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Allele-Specific Methylation and Expression in Lymphoma

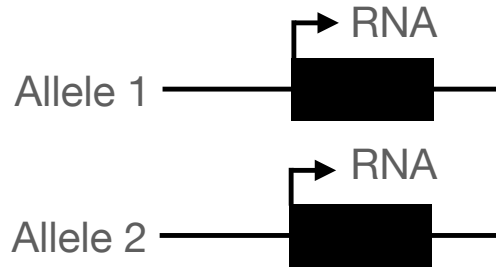
Winterseminar, 14.02.2023

Christiane Gärtner

Bioinformatics Group Uni Leipzig

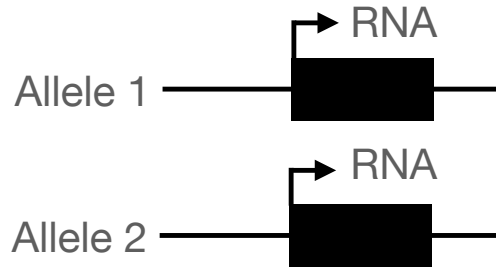
BACKGROUND

no methylation



BACKGROUND

no methylation

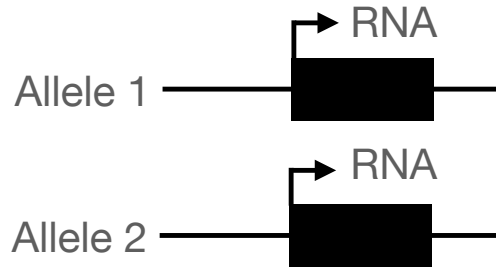


bi-allelic methylation

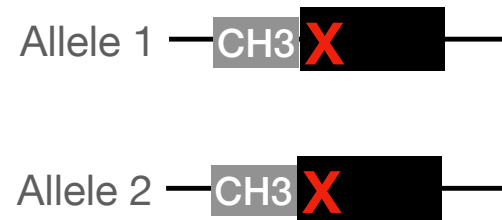


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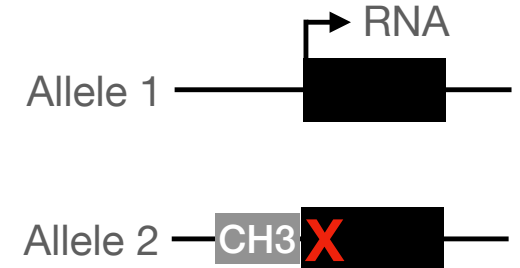
no methylation



