

Supplementary Table 1. Patient information¹.

| subject | age | gender | genotype I | genotype II | mean FEV ₁ (%predicted) for the year | BMI | diabetes | number of CFPE over the period months studied | CFPE | CFPE occurrence (days) from study start, across full collection period | short term medications | | | | long term medications | | | | | | | | | | | |
|---------|---------|--------|------------|-------------|-------------------------------------------------|------|----------|-----------------------------------------------|------|------------------------------------------------------------------------|------------------------|------------------------------|-----------|---------------|-----------------------|--------------------------|--------------|----------------------|-------------------------|-------|-------------------|--|--|--|--|--|
| | | | | | | | | | | | PO antibiotics | IV antibiotics | macrolide | colomycin neb | tobramycin neb | col/tob neb (alt months) | itraconazole | oral corticosteroids | inhaled corticosteroids | DNase | hypertonic saline | | | | | |
| 1 | 30 | male | phe508del | unknown | 54.9 | 29 | no | 3 | 1 | 95-130 | doxy, azit, cibr | fluc, gent, tobr, mero | no | no | no | no | no | no | yes | yes | no | | | | | |
| | | | | | | | | | 2 | 151-161 | cibr, fluc | | | | | | | | | | | | | | | |
| | | | | | | | | | 3 | 237-256 | cibr, doxy | | | | | | | | | | | | | | | |
| 2 | 45 | female | phe508del | unknown | 40.2 | 18.5 | yes | 3 (+1 ^a) | 1 | 1- 14 | | ceft, tobr | yes | yes | no | no | no | no | yes | no | no | | | | | |
| | | | | | | | | | 2 | 88-105 | | colo, tobr | | | | | | | | | | | | | | |
| | | | | | | | | | EI | 191-198 | doxy | | | | | | | | | | | | | | | |
| 3 | 254-268 | | colo, tobr | | | | | | | | | | | | | | | | | | | | | | | |
| 3 | 47 | male | phe508del | unknown | 33.9 | 20.7 | yes | 0 | 0 | | | | yes | yes | no | no | no | no | yes | yes | no | | | | | |
| 4 | 30 | female | phe508del | 711+3A7G | 38.2 | 25 | no | 3 | 1 | 175-189 | co-am, fluc | | yes | no | no | no | no | no | yes | yes | no | | | | | |
| | | | | | | | | | 2 | 235-249 | doxy | | | | | | | | | | | | | | | |
| | | | | | | | | | 3 | 349-362 | doxy | | | | | | | | | | | | | | | |
| 5 | 22 | female | phe508del | phe508del | 36.2 | 19 | no | 5 | 1 | 62-105 | | colo, ceft, mero, tobr, amik | yes | yes | no | no | yes | no | yes | yes | no | | | | | |
| | | | | | | | | | 2 | 126-135 | doxy | | | | | | | | | | | | | | | |
| | | | | | | | | | 3 | 153-167 | doxy | | | | | | | | | | | | | | | |
| | | | | | | | | | 4 | 215-239 | cibr | mero, amik | | | | | | | | | | | | | | |
| | | | | | | | | | 5 | 322-345 | doxy | mero, amik | | | | | | | | | | | | | | |
| 6 | 55 | male | phe508del | G85E | 52.2 | 24.5 | no | 2 | 1 | 210-220 | cibr | | yes | yes | no | no | no | no | yes | yes | no | | | | | |
| | | | | | | | | | 2 | 251-261 | | ceft, gent | | | | | | | | | | | | | | |

¹ “neb” – nebulised, “EI” – elective antibiotics, ^a - for sinus infection, ^b - for skin infection, ^c - as maintenance therapy, ^d - for haemoptysis. “amik” – amikacin, “amox” – amoxicillin, “azit” – azithromycin, “ceft” – ceftazidime, “cibr” – ciprofloxacin, “clar” – clarithromycin, “co-am” – co-amoxiclav, “colo” – colomycin, “doxy” – doxycycline, “eryt” – erythromycin, “fluc” – flucloxacillin, “mero” – meropenem, “metr” – metronidazole, “pipe” – piperacillin, “tazo” – tazobactam

