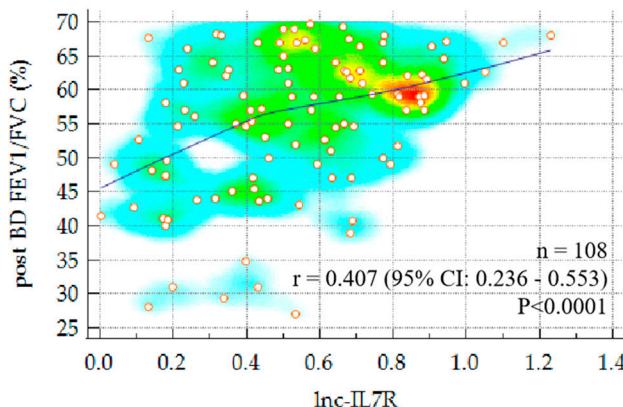
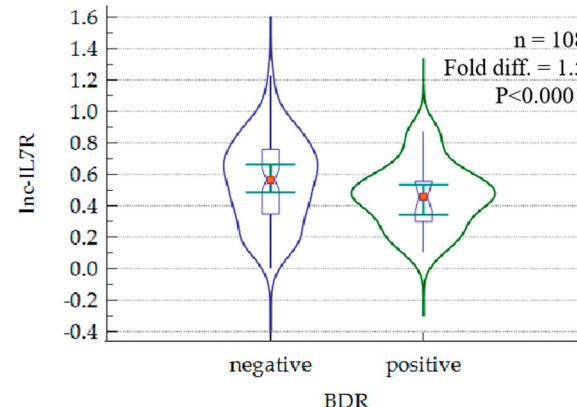
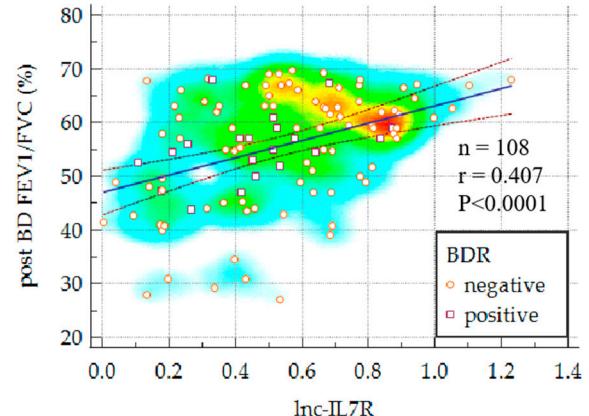


**Supplementary Table S1. Association of lnc-IL7R, with GOLD COPD severity, and pulmonary function in our cohort (n = 125)**