bi-allelic methylation



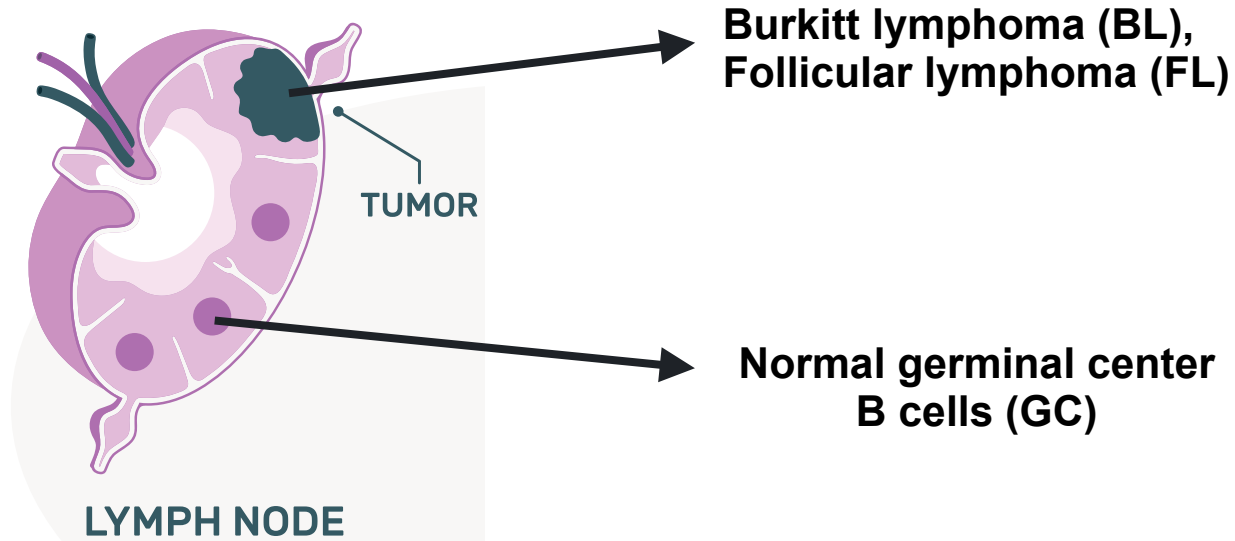
mono-allelic methylation



AIMS

- In which genes can we detect **allele-specific methylation** in lymphoma?
- Can we find **allele-specific expression** in lymphoma?
- Is there a relation of allele-specific methylation to allele-specific expression?

STUDY DESIGN



DETECTION OF ALLELE-SPECIFIC METHYLATION

Mapping

ATTTCGCGCG
ATTTCGCGCG
ATATCGCGCG
ATTTCGCGCG
ATATCGCGCG
ATATCGCGCG
ATATCGCGCG
ATTTCGCGCG
ATTTCGCGCG
ATATCGCGCG

DETECTION OF ALLELE-SPECIFIC METHYLATION

Mapping



SNP calling

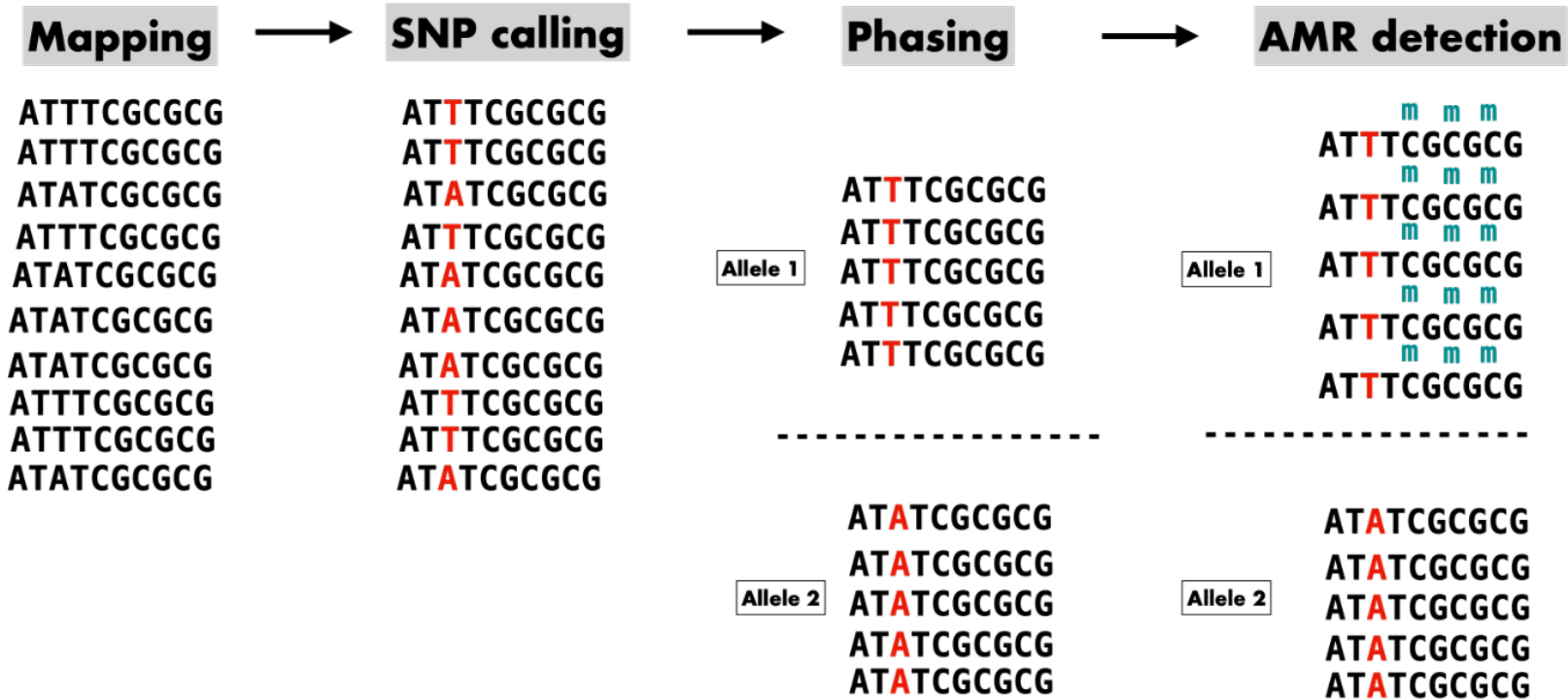
ATTTTCGCGCG
ATTTTCGCGCG
ATATCGCGCG
ATTTTCGCGCG
ATATCGCGCG
ATATCGCGCG
ATATCGCGCG
ATTTTCGCGCG
ATTTTCGCGCG
ATATCGCGCG

