



Differential Gene Expression Elicited by Children in Response to the 2015-16 Live Attenuated versus Inactivated Influenza Vaccine

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Background:

- In the influenza seasons preceding the ACIP's withdrawal of its recommendation for the live attenuated influenza vaccine (LAIV), it had not demonstrated the same level of vaccine effectiveness as the inactivated influenza vaccine (IIV) among children.

- This study compared the mRNA sequencing transcription profile (RNA seq) in children who received either IIV or LAIV during 2015, the last season in which LAIV was recommended for use in the U.S.

Methods:

- Children 3-17 years received the quadrivalent influenza vaccine of their choice.
- Blood samples were collected on Day 0 pre- & Day 7 (range 6-10 days) post vaccination.
- Total RNA was isolated from PAXgene tubes and sequenced for a custom panel of 89 transcripts.
- Fold differences in normalized RNA seq counts from Day 0 to Day 7 were calculated, log₂ transformed and compared between the two vaccine groups.

Results:

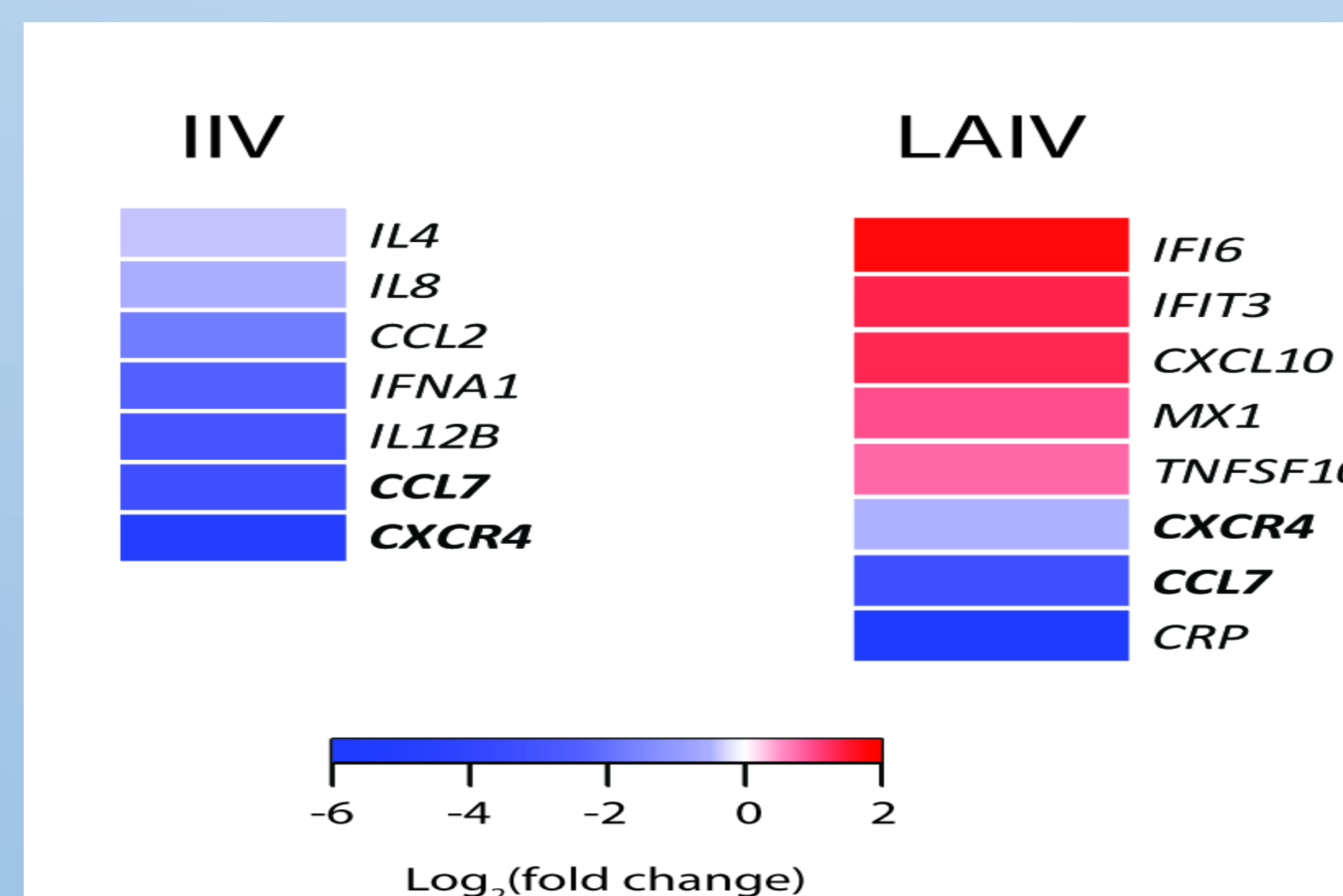
- 46 children received IIV and 26 received LAIV.
- Following IIV, 7 genes were significantly down-regulated at Day 7.
- Following LAIV vaccination, (5 genes were significantly up-regulated and 3 were down-regulated) at Day 7.
- Only two genes demonstrated similar patterns of regulation in both groups.

