415. Airway Gene-Expression Classifiers for Respiratory Syncytial Virus (RSV) Disease Severity in Infants

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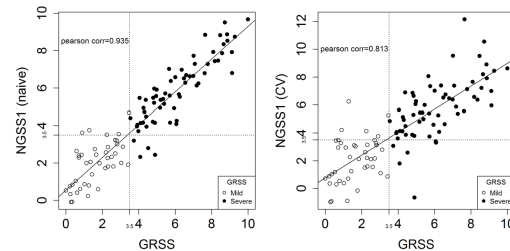
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Thursday, October 3, 2019: 12:15 PM

Background. RSV infection is common in infants with a majority of those affected displaying mild clinical symptoms. However, a substantial number develop severe symptoms requiring hospitalization. We currently lack sensitive and specific predictors to identify a majority of those who develop severe disease.

Methods. High throughput RNA sequencing (RNAseq) of nasal epithelial cells defined airway gene expression patterns in RSV-infected subjects. Using multivariate linear regression analysis with AIC-based model selection, we built a sparse linear predictor of RSV disease severity, the Nasal Gene Severity Score-NGSS1. Using a similar statistical approach, we built an alternate predictor based upon genes displaying stable expression over time (NGSS2). We evaluated predictive performance of both models using leave-one-out cross-validation analyses.

Results. We defined comprehensive airway gene expression profiles from 106 full-tem previously healthy RSV-infected subjects with a range of RSV disease severity prospectively enrolled in the AsPIRES study. Nasal samples were obtained during acute infection (day 1–10 of illness; 106 samples), and convalescence (day 14–28 of illness; 69 samples). All subjects had a primary infection and were assigned a cumulative clinical illness severity score (GRSS) (Table 1). From the RNA seq data 41 genes were identified as the NGSS1 which is strongly correlated with disease severity (GRSS) in both the naive (ρ=0.935) and cross-validated analysis (ρ of 0.813). As a binary classifier (mild vs. severe), NGSS1 correctly classifies 89.6% of the subjects following cross-validation (Figure 1). Next, we evaluated genes that were stably expressed in both acute illness and convalescence samples in 54 subjects with data from both time points. Repeating the regression based step wise model selection identified 13 genes as NGSS2, which was significantly correlated with GRSS (ρ = 0.741). This model has slightly less, but comparable, prediction accuracy with a cross-validated correlation of 0.741 and cross-validated classification accuracy of 84.0% (Figure 2).

Conclusion. Airway gene expression patterns, obtained following a minimally-invasive nasal procedure, have potential utility as prognostic biomarkers for severe infant RSV infections.

Table 1.Characteristics of RSV infected infants divided into mild or severe disease. *P*-values reported in the last column were either based on Fisher's exact test (if the variable is categorical) or Welch *t*-test (if the variable is continuous).

		mild (n=42)[a]		severe (n=64)[a]		
		n	Mean (SE) or %	n	Mean (SE) or %	p value
Global Respiratory Severity Score		42	1.63(0.15)	64	6.13(0.22)	<0.001
Visit Age (months)		42	3.52(0.31)	64	3.24(0.3)	0.5122
Gestational Age (weeks)		42	39.05(0.19)	64	38.8(0.18)	0.3437
Birth Weight (kg)		42	3.32(0.11)	64	3.36(0.07)	0.7468
Family Size		42	4.43(0.44)	64	3.98(0.22)	0.3703
Days Since Disease Onset		42	4.31(0.27)	64	4.86(0.22)	0.1209
Breast Feeding Summary		42	1.56(0.19)	63	1.53(0.16)	0.8979
Sex						
	Male	23	44.23	29	55.77	0.4275
	Female	19	35.19	35	64.81	
Ethnicity						
	Hispanic or Latino	8	42.11	11	57.89	0.8018
	Non-Hispanic or Non-Latino	34	39.08	53	60.92	
Race						
	Caucasian	23	37.1	39	62.9	0.3115
	Other race	19	47.5	21	52.5	
	Missing	-	0	4	100	
Delivery Type						
	Vaginal	29	36.71	50	63.29	0.3634
	C-section	13	48.15	14	51.85	
Smoking Exposure						
	True	14	38.89	22	61.11	1
	False	28	40	42	60	
RSV Strain						
	A	23	38.98	36	61.02	1
	B	18	39.13	28	60.87	
	Missing	1	100	-	0	

