



Title	High co-expression of IL-34 and M-CSF correlates with tumor progression and poor survival in lung cancers
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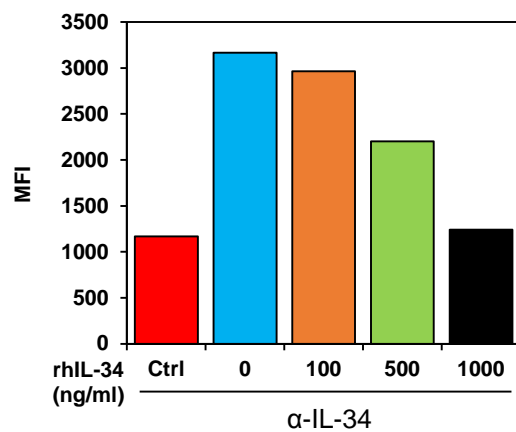
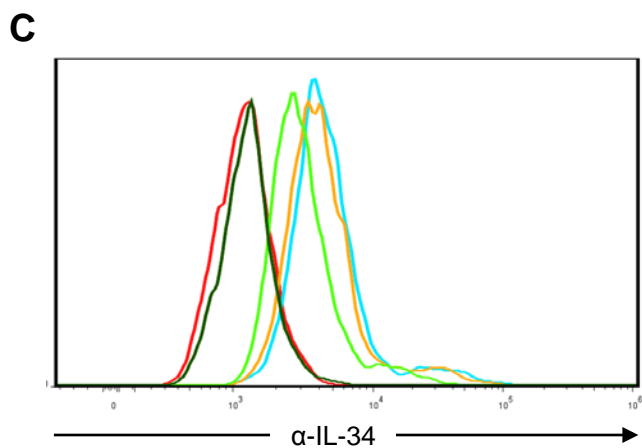
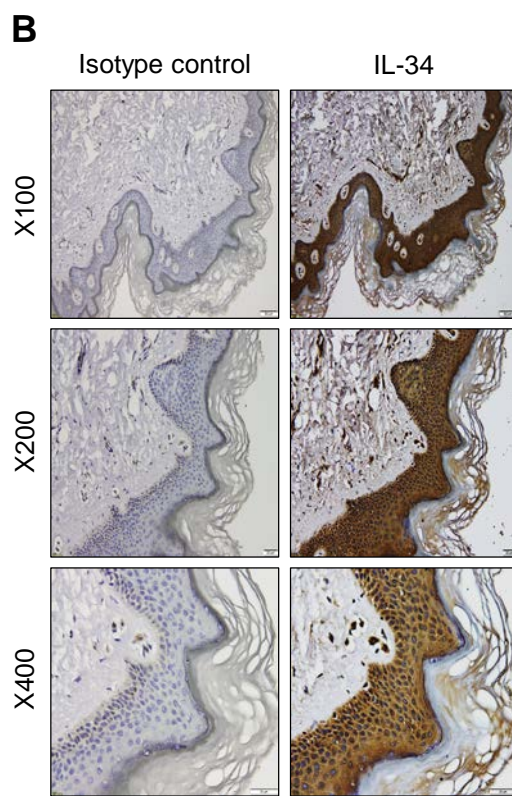
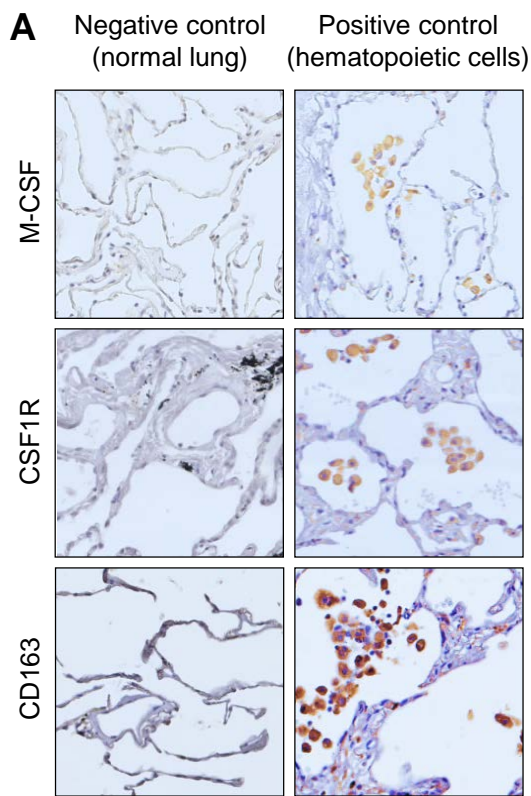


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Supplementary information

High co-expression of IL-34 and M-CSF correlates with tumor progression and poor survival in lung cancers

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Supplementary figure 1

Confirmation of antibodies specificity. **(A)** Immunohistochemistry staining of M-CSF, CSF1R or CD163 is shown in hematopoietic cells (positive control) compare to normal lung (negative control). **(B)** Specific staining of IL-34 in keratinocytes of normal skin is shown by immunohistochemistry. **(C)** Intracellular staining of IL-34 in IL-34-producing A549 cells as analyzed by flowcytometry (left) and bar graph (right). Adding soluble antigen (recombinant human IL-34) results in decreased staining levels of IL-34 in a dose-dependent manner, indicating antibody specificity.

