

xSpecies miRNA: outline / tasks

human (hsa)



chimp (ptr)

macaque (mml)



aim

- ▶ letter to Nature:

“mapping the microRNA landscape of the adult human, chimp, and macaque brain”

- ▶ ~1,500 words + 3 or 4 exhibits

6 parts

1. PTR/MML reannotation using HSA miRNAs
2. HSA/PTR/MML miRNAs detected in brain
3. brain specific miRNAs
4. DEX/delta-DEX between tissues/species
5. miRNA / mRNA network
6. validated miRNAs / mRNA interaction

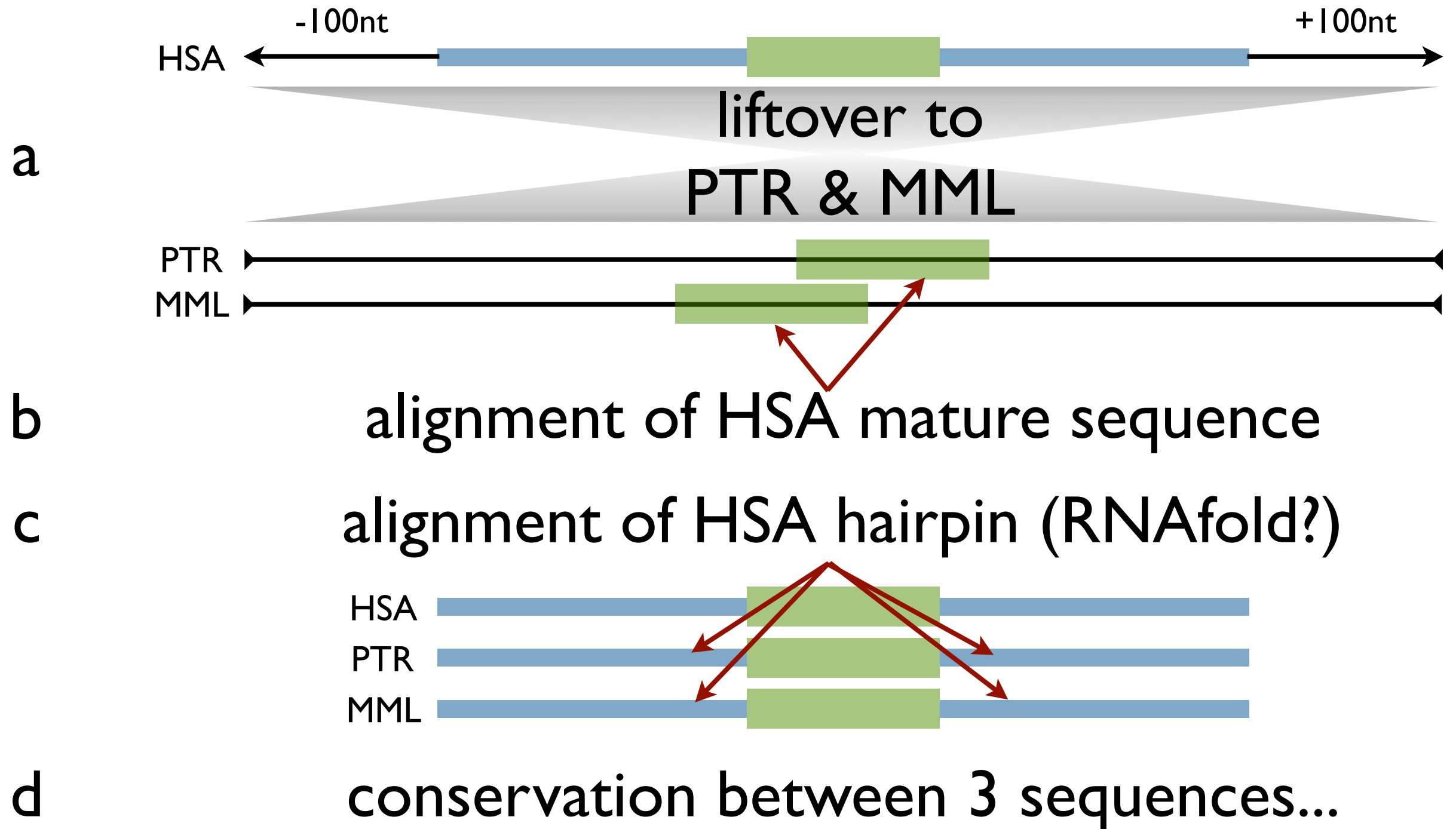
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1. reannotation

