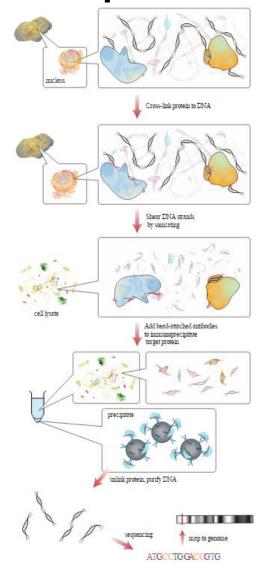
Comparison of ChIP-Seq Peak calling programs

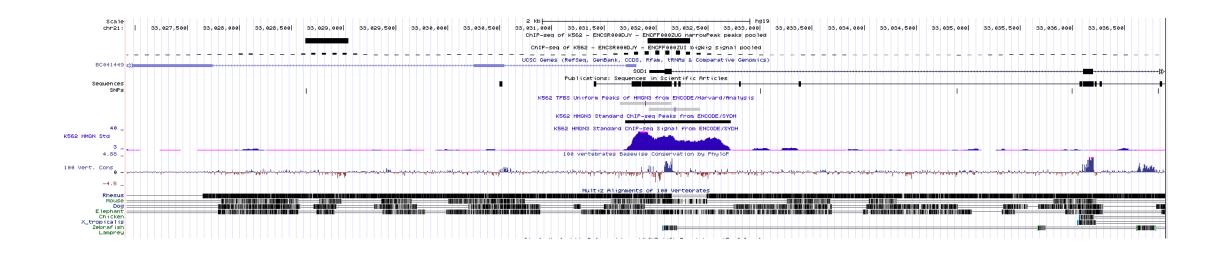
Kanishk Asthana

kasthana@eng.ucsd.edu

Overview of ChIP-seq



A genome wide histogram



ChIP-seq calling programs

- SISSRS: only get start position, end position and number of TAGs, no filtering method can be applied because of no score being returned.
- Spp: not user friendly, documentation inadequate.
- Quest: not user friendly, documentation inadequate.
- PeakSeq: documentation inadequate
- MACS: extremely user friendly and easy to use
- HOMER: a little less user friendly, but still very useful. The entire package is what makes it so useful, a lot of associated functions and functionality.
- Sole-search: documentation inadequate, not user friendly
- Hpeak: only works for human genome

Pair wise comparison of shared peaks

Data Set	HOMER (% of Peaks shared	MACS (% of Peaks shared with
	with MACS)	HOMER)
<u>PU.1</u>	93.24609	90.06348
ENCODE	74.55422	89.26311

	HOMER (% of Peaks shared with SISSRS)	SISSRS (% of Peaks shared with HOMER)
<u>PU.1</u>	82.0557	75.01613
ENCODE	80.47605	63.70693

Data Set	SISSRS (% of Peaks shared with	
	MACS)	SISSRS)
<u>PU.1</u>	82.8864	87.56901
ENCODE	63.42505	95.92693

Comparison of HOMER vs MACS: Does more peaks called mean more false positives?

Data Set	Type of Peaks	HOMER (% of Peaks shared with MACS)	MACS (% of Peaks shared with HOMER)
PU.1	<u>Average</u>	93.24609	90.06348
	Top 25 Percentile	90.48544	85.42430
	Top 5000 Peaks	82.57576	80.66000
	Bottom 25 Percentile	57.85524	51.35473
ENCODE	<u>Average</u>	74.55422	89.26311
	<u>Top 25 Percentile</u>	77.50584	91.39446
	Top 5000 Peaks	81.40521	80.64000
	Bottom 25 Percentile	24.38621	25.17400

Motif Analysis: Peaks Called by HOMER and MACS

Figure 1. PU.1 is the most ENRICHED known Motif found in peaks called by HOMER (Enrichement~44%)