Supplementary Table 2. Sample information.²

| subject | sample | days since study start | clinical status | subject | sample | days since study start | clinical status |
|----------|--------|------------------------|------------------------------|-----------|--------|------------------------|-----------------------|
| 1 | 1 | 1* | stable | 08 | 1 | 1* | stable |
| | 2 | 24 | stable | | 2 | 18 | stable |
| | 3 | 50 | stable | | 3 | 46 | stable |
| | 4 | 80 | 3 days prior CFPE | | 4 | 76 | stable |
| | 5 | 120 | 8 days post CFPE | | 5 | 109 | stable |
| | 6 | 141 | start of CFPE (prior to abx) | | 6 | 158 | stable |
| | 7 | 188 | stable | | 7 | 176 | stable |
| | 8 | 220 | 5 days prior CFPE | | 8 | 211 | stable |
| | 9 | 260 | 15 days post CFPE | | 9 | 237 | stable |
| | 10 | 286 | stable | | 10 | 270 | exacerbating (day 6) |
| | 11 | 323 | stable | | 11 | 305 | stable |
| | 12 | 344 | stable | | 12 | 349 | stable |
| 2 | 1 | 1 | 16 days post CFPE | 09 | 1 | 1 | stable |
| | 2 | 19* | stable | | 2 | 10* | stable |
| | 3 | 49 | 13 days prior CFPE | | 3 | 31 | stable |
| | 4 | 93 | 17 days post CFPE | | 4 | 57 | stable |
| | 5 | 119 | stable | | 5 | 89 | stable |
| | 6 | 145 | stable | | 6 | 176 | 12 days prior CFPE |
| | 7 | 175 | stable | | 7 | 218 | 15 days post CFPE |
| | 8 | 191 | stable | | 8 | 234 | 12 days prior CFPE |
| | 9 | 227 | exacerbating (day 3) | | 9 | 291 | stable |
| | 10 | 264 | stable | | 10 | 305 | stable |
| | 11 | 285 | stable | | 11 | 311 | 15 days prior CFPE |
| | 12 | 324 | stable | | 12 | 332 | exacerbating (day 6) |
| 3 | 1 | 1* | stable | 10 | 1 | 1* | stable |
| | 2 | 38 | stable | | 2 | 29 | stable |
| | 3 | 70 | stable | | 3 | 57 | stable |
| | 4 | 103 | stable | | 4 | 83 | 13 days prior CFPE |
| | 5 | 131 | stable | | 5 | 134 | 19 days post CFPE |
| | 6 | 161 | stable | | 6 | 144 | stable |
| | 7 | 189 | stable | | 7 | 181 | stable |
| | 8 | 220 | stable | | 8 | 204 | stable |
| | 9 | 257 | stable | | 9 | 221 | 16 days prior CFPE |
| | 10 | 283 | stable | | 10 | 270 | 16 days post CFPE |
| | 11 | 306 | stable | | 11 | 291 | stable |
| | 12 | 348 | stable | | 12 | 321 | 3 days prior CFPE |
| 4 | 1 | 1* | stable | 11 | 1 | 1* | stable |
| | 2 | 22 | stable | | 2 | 31 | stable |
| | 3 | 52 | stable | | 3 | 52 | stable |
| | 4 | 93 | stable | | 4 | 83 | exacerbating (day 10) |
| | 5 | 168 | exacerbating (day 2) | | 5 | 125 | stable |
| | 6 | 200 | 19 days post CFPE | | 6 | 150 | stable |
| | 7 | 213 | 13 days prior CFPE | | 7 | 162 | 9 days prior CFPE |
| | 8 | 226 | start of CFPE (prior to abx) | | 8 | 209 | exacerbating (day 10) |
| | 9 | 263 | stable | | 9 | 239 | stable |
| | 10 | 308 | 20 days prior CFPE | | 10 | 269 | stable |
| | 11 | 320 | 9 days prior CFPE | | 11 | 304 | stable |
| | 12 | 331 | stable | | 12 | 337 | stable |
| 5 | 1 | 1* | stable | 12 | 1 | 1* | 13 days prior CFPE |
| | 2 | 22 | stable | | 2 | 41 | 14 days post CFPE |
| | 3 | 51 | 7 days prior CFPE | | 3 | 62 | stable |
| | 4 | 87 | stable | | 4 | 98 | stable |

