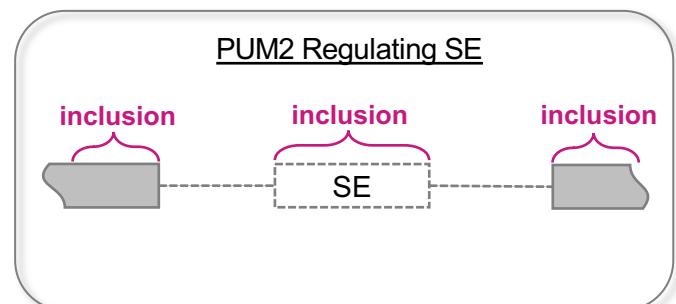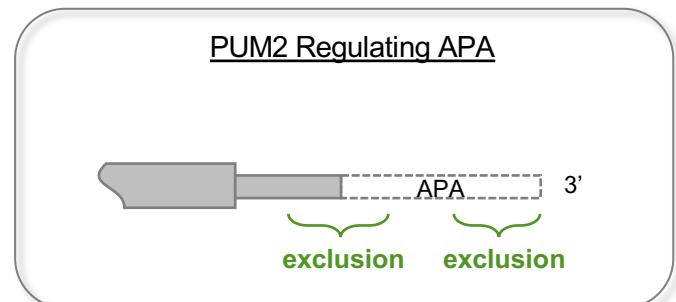
PUM2 leads to exclusion of APA site

- One example out of the 715 APA events
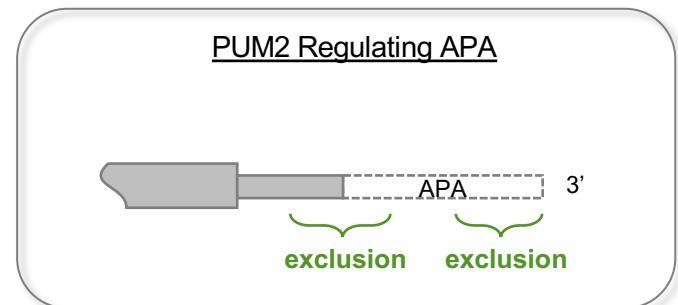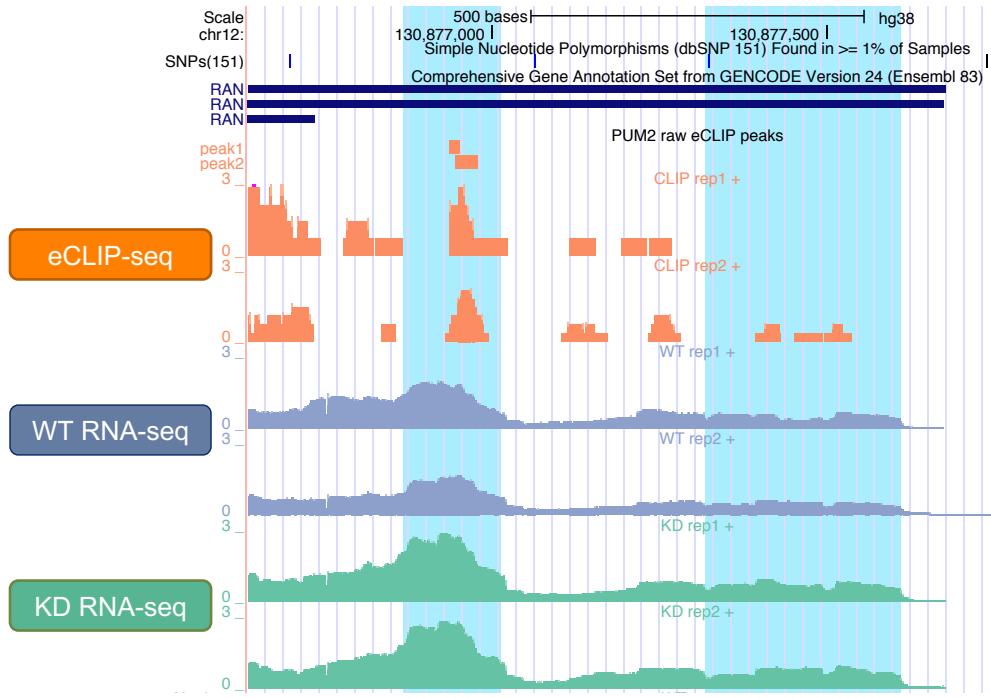
SURF is scalable,
so we can study many RBPs.