[a] based on GRSS ≤3.5 (mild) or > 3.5 (severe)

Figure 1. Correlating NGSS1 with GRSS. Left: naïve Pearson correlation between GRSS and NGSS1 is $\rho = 0.935$. Right: cross-validated Pearson correlation between GRSS and NGSS is $\rho = 0.813$. Solid dots are subjects with severe symptoms (defined by GRSS>3.5) and empty dots are those with mild symptoms (GRSS≤3.5).
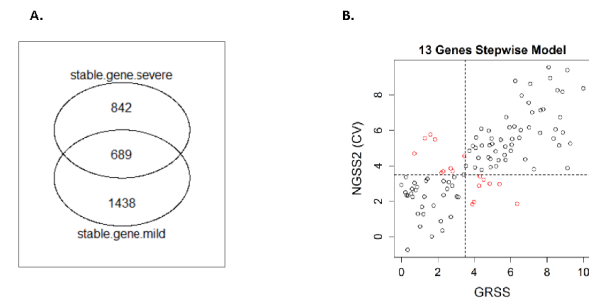
Figure 2. (A). Diagram indicating the stable genes for the mild (GRSS ≤3.5) and severe (GRSS >3.5) groups and the 689 intersecting stable genes common to both groups. (B). Correlating NGSS2 with GRSS. Naïve Pearson correlation between GRSS and NGSS2 is $\rho = 0.800$. Right: cross-validated Pearson correlation between GRSS and NGSS is $\rho = 0.741$. Solid dots are subjects with severe symptoms (defined by GRSS>3.5) and empty dots are those with mild symptoms (GRSS≤3.5).

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416. Improvement in Syphilis and HIV Screening Rates at a Community-Based Emergency Department in Columbus, Ohio: Six Month Post-Intervention Analysis

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Thursday, October 3, 2019: 12:15 PM

Background. Sexually transmitted infections (STIs) disproportionally affect individuals living in underserved areas and Emergency Departments (ED) can play a major role in STI screening. Given the overlapping risk factors for STIs, patients screened for gonorrhea and chlamydia should also be screened for syphilis and HIV. Rates of syphilis/HIV screening in the ED are very low and barriers include lack of knowledge about the risk/prevalence, difficulty with results interpretation, and concerns about follow-up.

Methods. The main study objective was to improve rates of syphilis/HIV screening in a community-based ED in Columbus, OH. A team of clinical providers, case managers, and social workers was formed to address barriers to screening. Using root cause analysis and data feedback, a multistep intervention that included provider education along with expert review of syphilis/HIV results was implemented to ensure proper screening, treatment and rapid linkage to care. Syphilis/HIV screening rates in the ED were compared between two periods: 2012–2017 (pre-intervention) and November 2018–April 2019 (post-intervention).

Results. Between 2012 and 2017, there were 24,427 ED encounters where any STI test was ordered. There were 23,652 (97%) tests for chlamydia, 23,637 (97%) for gonorrhea, 254 (1%) for syphilis, and 466 (2%) for HIV. Twenty-four (0.1%) encounters had screening that included all four tests. Six months after starting the intervention, there were 1,590 encounters where any STI test was ordered. There were 1,444 (91%) tests for chlamydia, 1,446 (91%) for gonorrhea, 493 (31%) for syphilis and 591 (37%) for HIV. Four hundred thirty-eight (28%) of encounters had screening that included all four tests.

Conclusion. Collaborative and practical interventions aimed at improving syphilis/HIV testing have resulted in dramatic increases in syphilis, HIV, and comprehensive STI screening (31-, 19-, 280-fold, respectively) over a relatively short post-intervention period. Additional steps are planned with the goal to further increase screening rates and improve linkage to prevention and treatment programs.

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