AT**T**TCGCGCG
AT**T**TCGCGCG
AT**A**TCGCGCG
AT**T**TCGCGCG
AT**A**TCGCGCG
AT**A**TCGCGCG
AT**A**TCGCGCG
AT**T**TCGCGCG
AT**T**TCGCGCG
AT**A**TCGCGCG

DETECTION OF ALLELE-SPECIFIC METHYLATION



DETECTION OF ALLELE-SPECIFIC METHYLATION



RNA EXPRESSION PATTERNS

Gene

ATCCGCGAGGCTTAGCGTTA

RNA EXPRESSION PATTERNS

Gene

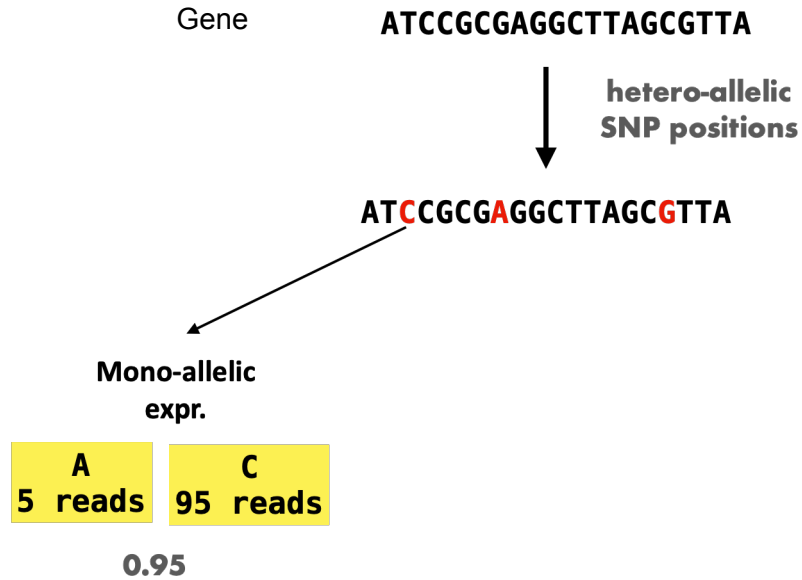
ATCCGCGAGGCTTAGCGTTA