Rank	Motif	Name	· . I	· .	q-value (Benjamini)	# Target Sequences with Motif		Sequences with	% of Background Sequences with Motif	Motif File	PDF
1	AGAGGAAGT		1e- 22448	-5.169e+04	0.0000	38652.0	44.72%	5065.1	6.10%	motif file (matrix)	pdf

Figure 2. PU.1 is the most ENRICHED known Motif found in peaks called by MACS (Enrichement~44%)

Rank	Motif	Name	· . I	log P- pvalue	(Reniamini)	•	% of Targets Sequences with Motif		% of Background Sequences with Motif	Motif File	PDF
1	AGAGGAAGT ©		1e- 23216	-5.346e+04	0.0000	39619.0	44.28%	5071.3	5.94%	motif file (matrix)	<u>pdf</u>

Motif Analysis: Peaks Called HOMER or MACS but not the other

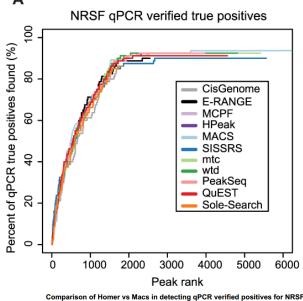
Figure 3. PU.1 is the most ENRICHED known Motif found in peaks found in HOMER and not MACS (Enrichment ~32%)

Rank	Motif	Name		log P- pvalue	I(Remiamini)	I_ ~	Sequences with	# Background Sequences with Motif	% of Background Sequences with Motif	Motif File	PDF
1		PU.1(ETS)/ThioMac-PU.1-ChIP- Seq(GSE21512)/Homer	1e- 829	-1.910e+03	0.0000	1874.0	32.09%	2492.7	5.81%	motif file (matrix)	<u>pdf</u>

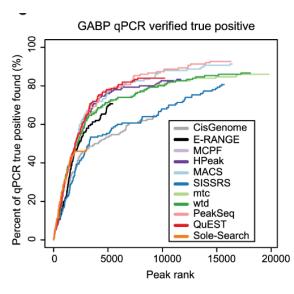
Figure 4. PU.1 is the most ENRICHED known Motif found in peaks found in MACS and not HOMER (Enrichment ~35%)

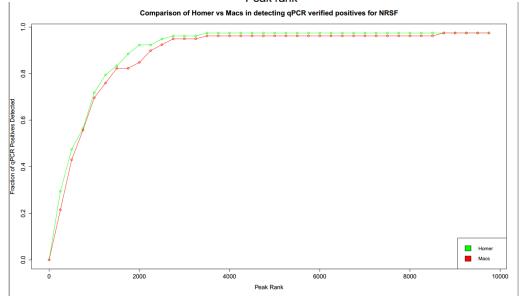
Rank	Motif	Name		log P- pvalue	q-value (Benjamini)	_	Sequences with	Sequences with	% of Background Sequences with Motif	Motif File	PDF
1		PU.1(ETS)/ThioMac-PU.1-ChIP- Seq(GSE21512)/Homer	1e- 1441	-3.320e+03	0.0000	3166.0	35.45%	2341.5	6.31%	motif file (matrix)	<u>pdf</u>

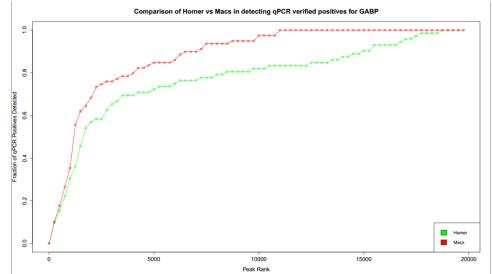
Detection of qPCR verified True Positives



Top Two figures are from Wilbanks et. al (2010) Plos One.







Conclusion: Which is better MACS or HOMER?

Not enough information to decide.

References

• Wilbanks, E. G., & Facciotti, M. T. (2010). Evaluation of algorithm performance in ChIP-seq peak detection. *PloS One*, *5*(7), e11471. doi:10.1371/journal.pone.0011471