- ▶ liftover HSA miRNA regions to PTR/MML
- ▶ blast within regions to find mature seq
- ▶ use RNAfold to determine precursor
- ▶ compare HSA/PTR/MML mature/precursor sequence to find mutations / rate
- ▶ create updated PTR/MML miRNA reference

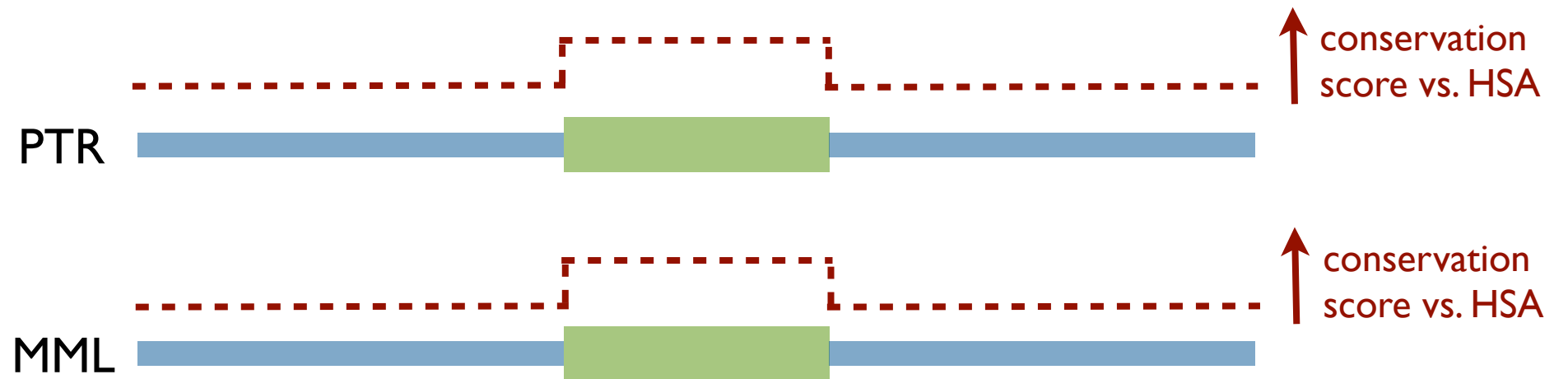
1. reannotation



1. reannotation

d

identity between
PTR/HSA and MML/HSA



e

3' or 5' conservation bias?

f

mature sequence divergence sufficient to
require re-mapping PTR/MML reads to new
reference?

in chimp and macaque, the 1789 and 1692 are the mature miRNAs with >50% identity to human

