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3 **The utility of resolving asthma molecular signatures using tissue-specific transcriptome data**
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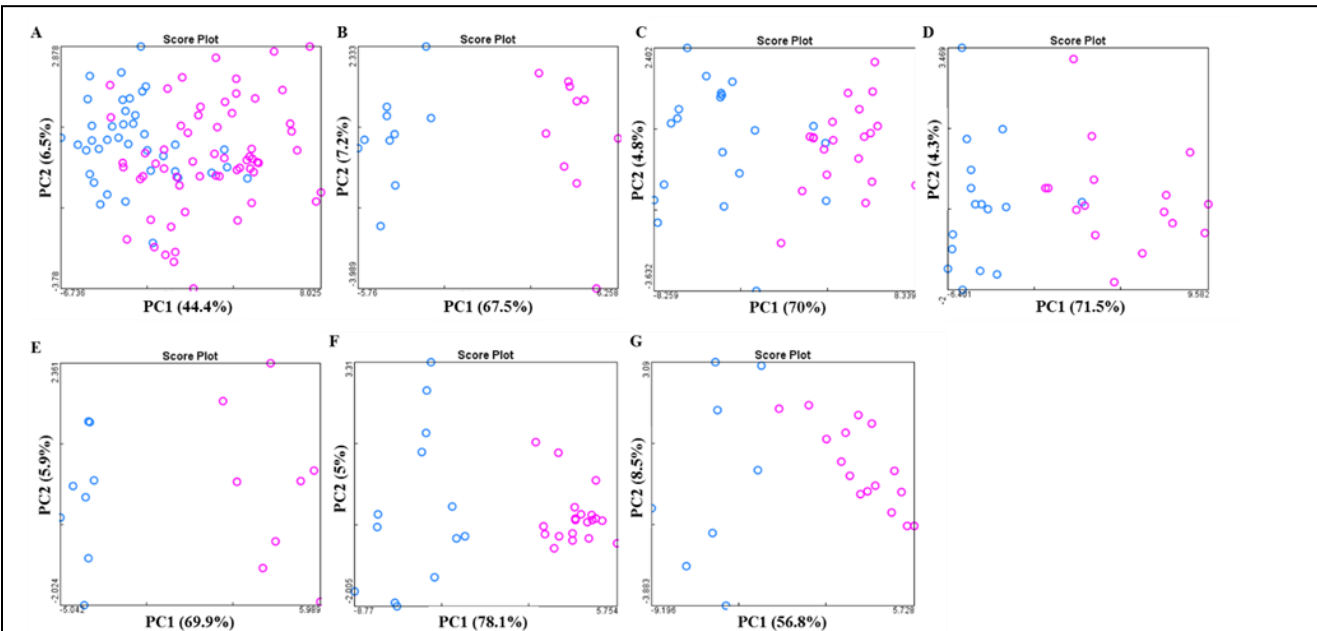41
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46 **Figure S1**
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Figure S1. Tissue combined (A) and tissue-specific (B-G) DEGs-based principal component analysis (PCA). Tissue-resolved approach shows distinct separation of samples.
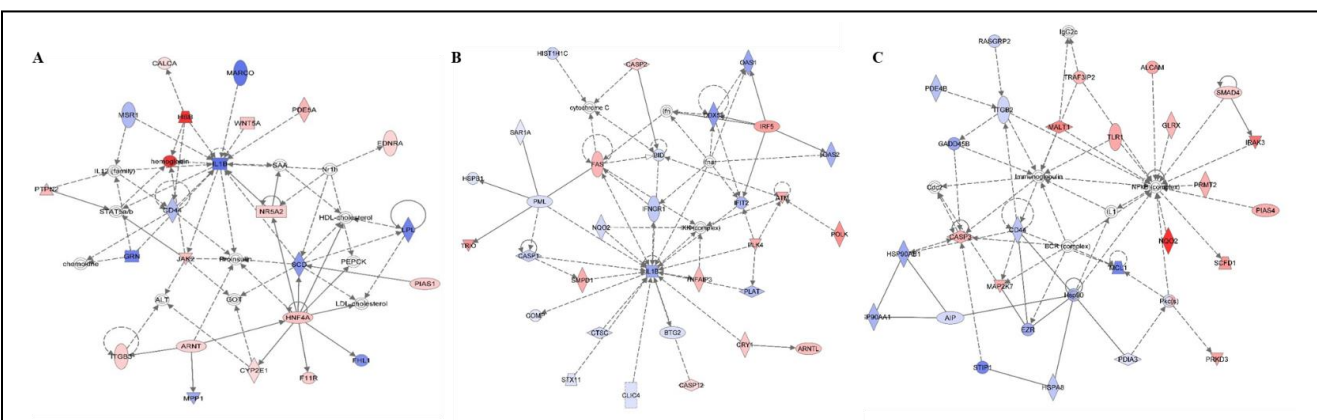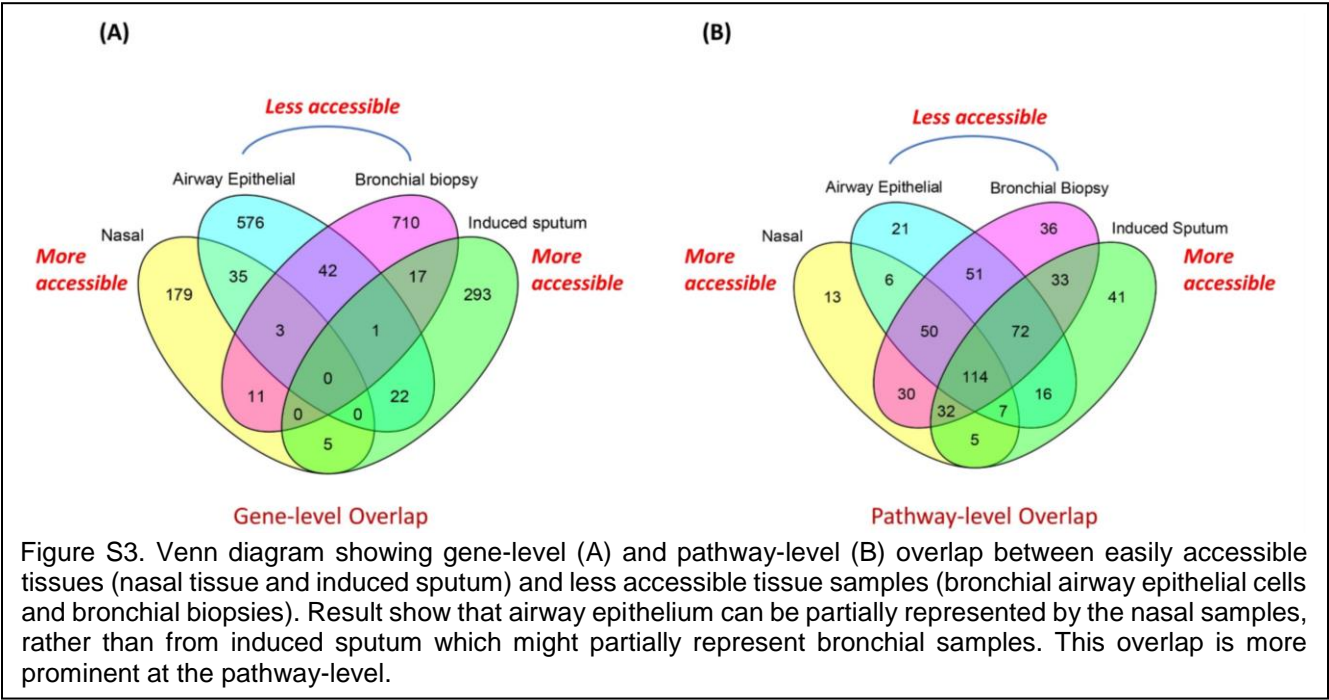
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51 **Figure S2**
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Figure S2. Tissue-specific gene networks in asthma: IL-12 and ERK are the major hub genes in Macrophages (A) indicating the role of sustained inflammation via the IL12 pathway and control of cell proliferation via ERK pathway in this cell type. The up-regulation of extracellular matrix-associated molecules and actin binding as well as cytoskeletal protein molecules have been previously reported in case of proximal (B) and distal (C) lung fibroblasts, respectively.