| Univariate       |     |                                | Multivariate, correlation coefficient (95% CI) |                      |                      |                      |                      |                      |                          |                       |                      |  |
|------------------|-----|--------------------------------|--|----------------------|----------------------|----------------------|----------------------|----------------------|--------------------------|-----------------------|----------------------|--|
| Variable         | N   | Mean (95% CI)                  | FEV1(%)  | FEV1(L)              | FVC(%)               | FVC(L)               | post-BD_FEV1/FVC     | Total LAA(%)         | %LAA- <sub>950insp</sub> | lnc-IL7R              | COPD severity (GOLD) |  |
| Sex              | 125 | 0.89 ± 0.32 (0.00 – 1.00)      | 0.19 (0.01 – 0.35)                             | 0.30 (0.13 – 0.45)   | 0.23 (0.05 – 0.39)   | 0.36 (0.20 – 0.51)   | 0.05 (–0.13 – 0.22)  | –0.05 (–0.22 – 0.13) | –0.08 (–0.25 – 0.10)     | –0.003 (–0.19 – 0.19) | –0.22 (–0.43 – 0.02) |  |
| Age              | 125 | 69.09 ± 7.76 (41.00 – 87.00)   | –0.02 (–0.19 – 0.16)                           | –0.31 (–0.46 – 0.14) | –0.05 (–0.22 – 0.13) | –0.39 (–0.53 – 0.23) | –0.06 (–0.23 – 0.12) | 0.04 (–0.14 – 0.21)  | 0.11 (–0.07 – 0.28)      | –0.09 (–0.27 – 0.10)  | –0.02 (–0.26 – 0.22) |  |
| BMI              | 122 | 23.54 ± 4.07 (15.80 – 36.20)   | 0.21 (0.04 – 0.38)                             | 0.27 (0.10 – 0.43)   | 0.10 (–0.07 – 0.28)  | 0.18 (0.00 – 0.35)   | 0.30 (0.13 – 0.45)   | –0.46 (–0.59 – 0.30) | –0.47 (–0.60 – 0.32)     | –0.08 (–0.11 – 0.27)  | –0.41 (–0.59 – 0.19) |  |
| Smoking_Hx       | 125 | 1.384 ± 0.63 (0.00 – 2.00)     | –0.11 (–0.28 – 0.07)                           | –0.15 (–0.31 – 0.03) | –0.01 (–0.18 – 0.17) | –0.10 (–0.28 – 0.07) | –0.23 (–0.39 – 0.05) | 0.26 (0.09 – 0.42)   | 0.26 (0.09 – 0.42)       | –0.11 (–0.29 – 0.08)  | 0.11 (–0.13 – 0.34)  |  |
| pack-year        | 125 | 48.98 ± 35.97 (0.00 – 180.00)  | –0.03 (–0.20 – 0.15)                           | 0.02 (–0.15 – 0.20)  | –0.01 (–0.18 – 0.17) | 0.08 (–0.09 – 0.26)  | –0.05 (–0.22 – 0.13) | 0.17 (–0.01 – 0.33)  | 0.17 (–0.01 – 0.34)      | –0.04 (–0.23 – 0.15)  | –0.02 (–0.26 – 0.22) |  |
| FEV1 (%)         | 125 | 56.26 ± 19.16 (17.50 – 97.70)  |  | 0.86 (0.80 – 0.90)   | 0.86 (0.80 – 0.90)   | 0.68 (0.58 – 0.77)   | 0.77 (0.69 – 0.83)   | –0.39 (–0.53 – 0.23) | –0.26 (–0.42 – 0.09)     | 0.52 (0.37 – 0.65)    | –0.92 (–0.95 – 0.88) |  |
| FEV1 (L)         | 125 | 1.41 ± 0.55 (0.43 – 3.07)      |  |                      | 0.70 (0.59 – 0.78)   | 0.89 (0.85 – 0.92)   | 0.74 (0.65 – 0.81)   | –0.41 (–0.55 – 0.25) | –0.29 (–0.45 – 0.13)     | 0.37 (0.20 – 0.53)    | –0.78 (–0.86 – 0.67) |  |
| FVC(%)           | 124 | 79.80 ± 18.47 (38.50 – 117.70) |  |                      |                      | 0.71 (0.61 – 0.79)   | 0.37 (0.21 – 0.51)   | –0.15 (–0.32 – 0.03) | –0.09 (–0.27 – 0.08)     | 0.45 (0.28 – 0.59)    | –0.83 (–0.90 – 0.74) |  |
| FVC(L)           | 124 | 2.51 ± 0.71 (1.20 – 4.61)      |  |                      |                      |                      | 0.41 (0.25 – 0.55)   | –0.23 (–0.39 – 0.05) | –0.15 (–0.32 – 0.03)     | 0.31 (0.13 – 0.47)    | –0.69 (–0.80 – 0.54) |  |
| post-BD_FEV1/FVC | 125 | 54.66 ± 10.45 (27.00 – 69.72)  |  |                      |                      |                      |                      | –0.57 (–0.68 – 0.44) | –0.41 (–0.55 –           | 0.41 (0.24 – 0.55)    | –0.66 (–0.77 – 0.49) |  |

|                    |     |                                   |  |  |  |  |  |  |                             |                             |                          |
|--------------------|-----|-----------------------------------|--|--|--|--|--|--|-----------------------------|-----------------------------|--------------------------|
|                    |     |                                   |  |  |  |  |  |  | -0.25)                      |                             |                          |
| Total LAA (%)      | 125 | 14.71 ± 8.64<br>(0.41 –<br>45.65) |  |  |  |  |  |  | 0.82<br>(0.75 –<br>0.87)    | -0.35<br>(-0.50 --<br>0.17) | 0.38<br>(0.15 –<br>0.56) |
| %LAA-950insp       | 125 | 1.34 ± 0.73<br>(0.00 –<br>2.00)   |  |  |  |  |  |  | -0.30<br>(-0.46 --<br>0.12) | 0.30<br>(0.06 –<br>0.50)    |                          |
| ln-IL7R            | 108 | 0.54 ± 0.26<br>(0.005 –<br>1.23)  |  |  |  |  |  |  |                             | -0.59<br>(-0.74 -- 0.38)    |                          |
| COPD severity_GOLD | 67  | 1.51 ± 101.0<br>(0.00 –<br>3.00)  |  |  |  |  |  |  |                             |                             |                          |

COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; M, male; F, female; FEV<sub>1</sub>, forced expiratory volume in 1 s; FVC, forced vital capacity; BMI, body mass index; Hx, history; Post-BD, post-bronchodilator; LAA, low attenuation area; %LAA-<sub>950insp</sub>, percentages of low attenuation area below - 950 Hounsfield units; GOLD, Global Initiative for Chronic Obstructive Lung Disease. The values of FEV<sub>1</sub>/FVC % and FEV<sub>1</sub> % were analyzed by Kruskal-Wallis tests and Dunn's multiple comparisons