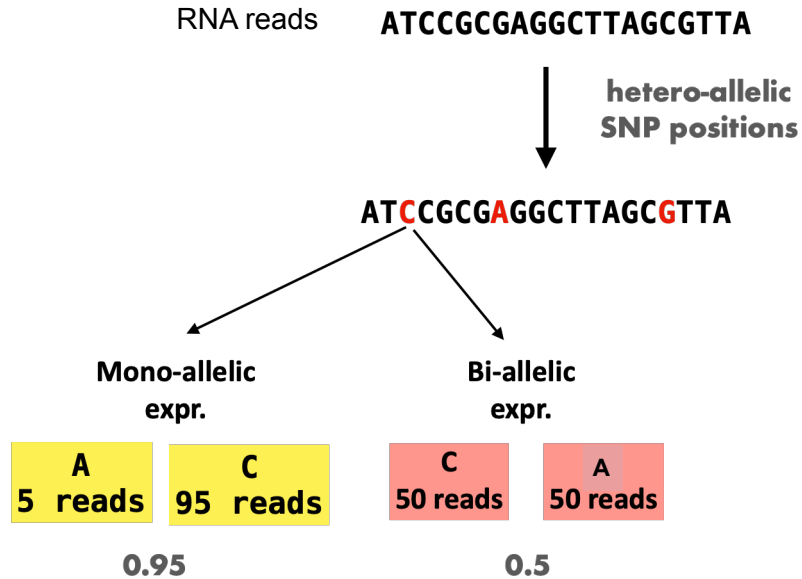
hetero-allelic
SNP positions

ATCCGCGAGGCTTAGCGTTA

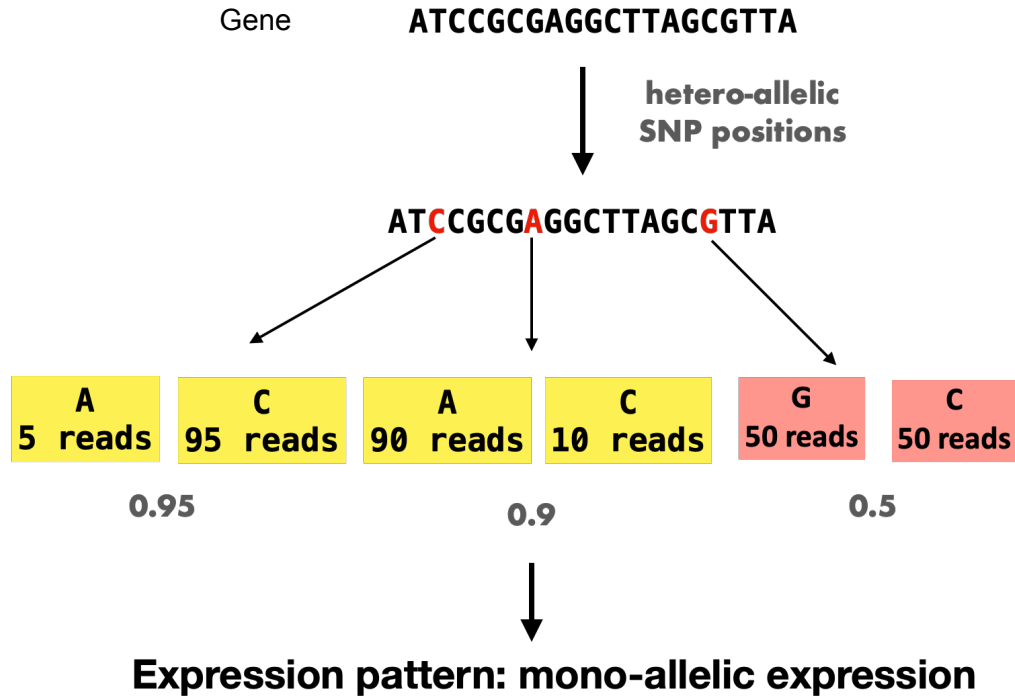
RNA EXPRESSION PATTERNS



RNA EXPRESSION PATTERNS



RNA EXPRESSION PATTERNS

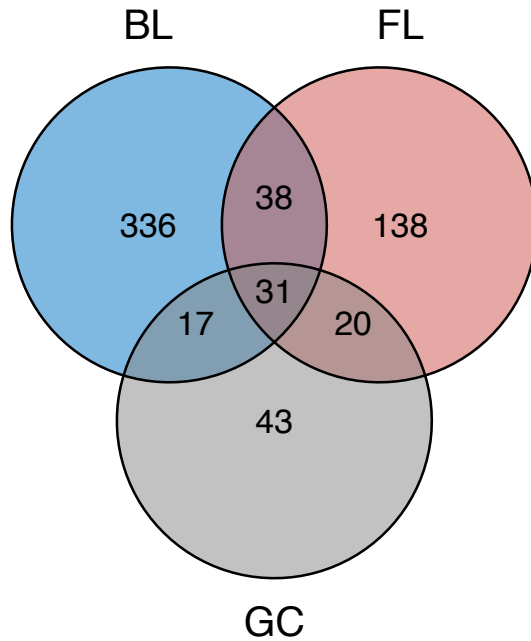


RESULTS

	Burkitt lymphoma (BL)	Follicular lymphoma (FL)	Normal germinal center B cells (GC)
Allele-specific methylated regions (AMR)	750	489	212