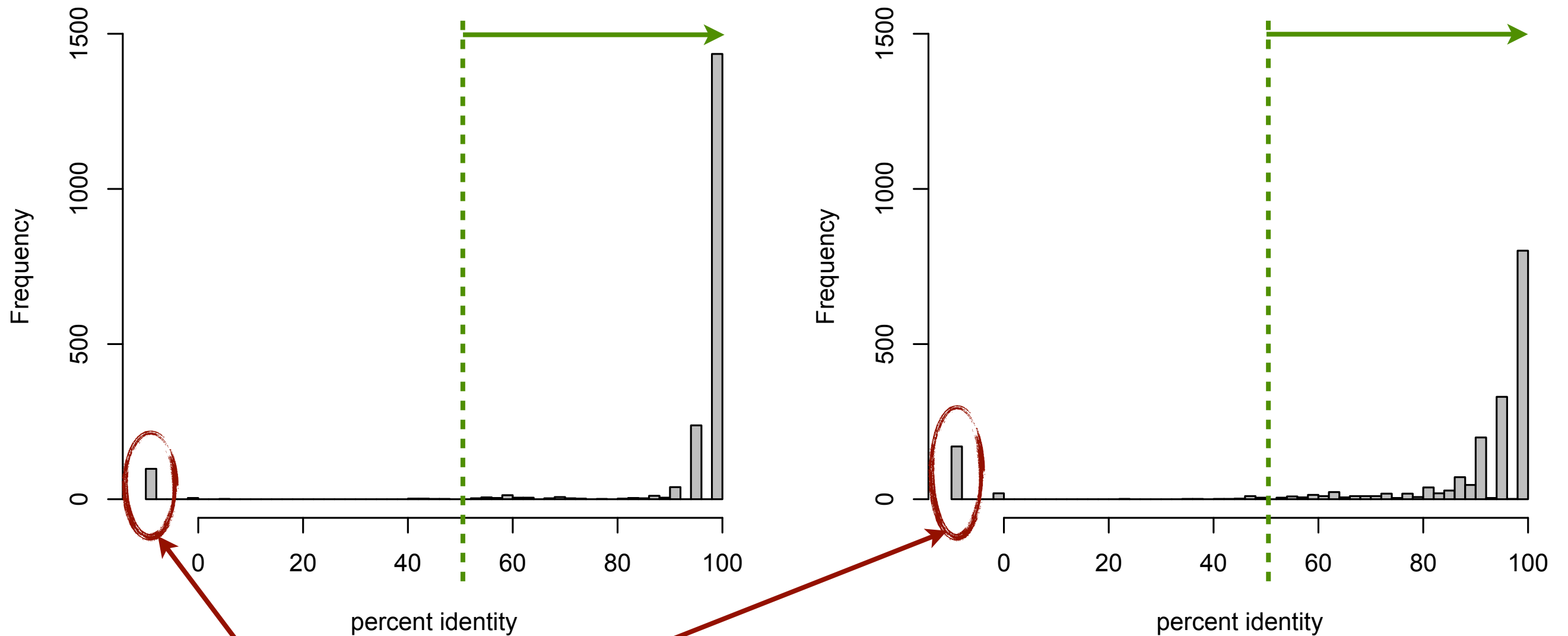
liftover

liftover require >50% sequence identity...

difference between HUMAN miRBase miRNAs and liftover miRNAs is removal of duplicate

source	human	chimp	
miRBase pre-miRNAs	1,523	600	479
liftover pre-miRNAs	1,494	1,451	1,375
miRBase mature miRNAs	1,921	525	488
liftover mature miRNAs	1,898	1,789	1,692