Supplementary table. 1**The relation between IL-34 / M-CSF / CD163 expression in lung cancer tissues****A. Relation between IL-34 and M-CSF expression in lung cancer tissues**

	Total	IL-34 expression			P-value
		High	Weak	Absent	
	n = 332	n = 83	n = 79	n = 170	
M-CSF expression					
High	71	40	15	16	< 0.0001*
Weak	147	36	47	64	
Absent	114	7	17	90	

* $P < 0.05$ (Fisher's exact test)

B. Relation between M-CSF and CD163 expression in lung cancer tissues

	Total	M-CSF expression		P-value
		Positive	Negative	
	n = 332	n = 218	n = 114	
CD163 expression				
High	113	98	15	< 0.0001*
Weak or absent	219	120	99	

* $P < 0.05$ (Fisher's exact test)

C. Relation between IL-34 and CD163 expression in lung cancer tissues

	Total	IL-34 expression		P-value
		Positive	Negative	
	n = 332	n = 162	n = 170	
CD163 expression				
High	113	64	49	0.0488*
Weak or absent	219	98	121	

* $P < 0.05$ (Fisher's exact test)

Supplementary table. 2

Association between IL-34 expression and disease stages in lung cancer

	Total n = 332	High n = 83	Weak n = 79	Absent n = 170	P-value High vs. W/A
Gender					
Male	181	48	44	89	0.5257
Female	151	35	35	81	
Age (years)					
< 65	143	38	32	73	0.6094
65 ≥	189	45	47	97	
Histology					
ADC	277	66	70	141	0.1148 [#]
SCC	32	10	7	15	
LCC	5	2	1	2	
Others	18	5	1	12	
Stage					
IA	157	27	39	91	0.0004*, ^{##}
IB	100	25	25	50	
IIA	30	12	5	13	
IIB	16	6	2	8	
IIIA	29	13	8	8	
pT					
T1	176	35	42	99	0.0305*
T2-T3	156	48	37	71	
pN					
N0	277	58	68	151	0.0003*
N1-N2	55	25	11	19	
Smoking status					
Never smoker	138	32	35	71	0.6064 ^{###}
Ex-smoker	157	42	40	75	
Current smoker	35	8	4	23	
Unknown	2	1	0	1	

*P < 0.05 (Fisher's exact test)

[#] ADC vs non-ADC

^{##}stage I vs stage II-III A

^{###}Never vs. Ex/Current smoker

Supplementary table. 3

Association between M-CSF expression and disease stages in lung cancer

	Total n = 332	High n = 71	Weak n = 147	Absent n = 114	P-value High vs. W/A
Gender					
Male	181	52	73	56	0.004*
Female	151	19	74	58	
Age (years)					
< 65	143	30	64	49	0.8934
65 ≥	189	41	83	65	
Histology					
ADC	277	44	126	107	<0.0001*,##
SCC	32	17	12	3	
LCC	5	3	2	0	
Others	18	7	7	4	
Stage					
IA	157	24	71	62	0.0062*,##
IB	100	22	47	31	
IIA	30	6	13	11	
IIB	16	8	4	4	
IIIA	29	11	12	6	
pT					
T1	176	27	79	70	0.049*
T2-T3	156	44	68	44	
pN					
N0	277	53	124	100	0.0308*
N1-N2	55	18	23	14	
Smoking status					
Never smoker	138	19	64	55	0.0061###
Ex-smoker	157	44	69	44	
Current smoker	35	7	13	15	
Unknown	2	1	0	1	

*P < 0.05 (Fisher's exact test)

ADC vs non-ADC

##stage I vs stage II-III A

###Never vs. Ex/Current smoker

Supplementary table. 4

Correlation between IL-34 and M-CSF expression and stages in lung cancer patients

A. Correlation between IL-34 expression and stages in lung cancer patients

	Total	High	Weak	Absent	<i>P</i> -value
	n = 332	n = 83	n = 79	n = 170	High vs. Weak/Absent
Stage					
IA	157	27	39	91	
IB	100	25	25	50	
IIA	30	12	5	13	0.0004*, #
IIB	16	6	2	8	
IIIA	29	13	8	8	

**P* < 0.05 (Fisher's exact test) #stage I vs stage II-III A

B. Correlation between M-CSF expression and stages in lung cancer patients

	Total	High	Weak	Absent	<i>P</i> -value
	n = 332	n = 71	n = 147	n = 114	High vs. Weak/Absent
Stage					
IA	157	24	71	62	
IB	100	22	47	31	
IIA	30	6	13	11	0.0062*, #
IIB	16	8	4	4	
IIIA	29	11	12	6	

**P* < 0.05 (Fisher's exact test) #stage I vs stage II-III A

C. Correlation between IL-34 / M-CSF expression and stages in lung cancer patients

	Total	IL-34 W/A	IL-34 High	IL-34 W/A	IL-34 High	<i>P</i> -value
	n = 332	M-CSF W/A	M-CSF W/A	M-CSF High	M-CSF High	High vs. others
	n = 332	n = 71	n = 147	n = 114		
Stage						
IA	157	119	14	11	13	
IB	100	64	14	11	11	
IIA	30	17	7	1	5	0.0081*, #
IIB	16	6	2	4	4	
IIIA	29	12	6	4	7	

**P* < 0.05 (Fisher's exact test) #stage I vs stage II-III A W/A: Weak or Absent