A systematical analysis to the ENCODE consortium.

# ENCODE is generating lots of these data

105 RBPs (K562 cell)
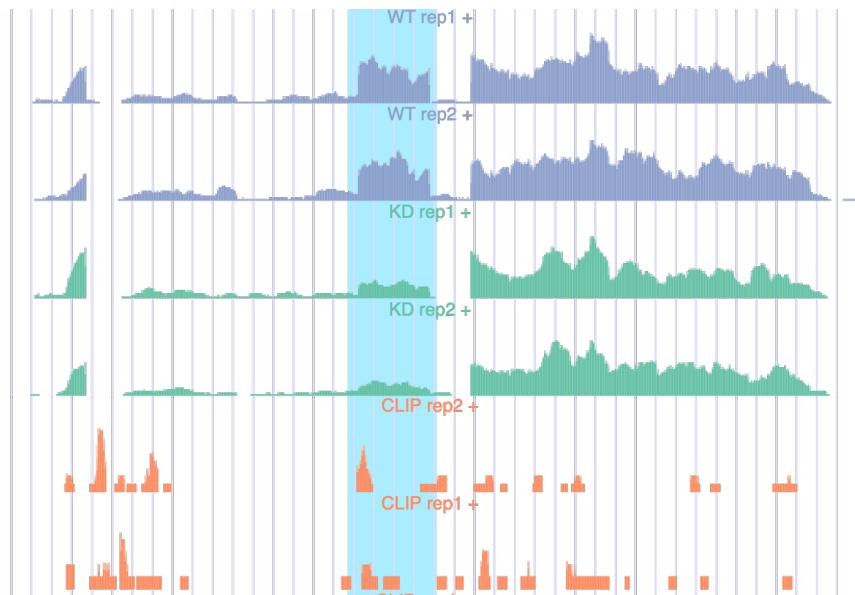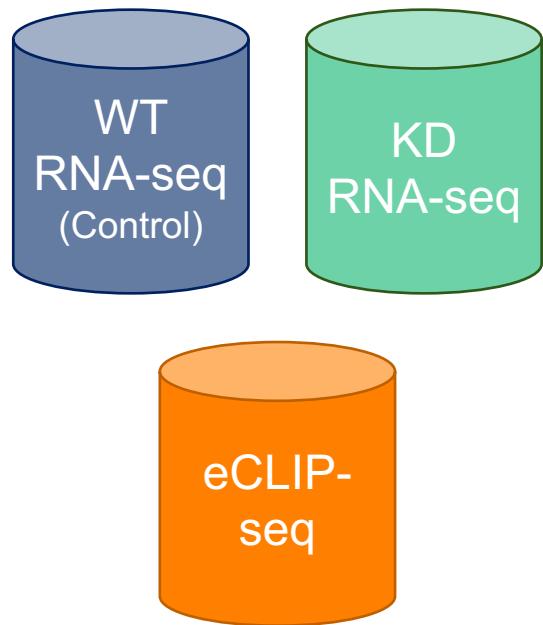
Profiling 68 RBPs in alternative regulations