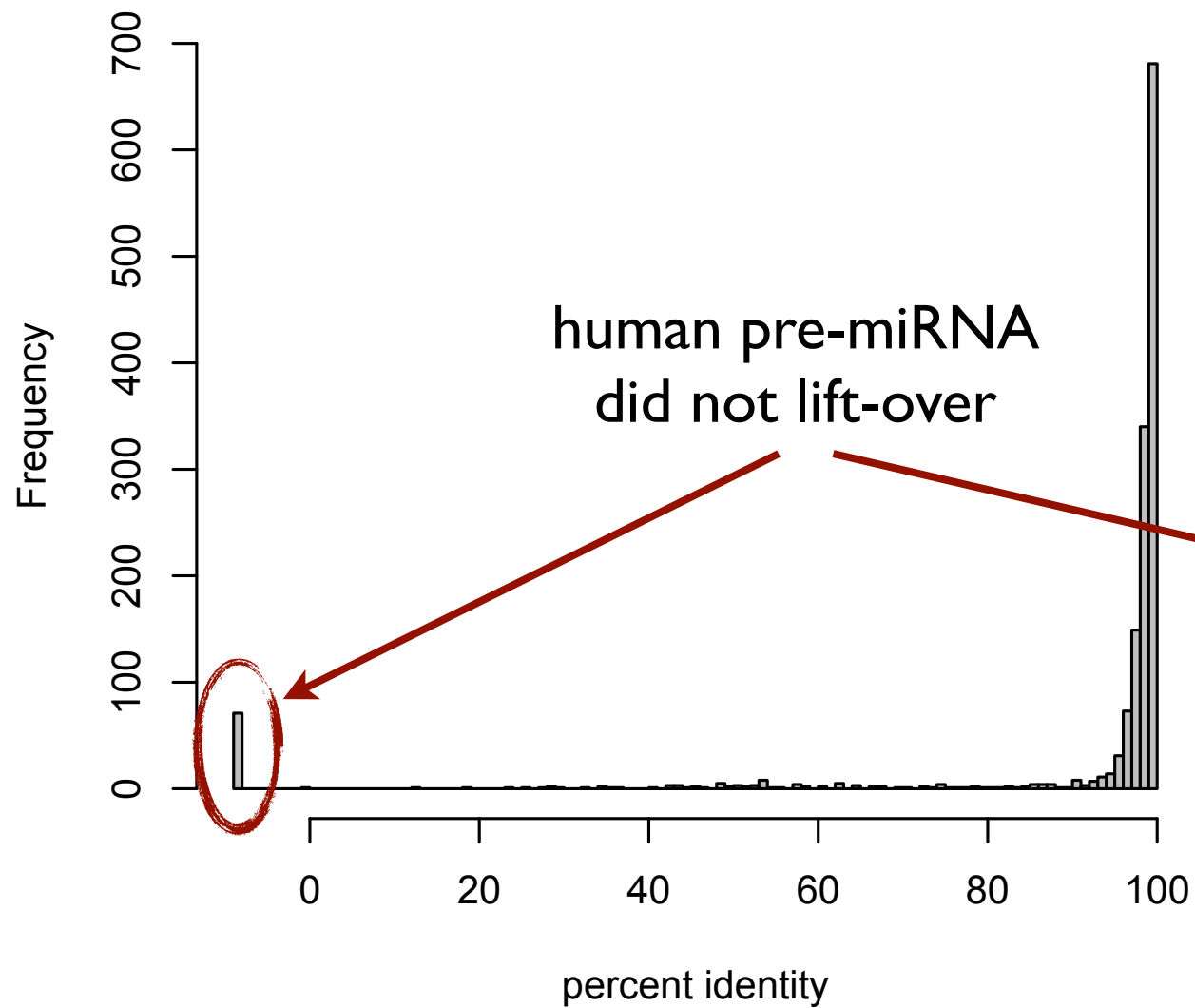
mature miRNA identity



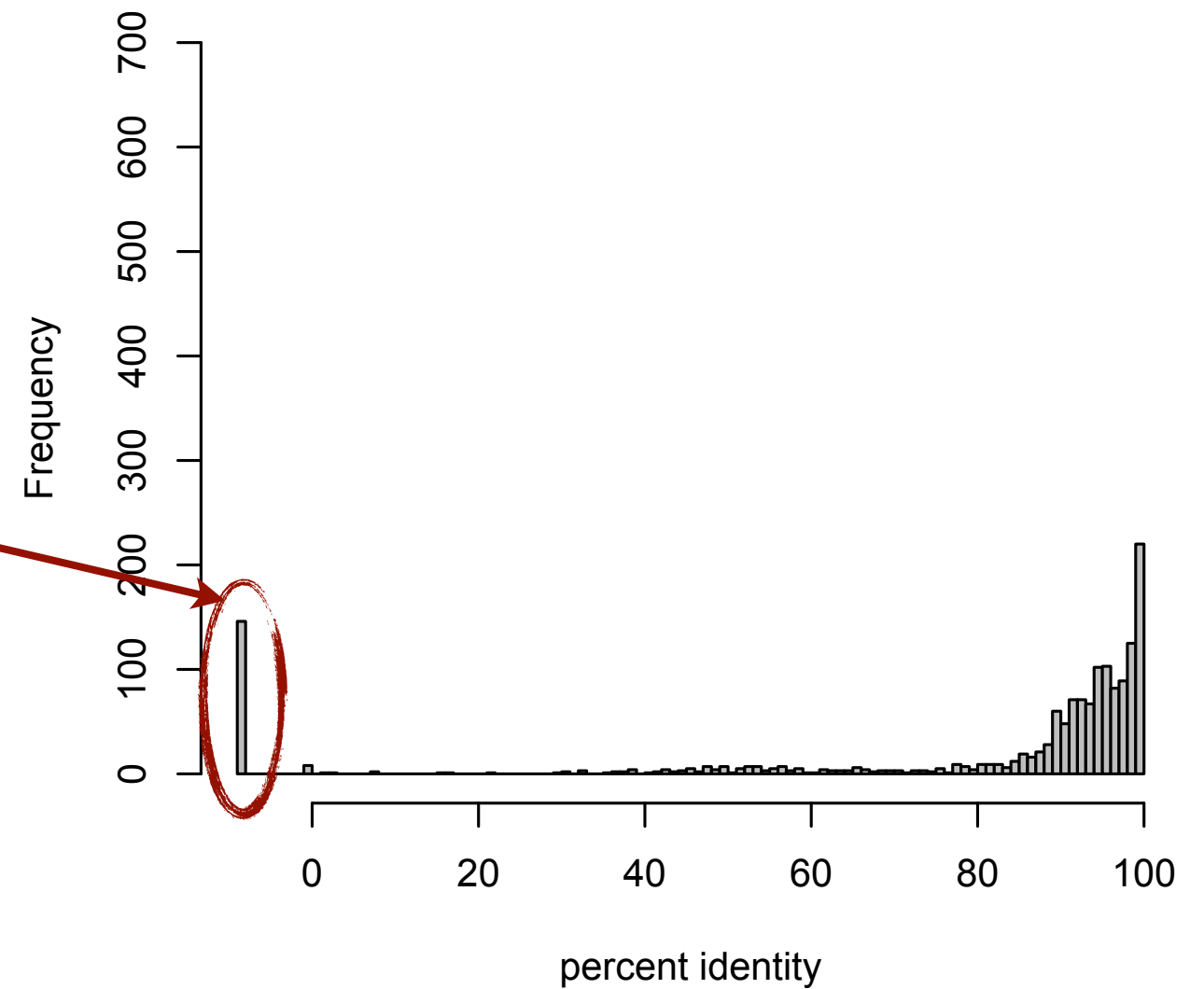
human pre-miRNA
did not lift-over

pre-miRNA identity

Chimp pre-miRNA



Macaque pre-miRNA



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2. detected in brain

- ▶ depends on mature sequence conservation...
- ▶ if high:
 - map PTR/MML reads onto HSA reference
 - done this already
- ▶ if low:
 - re-map reads to new mature sequences determined in part 1

2. detected in brain

634	660	681	704	702	720	704	709	669	680	683	691	689	689	697	694	HSA
355	365	372	391	401	416	416	430	444	415	416	416	419	415	425	431	PTR
369	391	399	432	405	417	407	407	427	412	422	420	421	435	424	429	MML
CBC	V1C	STR	DFC	S1C	M1C	VFC	IPC	MD	A1C	OFC	STC	ITC	MFC	HIP	AMY	

2. detected

Using single STR sample in each species

>90% = homology to a human mature sequence

percentage on bottom row is w.r.t. number of 90%+ homology miRNAs


source			
miRBase mature miRNAs	1,898	514	472
miRBase detected	917	360	341
miRBase detected (> 1 read)	739 (39%)	332 (65%)	319 (68%)
liftover mature miRNAs	1,898	1,789	1,692
liftover mature miRNAs (>90%)	1,898	1,713	1,348
liftover detected	917	816	651
liftover detected (> 1 read)	739 (39%)	678 (40%)	553 (41%)