Table 1. Demographic Characteristics of Participants Overall and by 2015-2016 Influenza Vaccine Type

Variable	Total N=72	LAIV* N=26	IIV** N=46	P-value [†]
	n (%)	n (%)	n (%)	
Age 9-17 years, ref. = 3-8 years	58 (80.6)	20 (76.9)	38 (82.6)	0.558
Male, ref. = female	31 (43.1)	9 (34.6)	22 (47.8)	0.277
Black race, ref. = white and others	62 (86.1)	22 (84.6)	40 (87.0)	0.783
Parent's education ≥ some college, ref. = high school or less	40 (55.6)	16 (61.5)	24 (52.2)	0.442
Public health insurance, ref. = private insurance	64 (88.9)	24 (92.3)	40 (87.0)	0.488
Smoker in household	31 (43.1)	8 (30.8)	23 (50.0)	0.113

*Live attenuated influenza vaccine; **Inactivated influenza vaccine; [†]By Chi-square test

Figure. Heat maps of RNA-seq responses to IIV and LAIV



Heat maps representing differential expression of genes between Day 0 (pre) and Day 7 (post) vaccination based on P<0.05. IIV = inactivated influenza vaccine; LAIV = live attenuated influenza vaccine

Table 2. Differential Gene Expression in Response to Vaccination with Inactivated Influenza Vaccine (IIV) and Live Attenuated Influenza Vaccine (LAIV)

Gene Name	Inactivated Influenza Vaccine (IIV)						Live Attenuated Influenza Vaccine (LAIV)					
	Normalized Mean Counts		Fold Change	Log ₂ Fold Change	P-value	Q-value	Normalized Mean Counts		Fold Change	Log ₂ Fold Change	P-value	Q-value
	Day 0	Day 7					Day 0	Day 7				
CCL 2	2250.4	666.4	0.30	-1.76	0.000	0.000	1222.5	982.8	0.80	-0.31	0.418	0.995
CCL 7	218.2	21.7	0.10	-3.33	0.000	0.000	148.2	15.2	0.10	-3.29	0.000	0.000
CRP	0.0	0.3	10.8	3.44	0.469	0.964	4.0	0.0	0.01	-6.77	0.009	0.127
CXCL 10	194.5	214.3	1.10	0.14	0.699	0.964	118.6	297.5	2.50	1.33	0.016	0.186
CXCR 4	85358.2	65535.9	0.77	-5.06	0.005	0.090	96750.5	69100.4	0.71	-0.49	0.024	0.208
IFI 6	5583.3	5884.0	1.10	0.08	0.891	0.964	3132.5	10545.8	3.40	1.75	0.000	0.007
IFIT 3	5185.3	5437.8	1.00	0.07	0.697	0.964	3065.8	7878.8	2.60	1.36	0.001	0.036
IFNA 1	13.3	2.5	0.19	-2.40	0.014	0.175	11.3	5.6	0.50	-1.01	0.449	0.995
IL 12B	13.9	1.7	0.12	-3.02	0.011	0.163	3.6	5.5	1.50	0.62	0.635	0.995
IL 4	5.3	0.2	0.03	-0.38	0.001	0.038	79.5	96.3	1.20	0.28	0.597	0.995
IL 8	33833.4	23295.4	0.69	-0.54	0.002	0.038	30873.1	26617.8	0.86	-0.21	0.309	0.995
MX 1	6148.1	6471.1	1.10	0.07	0.707	0.964	4289.6	8382.4	2.00	0.97	0.022	0.208
TNFSF 10	29765.0	35952.3	1.20	0.27	0.102	0.665	22680.5	39467.1	1.70	0.80	0.025	0.208

NOTE: The two genes that are common between the two vaccine types are highlighted yellow; bolded P-values indicate significance. Normalized mean counts obtained for each gene on Day 0 pre-, or Day 7 post influenza vaccination; fold change refers to the ratio of mean counts on Day 0 and mean counts on Day 7.

Conclusions:

Differential regulation of genes was observed between 2015-16 LAIV and IIV recipients. These results may be related to the difference in vaccine effectiveness observed in recent years between LAIV and IIV.

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