✓ **RBPs typically have impacts on multiple AR events**

✓ **Individual RBP is involved in different types of AR events**
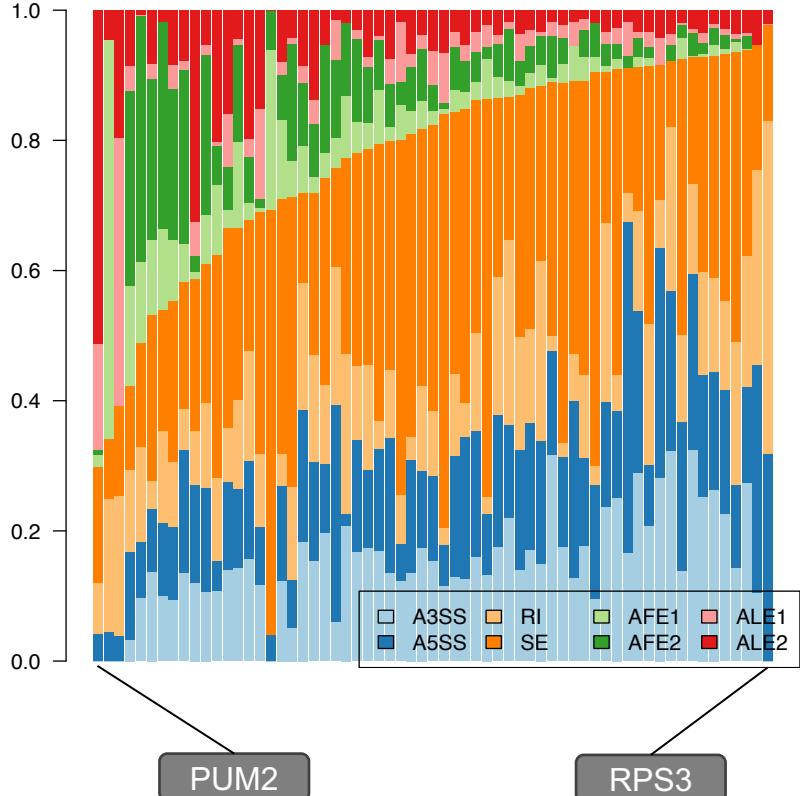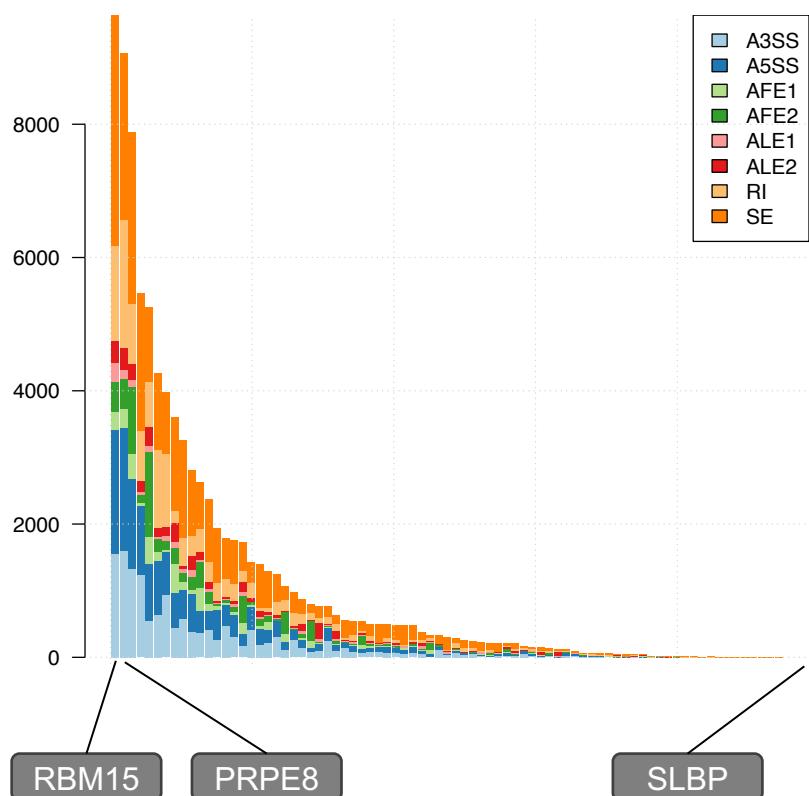
Inferenced regulatory functions of 68 RBPs

Sanity checks

HNRNPC Regulating SE
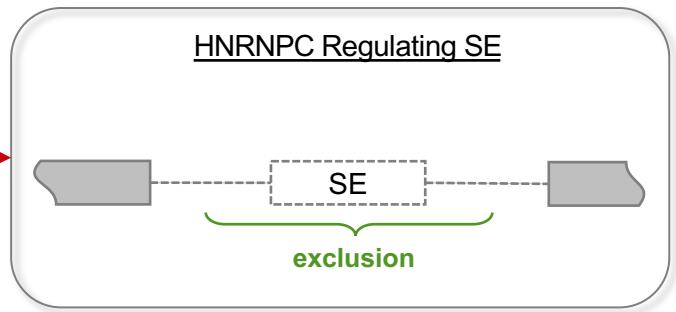
How about RBP relationships?

