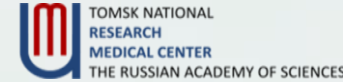


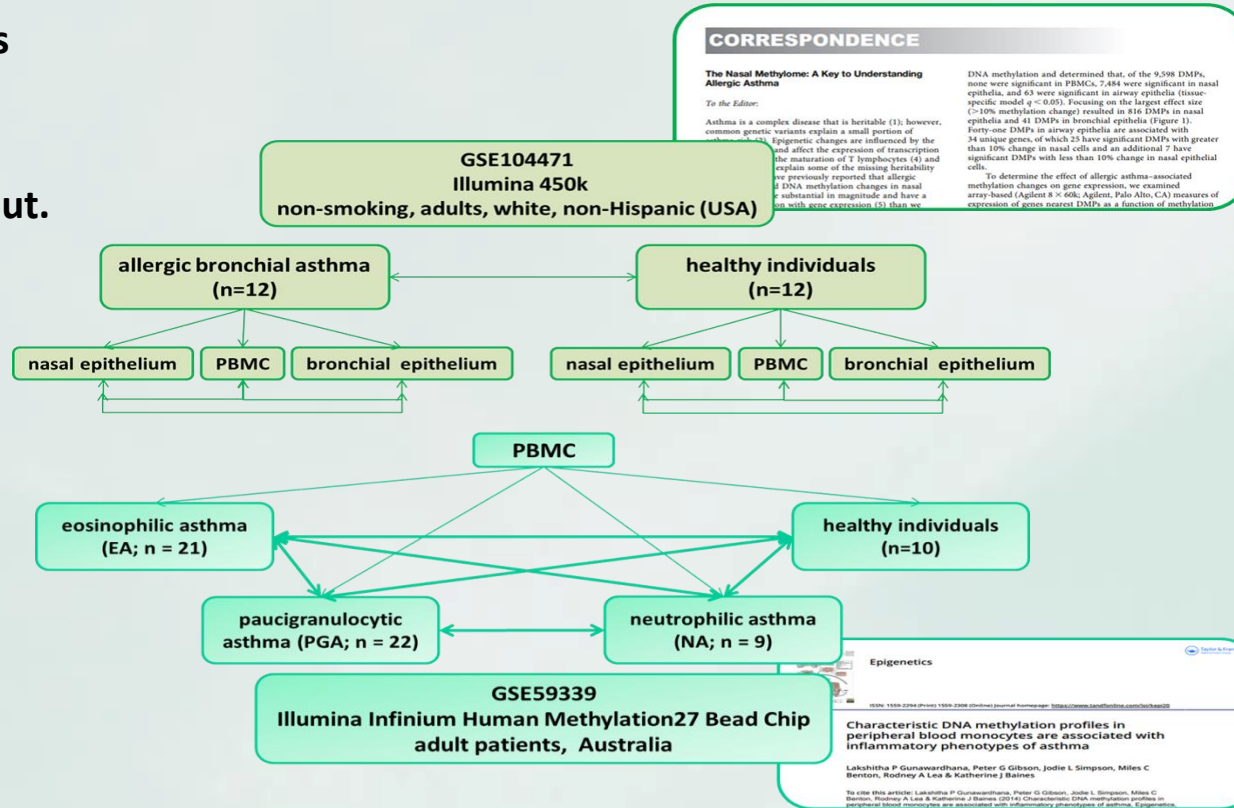
Re-analysis of DNA methylation in genes associated with bronchial asthma

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Re-analysis of two DMG datasets presented in the public repository of functional genomic data **Gene Expression Omnibus** was carried out.



Methods and Algorithms:

The analyzed target genes are divided into 3 subgroups:

1

associated with
asthma/tuberculosis
(*IFNG, SOCS5, TNFB,*
TNFRSF1B, PIAS3,
PIASY, CXCL10, ATM, ,
NBN, MRE11, MLH1,
PMS2, TP53BP1)

all groups
comparison of
GSE104471 and
GSE59339 datasets

2

interesting from the
point of view of atopy
(*TNF, IL13, IL4, IL4R,*
TGFB1, MS4A2, HLA-
DRB1, HLA-DQB1, CD14,
LTC4S, IL10, TLR2, CTLA4,
HLA-DQA1)

all groups comparisons
of the GSE104471 data
set and in the
comparison groups of
the GSE59339 set with
eosinophilic asthma

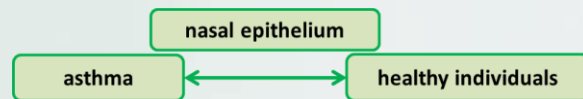
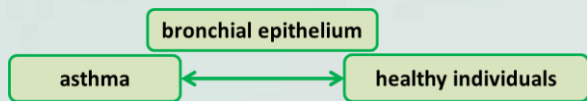
3

interesting from the point
of view of syntropy of
asthma and diseases of the
cardiovascular system
(*ANG, RNASE4,*
LOC105376244, TLR4,
AL160272.2, ABTB2, CAT)

groups of the GSE59339
set, with neutrophilic and
paucigranulocytic asthma

Results:

Significant differences in the level of DNA methylation of target genes, taking into account the **FDR correction**, were obtained **only** when comparing methylation **between asthma patients and healthy individuals - in both nasal and bronchial epithelial cells.**



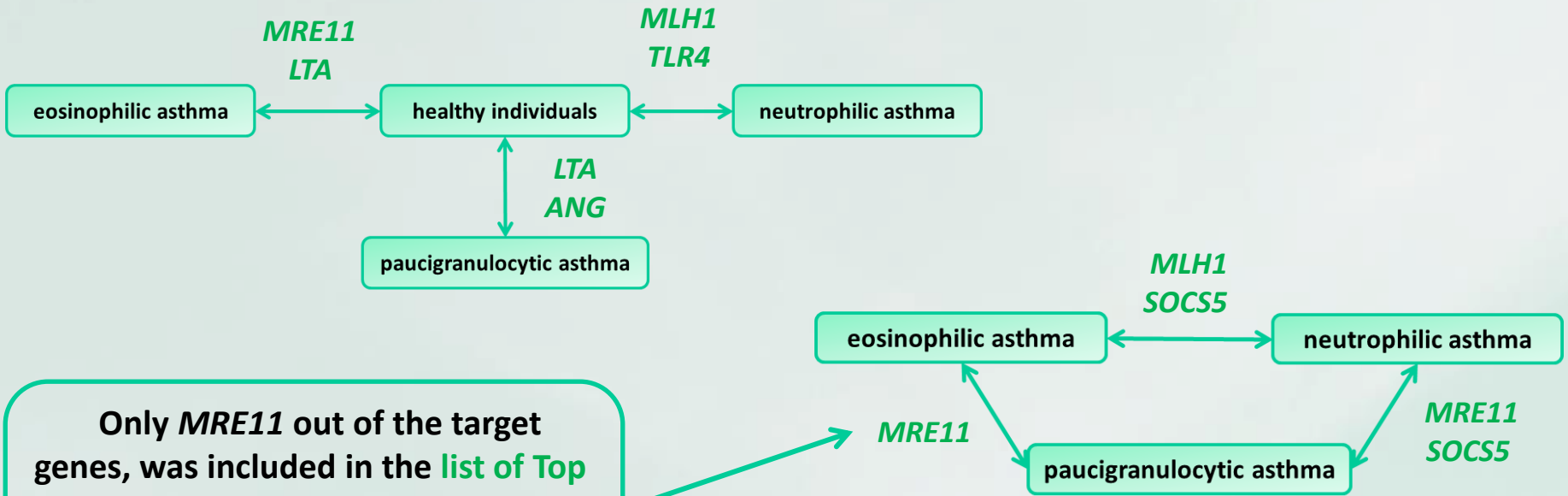
of 175 CpG-sites in 8 genes (*MRE11*, *MLH1*, *TP53BP1*, *TNF*, *TGFB1*, *HLA-DRB1*, *HLA-DQB1*, *CD14*), **differential methylation** was shown with $p < 0.05$ - for 41 CpG-sites, with $pFDR < 0.05$ - for 6 CpG-sites: 3 in the *MLH1* gene, one site each in the *TNF*, *TGFB1*, and *HLA-DRB1* genes

of 228 CpG-sites in 13 genes, **differential methylation** was shown with $p < 0.05$ - for 18 CpG-sites in the *ATM*, *MLH1*, *MRE11*, *PMS2*, *TP53BP1*, *IL13*, *IL4*, *TGFB1*, *HLA-DRB1*, *HLA-DQB1*, *TLR2*, *CTLA4*, *HLA-DQA1* genes, with $pFDR < 0.05$ all differences do not reach a significant level.

of 103 CpG-sites in 11 genes (*ATM*, *TP53BP1*, *IFNG*, *LTA*, *TNFRSF1B*, *PIAS3*, *IL4R*, *TGFB1*, *CD14*, *LTC4S*, *TLR2*), **differential methylation** was shown with $p < 0.05$ - for 39 CpG-sites in these genes, with $pFDR < 0.05$ - for 18 CpG-sites

Results:

- When analyzing the GSE59339 dataset **after the FDR correction, no statistically significant differences** were found for any of the CpG-sites of the target genes. However, **without an FDR test, differences in methylation are detected in all types of comparisons:**



Only *MRE11* out of the target genes, was included in the list of Top 50 differentially methylated genes (DMG) when comparing EA and PGA ($p=0.00028$)

Conclusion:

- ✓ **The data obtained as a result of reanalysis on differences in the level of DNA methylation of a number of genes associated with bronchial asthma indicate the potential significance of epigenetic modifications in predisposition to this pathology.**

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