AMR IN LYMPHOMA

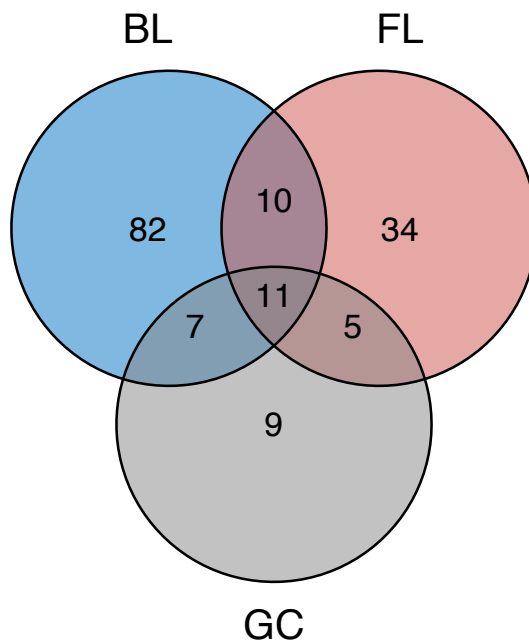
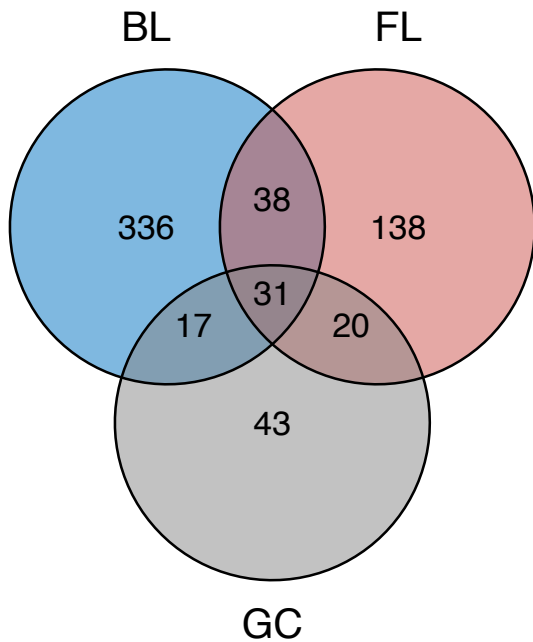
All genes containing AMR