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3. brain-specific miRNA

miRNA body map



Dissecting miRNA function through integrative genomics

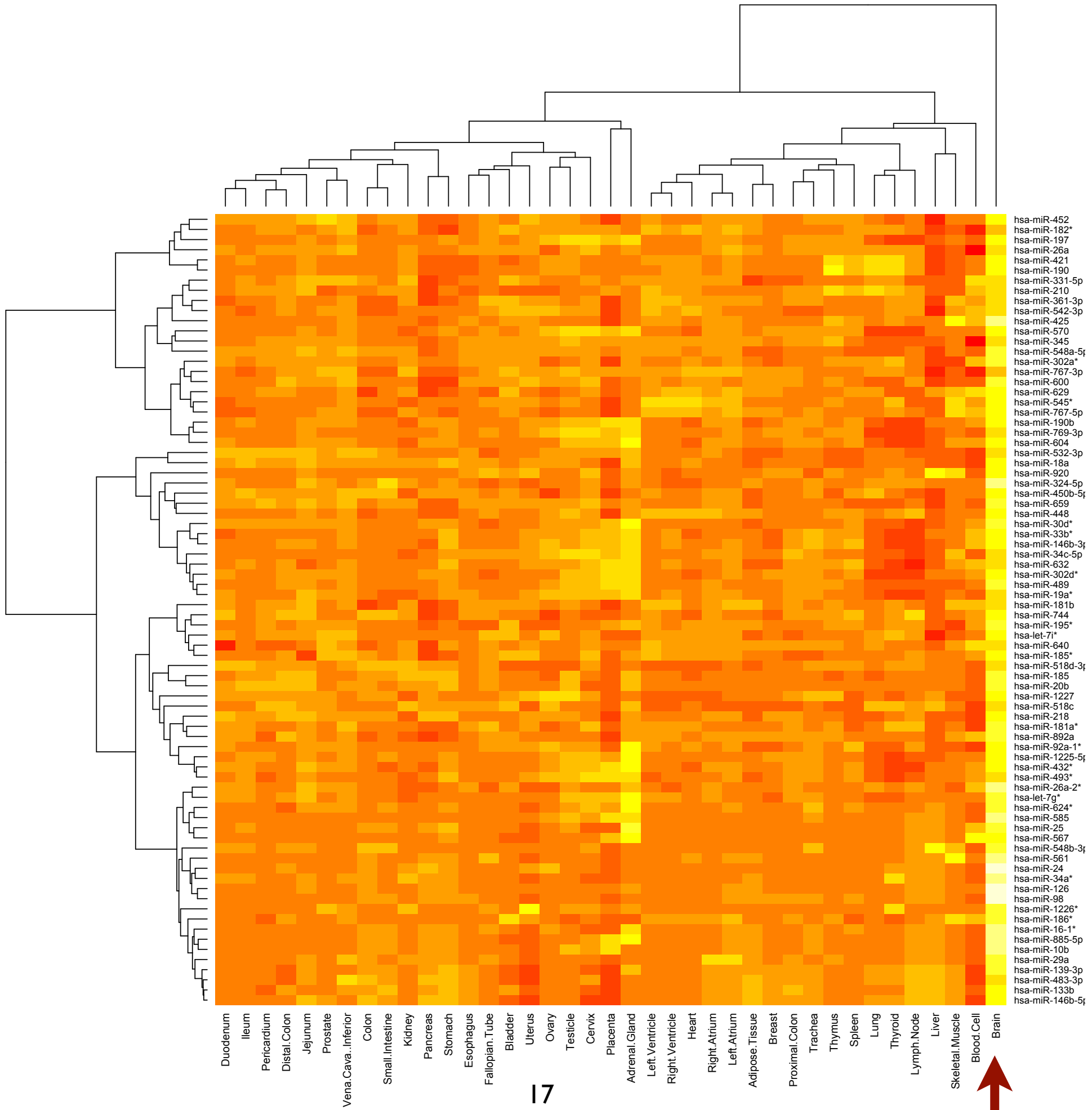


release 1.1

- 22 datasets
- 938 samples
- 328,338 datapoints

mirBase release 14
TargetScan 5.1
miRDB 3.0
MicroCosm v5
DIANA 3.0
TarBase v.5c
Gene Ontology april 2010
KEGG march 2010
PITA catalog v6
RNA22 (august 2007)
miRecords v2
PubMed

- ▶ use tissue-specific expression info in mirnabodymap.org to determine brain-specific miRNAs
- ▶ any of these DEX in hsa/ptr/mml?



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4. DEX & delta-DEX

- ▶ pairwise between tissues and between species

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5. network

- ▶ cluster / network miRNA / mRNA based on fold-change between pairs of tissues
- ▶ in parallel between HSA/PTR/MML
- ▶ match mRNAs by orthologs

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6. **validated miRNAs / mRNA interaction**

6. validation

- ▶ validate expression levels of selected miRNAs in selected tissues / species by qPCR
- ▶ validate mRNA targets using luciferase miRNA over-expression