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Figure S3

Figure S3. Venn diagram showing gene-level (A) and pathway-level (B) overlap between easily accessible tissues (nasal tissue and induced sputum) and less accessible tissue samples (bronchial airway epithelial cells and bronchial biopsies). Result show that airway epithelium can be partially represented by the nasal samples, rather than from induced sputum which might partially represent bronchial samples. This overlap is more prominent at the pathway-level.

Figure S4

Figure S4. Support Vector Machine based prediction accuracy of DEGs in discriminating asthma from control samples in each tissue. The dashed lines are for testing data.
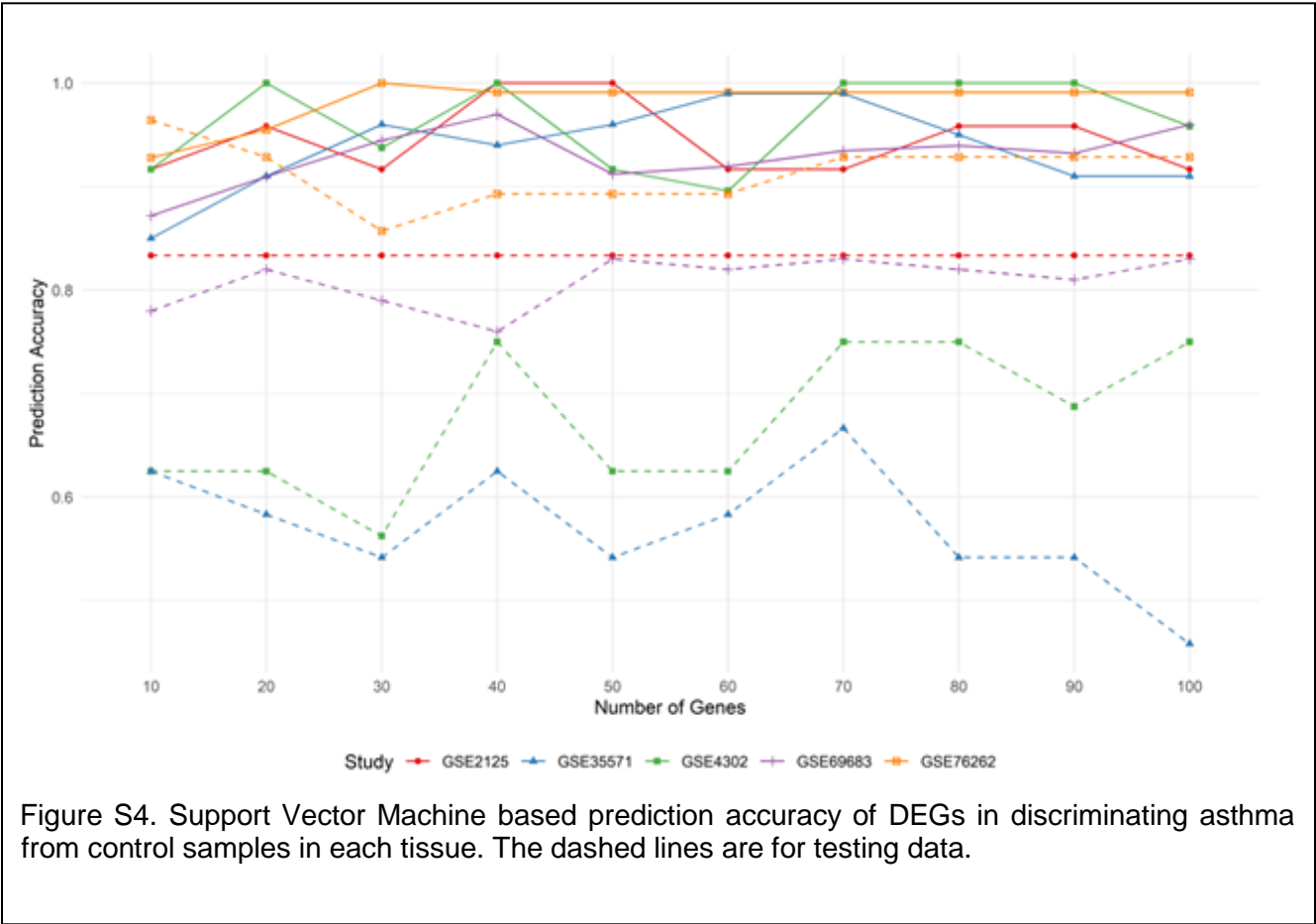
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Table S1. Connectivity scores of perturbagens that connected with at least 3 different tissue/ samples types of asthmatics. Positive and negative scores are shown in red and blue background respectively.