AMR IN LYMPHOMA

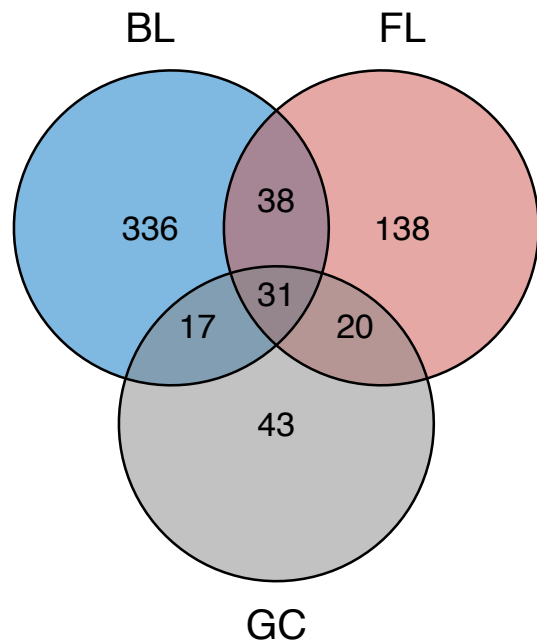
All genes containing AMR

lncRNA genes containing AMR

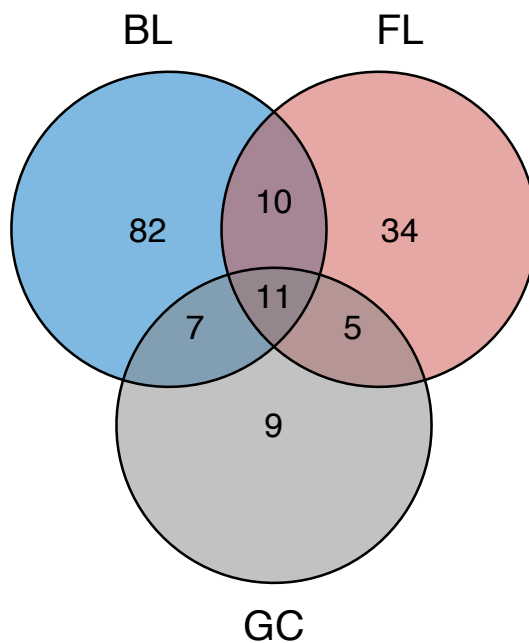


AMR IN LYMPHOMA

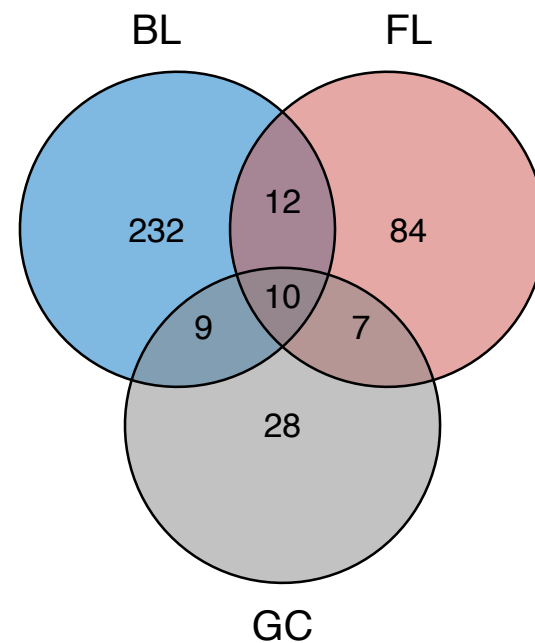
All genes containing AMR



lncRNA genes containing AMR



protein-coding genes containing AMR



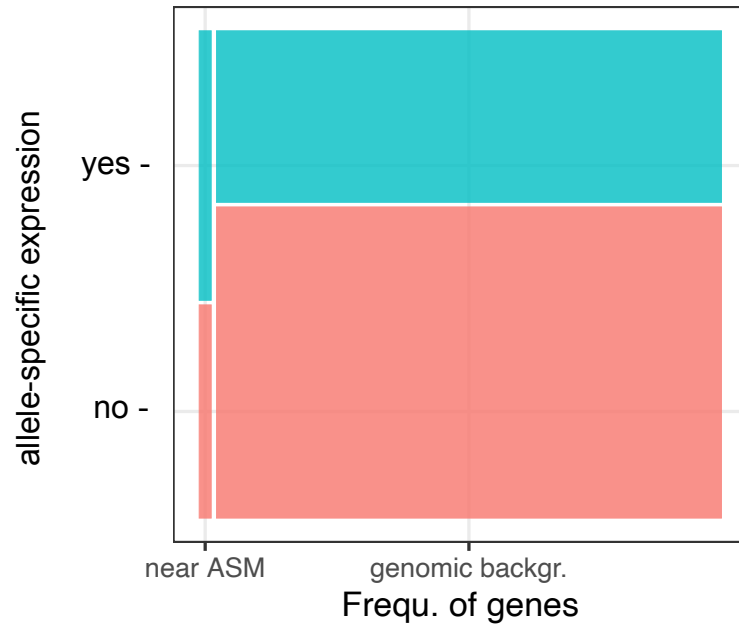
RESULTS

- Partizipation of genes containing AMRs in pathways / cellular functions:
 - **BL:** Wnt signaling pathway, mismatch repair, DNA replication, B receptor signaling pathway
 - **FL:** Wnt signaling pathway, Regulation of hematopoietic stem cell differentiation, interleukin-1-mediated signaling pathway

RESULTS

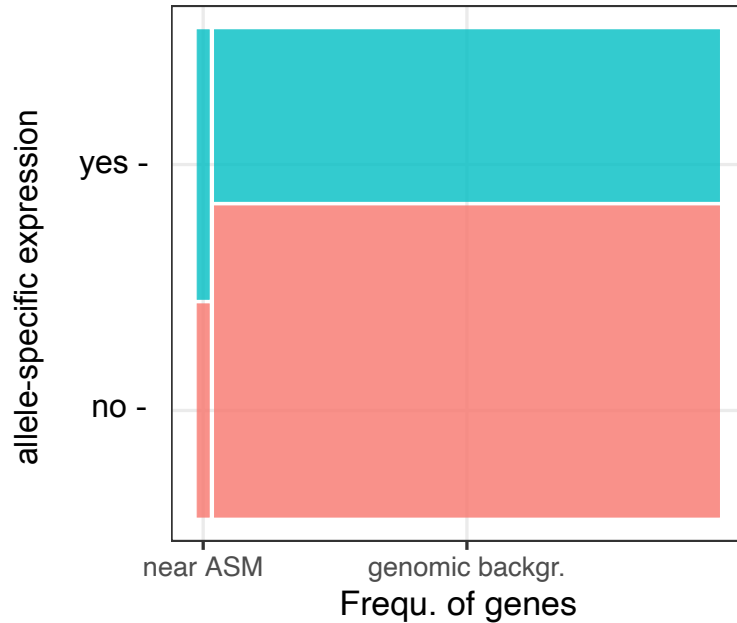
	Burkitt lymphoma (BL)	Follicular lymphoma (FL)	Normal germinal center B cells (GC)
allele-specific expression	1.521	2.754	1.692
bi-allelic expression	4.501	4.210	3.046