An example of CPSF6 in regulating APA

CPSF6 has dual functions in regulating APA

Fan Chen (Wisconsin)
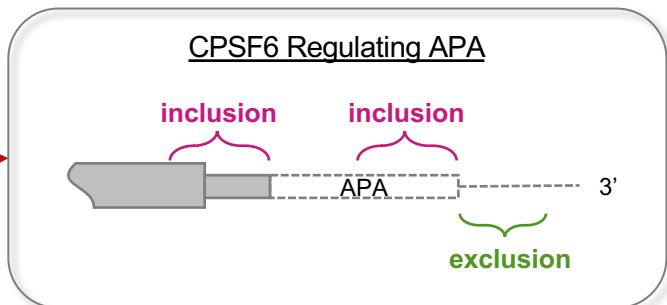
- **inclusion** supported by 1301 APA events
- **exclusion** supported by 580 APA events

# Pairwise screening indicates an association between CPSF6 and PUM2
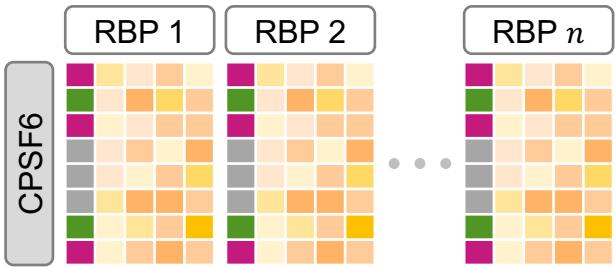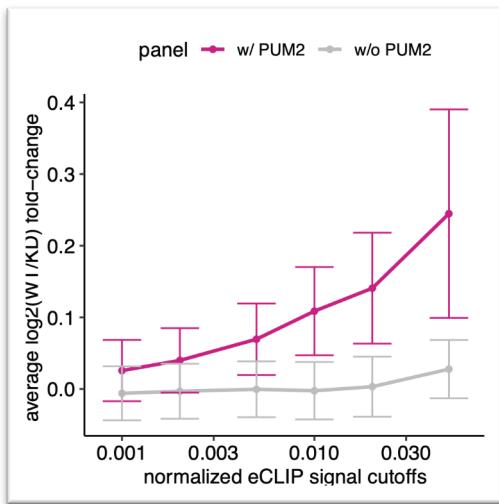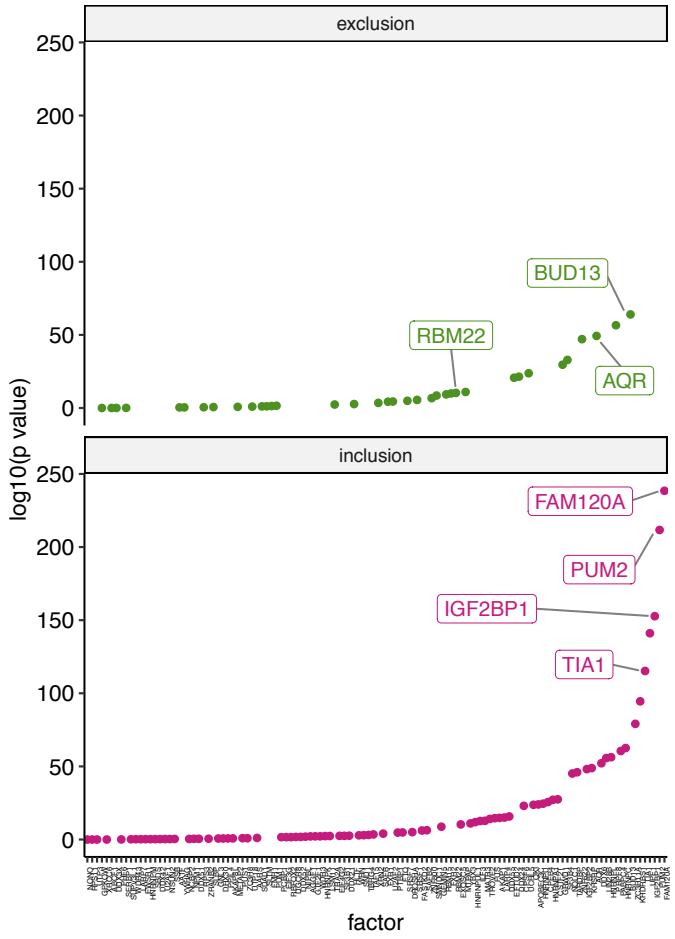
The inclusion function of CPSF6 associates with PUM2