Perturbagens	FibroDistal	CD8	Nasal	Blood	Bronchial	Sputum	AirEpi	CD4	Macrophage	FibroProximal
KLF6	96.61	96.58	99.58	41.78	0	0	96.94	0	99.16	0
entinostat	98.77	86	88.91	-89.98	1.48	-93.42	-0.63	8.04	98.97	43.02
HOXB13	98.84	75.31	86.31	66.66	0	86.6	0	12.12	98.82	37.36
BCL10	97.31	6.16	5.83	96.34	0	39.75	7.32	88.47	97.66	70.35
IFNB1	98.52	86.38	77.85	93.62	5.79	94.33	80.89	51.65	-45.14	80.06
YWHAZ	0	2.53	93.94	-42.28	92.14	41.38	96.69	-29.4	-84.74	-93.49
PPP2R3C	44	-2.97	1.62	94.67	57.61	12.53	96.53	3.08	99.18	0
DTX2	-55.57	0	88.84	-20.19	0	90.86	96.07	0	-36.99	0
LASP1	16.38	86.23	3.55	-86.95	2.76	-4.55	93.02	-4.69	94.87	0
XPO7	-5.14	47.49	0	-43.59	87.25	85.99	88.72	68.17	-68.21	26.71
LOXL1	-84.63	0	71.07	94.6	-68.73	95.36	86.11	-5.16	-60.55	0
CDCA8	7.69	-65.65	76.62	88.71	0	2.96	85.32	34.52	68.63	3.56
PUF60	45.69	89.38	96.43	-32.01	4.5	-66.63	-4.68	40.53	99.66	4.72
TRIP10	22.61	35.18	5.72	-62.88	87.4	-26.13	0	0	99.4	0
calyculin	99.61	-53.54	-96.17	98.38	0	-95.02	-98.66	10.68	98.13	2.64
PREB	93.22	0	-14.74	5.98	0	0	0	0	97.89	90.34
BAMBI	18.34	0	0	-34.17	0	93.66	0	17.65	97	0
SORBS3	28.59	0	92.58	-11.45	10.31	-36.43	79.52	4.58	96.71	91.17
importazole	-29.71	97.49	93.9	-71.03	0	-99.65	11.65	30.11	90.3	-0.63
CCNL1	93.65	88.84	23.06	2.28	0	-27.58	-2.18	1.2	89.35	0
DHX8	-69.08	0	0	87.31	85.23	95.58	10.08	45.59	-18.98	0
KLF3	96.97	94.41	29.1	32.37	0	-71.85	29.9	0	45.04	0
BMS-345541	92.82	96.93	93.65	-87.24	0	-54.89	49.87	58.53	-60.92	53.65
ATOX1	86.39	0	1.99	2.18	0	-10.93	20.12	86.52	27.22	0
topotecan	19.32	98.48	97.96	-29.64	0	-86.33	32.73	90.06	57.41	0

Table S2. Description of connected perturbagens relevant for asthma. Type (based on biological / chemical function drug), location and entrez names of genetic perturbagens have been shown. Twenty-five perturbagens (listed in Table 3) associated with at least three different asthma-relevant tissue/ sample types have been listed here.

Perturbagen	Type(s)	Location*	Entrez Gene Name*
ATOX1	transporter	Cytoplasm	AI256639 antioxidant 1 copper chaperone Atx1
BAMBI	TGF–beta psudoreceptor	Plasma Membrane	2610003H06Rik BMP and activin membrane-bound inhibitor
BCL10	transcription regulator	Cytoplasm	BCL10 immune signaling adaptor
BMS-345541	chemical drug (IKK-2 inhibitor)	Other	
calyculin A	chemical toxicant	Other	
CCNL1	other	Nucleus	cyclin L1
CDCA8	other	Nucleus	cell division cycle associated 8
DHX8	enzyme	Nucleus	DEAH-box helicase 8
DTX2	other	Nucleus	deltex E3 ubiquitin ligase 2
entinostat	chemical drug	Other	
HOXB13	transcription regulator	Nucleus	homeobox B13
IFNB1	cytokine	Extracellular Space	interferon beta 1
Importazole	chemical drug (Inhibitor of importin-β)	Other	
KLF3	transcription regulator	Nucleus	Kruppel like factor 3
KLF6	transcription regulator	Nucleus	Kruppel like factor 6
LASP1	cytoskeletal activities	Cytoplasm	LIM and SH3 protein 1
LOXL1	enzyme	Extracellular Space	lysyl oxidase like 1
PPP2R3C	other	Cytoplasm	protein phosphatase 2 regulatory subunit B''gamma
PREB	transcription regulator	Nucleus	prolactin regulatory element binding
PUF60	other	Nucleus	poly(U) binding splicing factor 60
SORBS3	other	Cytoplasm	sorbin and SH3 domain containing 3
topotecan	biologic drug (topoisomerase inhibitor)	Other	
TRIP10	other	Cytoplasm	thyroid hormone receptor interactor 10
XPO7	transporter	Nucleus	exportin 7
YWHAZ	enzyme	Cytoplasm	tryptophan 5-monooxygenase activation protein zeta

*For genetic perturbagens