**A****B****C****D****Regression**

|               |                      |
|---------------|----------------------|
| Dependent Y   | post_BD_FEV1_FVC_%   |
| Independent X | post BD FEV1/FVC (%) |
|               | lnc_IL7R             |
|               | lnc-IL7R             |

**Least squares regression****All cases**

|   |        |
|---|--------|
| Sample size                                 | 108    |
| Coefficient of determination R <sup>2</sup> | 0.1654 |
| Residual standard deviation                 | 9.4755 |

**Regression Equation**

|                         |             |            |                    |         |         |
|-------------------------|-------------|------------|--------------------|---------|---------|
| y = 47.0116 + 16.1211 x |             |            |                    |         |         |
| Parameter               | Coefficient | Std. Error | 95% CI             | t       | P       |
| Intercept               | 47.0116     | 2.0909     | 42.8662 to 51.1570 | 22.4840 | <0.0001 |
| Slope                   | 16.1211     | 3.5167     | 9.1488 to 23.0933  | 4.5841  | <0.0001 |

**Analysis of Variance**

| Source             | DF  | Sum of Squares | Mean Square |
|--------------------|-----|----------------|-------------|
| Regression         | 1   | 1886.7906      | 1886.7906   |
| Residual           | 106 | 9517.3152      | 89.7860     |
| F-ratio            |     |                | 21.0143     |
| Significance level |     |                | P<0.0001    |

**Residuals**

|  |  |
|--|--|
| Chi-squared test for Normal distribution | accept Normality (P=0.8029)<br>(Chi-squared=8.594 DF=13) |
|--|--|

**Subgroup: BDR = negative**

|   |         |
|---|---------|
| Sample size                                 | 88      |
| Coefficient of determination R <sup>2</sup> | 0.1700  |
| Residual standard deviation                 | 10.1639 |

**Regression Equation**

|                         |             |            |                    |         |         |
|-------------------------|-------------|------------|--------------------|---------|---------|
| y = 46.3389 + 16.9432 x |             |            |                    |         |         |
| Parameter               | Coefficient | Std. Error | 95% CI             | t       | P       |
| Intercept               | 46.3389     | 2.4767     | 41.4154 to 51.2624 | 18.7101 | <0.0001 |
| Slope                   | 16.9432     | 4.0366     | 8.9188 to 24.9677  | 4.1974  | 0.0001  |

**Analysis of Variance**

| Source             | DF | Sum of Squares | Mean Square |
|--------------------|----|----------------|-------------|
| Regression         | 1  | 1820.0659      | 1820.0659   |
| Residual           | 86 | 8884.1782      | 103.3044    |
| F-ratio            |    |                | 17.6185     |
| Significance level |    |                | P=0.0001    |

**Subgroup: BDR = positive**

|   |        |
|---|--------|
| Sample size                                 | 20     |
| Coefficient of determination R <sup>2</sup> | 0.1546 |
| Residual standard deviation                 | 5.7286 |

**Regression Equation**

|                         |             |            |                    |         |         |
|-------------------------|-------------|------------|--------------------|---------|---------|
| y = 50.0128 + 11.7084 x |             |            |                    |         |         |
| Parameter               | Coefficient | Std. Error | 95% CI             | t       | P       |
| Intercept               | 50.0128     | 3.2435     | 43.1986 to 56.8270 | 15.4196 | <0.0001 |
| Slope                   | 11.7084     | 6.4546     | -1.8522 to 25.2691 | 1.8140  | 0.0864  |

**Analysis of Variance**

| Source             | DF | Sum of Squares | Mean Square |
|--------------------|----|----------------|-------------|
| Regression         | 1  | 107.9815       | 107.9815    |
| Residual           | 18 | 590.7006       | 32.8167     |
| F-ratio            |    |                | 3.2904      |
| Significance level |    |                | P=0.0864    |

**Supplementary Figure S1.** Correlation between lnc-IL7R and bronchodilator response. (A) Scatter diagram showing the correlation between post-BD FEV1/FVC (%) and lnc-IL7R expression in our COPD cohort. (B) Combined notched box-and-whisker and violin plots comparing lnc-IL7R expression profile in patients with negative and positive BDR. (C) Scatter diagram with regression line showing the correlation between BDR-delineated post-BD FEV1/FVC (%) and lnc-IL7R levels in our COPD cohort. (D) Statistical chart showing the regression-based estimation of relationships between post-BD FEV1/FVC (%), BDR status, and lnc-IL7R expression levels in our cohort.