- PUM2 is enriched in APA where CPSF6 promotes inclusion
- Supported by 693 APA events
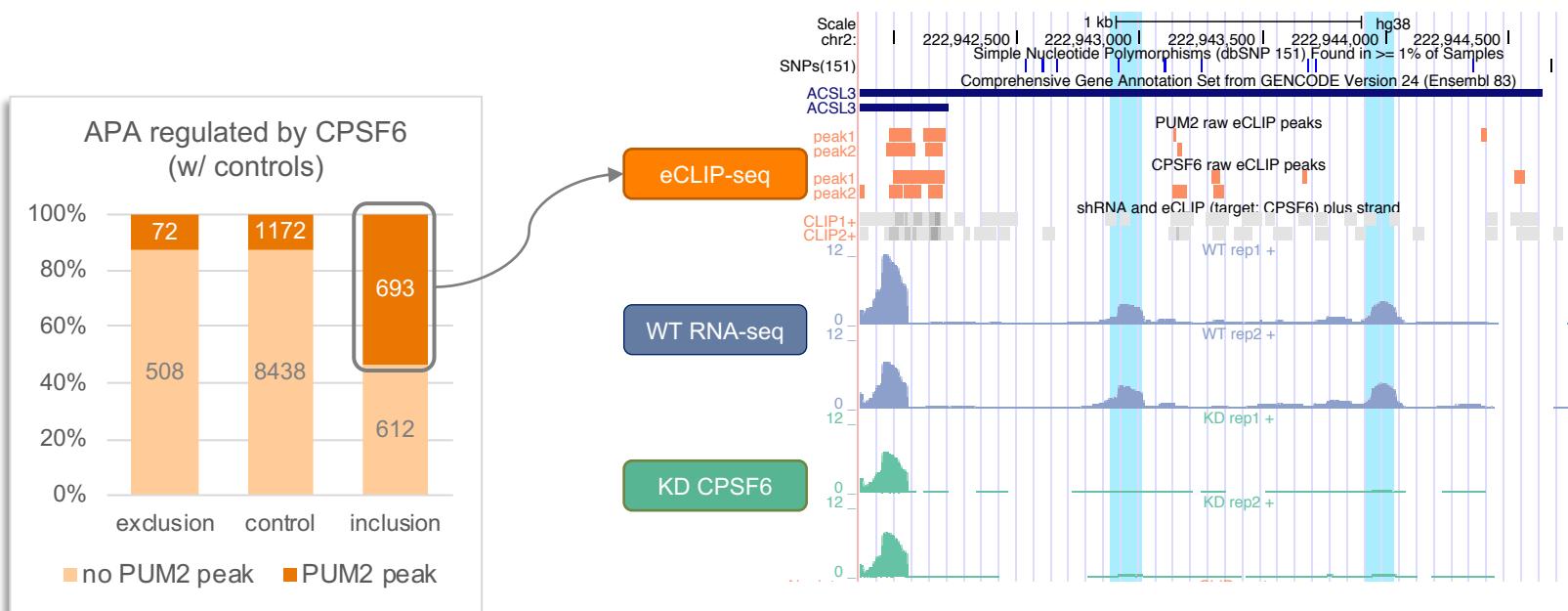
Summary

The SURF

- Utilizes abundant AR events to study RBP.
- Inferences RBP's regulatory functions.
- Screens for potential RBP interactions.

Thank you!

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Open to questions.

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