EXPRESSION PATTERN IN RELATION TO METHYLATION



(example BL)

EXPRESSION PATTERN IN RELATION TO METHYLATION



Genes that are close to an AMR are significantly more likely to be allele-specifically expressed in all conditions.

(example BL)

RESULTS

- Partizipation of ASE genes close to AMR in pathways / cellular functions:
 - **BL:** Wnt signaling pathway, MAPK signaling pathway, transcription machinery, B cell receptor signaling pathway
 - **FL:** Wnt signaling pathway, PI3K-Akt signaling pathway, DNA replication

CONCLUSION AND OUTLOOK

- Genes from pathways involved in cancer initiation and progression contain **allele-specific methylated regions** and/or are **allele-specifically expressed** in lymphoma
- Genes **close to AMR** are more likely to be **mono-allelic expressed**
- Are the results **transferable** to other types of cancer?



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Acknowledgements:

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Jörg Fallmann
Peter F. Stadler





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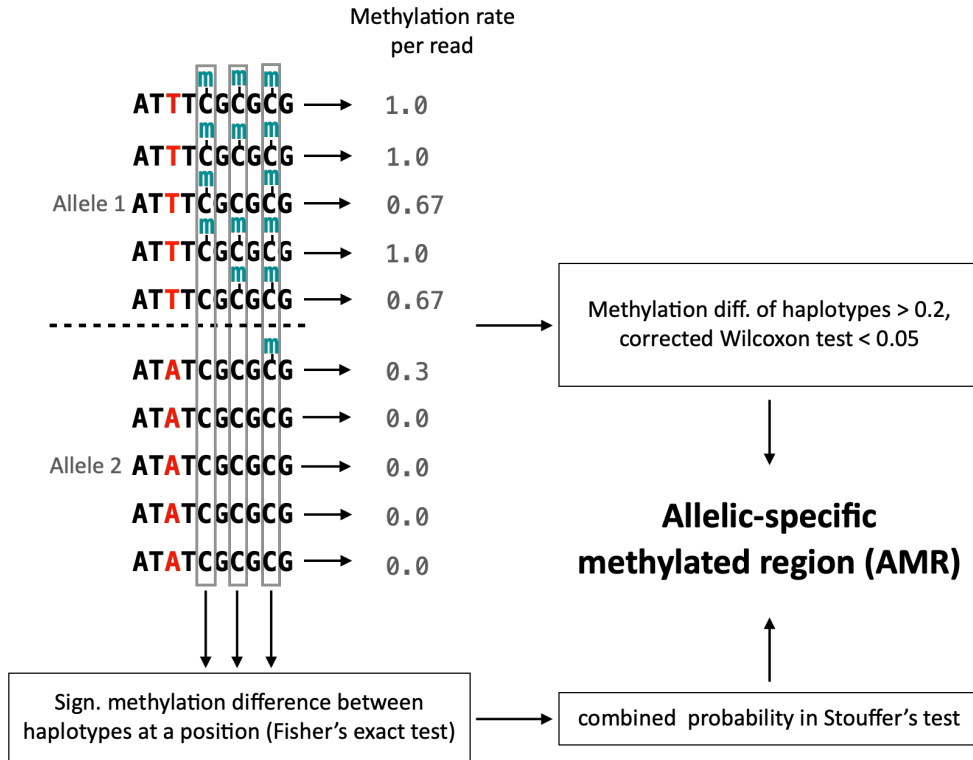
Acknowledgements:

Stephan H. Bernhart
Jörg Fallmann
Peter F. Stadler



THANK YOU

FAME ALGORITHM



RESULTS

	Burkitt lymphoma (BL)	Follicular lymphoma (FL)	Normal germinal center B cells (GC)
Allele-specific methylated regions (AMR)	750	489	212
Allele-specific expressed (ASE) genes	9240	3639	1107
ASE close to AMR	557	157	61