² * - sequenced for assignment of species identities to T-RF band lengths. Where samples were collected between two CFPE less than 42 days apart, the days to the nearest CFPE in time are shown. Samples taken at the start of CFPE were obtained before antibiotics (abx) were given.

| | | | |
|----------|----|-----|-----------------------|
| | 5 | 113 | 12 days post CFPE |
| | 6 | 138 | 7 days post CFPE |
| | 7 | 176 | 13 days post CFPE |
| | 8 | 204 | 7 days prior CFPE |
| | 9 | 228 | exacerbating (day 17) |
| | 10 | 255 | 19 days post CFPE |
| | 11 | 285 | stable |
| | 12 | 311 | stable |
| 6 | 1 | 1* | stable |
| | 2 | 19 | stable |
| | 3 | 52 | stable |
| | 4 | 84 | stable |
| | 5 | 113 | stable |
| | 6 | 138 | stable |
| | 7 | 171 | stable |
| | 8 | 190 | 9 days prior CFPE |
| | 9 | 229 | 19 days post CFPE |
| | 10 | 264 | 13 days post CFPE |
| | 11 | 311 | stable |
| | 12 | 351 | stable |
| 7 | 1 | 1 | stable |
| | 2 | 29* | stable |
| | 3 | 48 | stable |
| | 4 | 80 | stable |
| | 5 | 111 | stable |
| | 6 | 143 | exacerbating (day 3) |
| | 7 | 171 | stable |
| | 8 | 192 | stable |
| | 9 | 213 | 13 days prior CFPE |
| | 10 | 272 | stable |
| | 11 | 310 | exacerbating (day 1) |
| | 12 | 351 | stable |

| | | | |
|-----------|----|-----|------------------------------|
| | 5 | 132 | exacerbating (day 13) |
| | 6 | 148 | exacerbating (day 12) |
| | 7 | 170 | 2 days post CFPE |
| | 8 | 193 | 2 days prior CFPE |
| | 9 | 225 | 20 days post CFPE |
| | 10 | 245 | stable |
| | 11 | 358 | stable |
| | 12 | 371 | stable |
| 13 | 1 | 1* | stable |
| | 2 | 24 | 16 days prior CFPE |
| | 3 | 76 | exacerbating (day 5) |
| | 4 | 112 | stable |
| | 5 | 139 | stable |
| | 6 | 160 | 14 days prior CFPE |
| | 7 | 199 | 13 days post CFPE |
| | 8 | 223 | stable |
| | 9 | 234 | 12 days prior CFPE |
| | 10 | 247 | exacerbating (day 1) |
| | 11 | 316 | stable |
| | 12 | 339 | stable |
| 14 | 1 | 1 | exacerbating (day 1) |
| | 2 | 50 | stable |
| | 3 | 62* | stable |
| | 4 | 90 | stable |
| | 5 | 120 | exacerbating (day 3) |
| | 6 | 155 | stable |
| | 7 | 181 | stable |
| | 8 | 207 | stable |
| | 9 | 231 | start of CFPE (prior to abx) |
| | 10 | 267 | stable |
| | 11 | 316 | 13 days post CFPE |
| | 12 | 351 | stable |

Supplementary Table 3. Microbiological culture data.

| patient | sample | gram negative bacilli | | | | | gram positive cocci | | | mixed organisms | | fungi and yeasts | | | |
|---------|--------|-----------------------|------------------------------------|--------------------------------|---------------------------|-----------------------|------------------------------------------|------------------------------|---------------------------------|-----------------|--------------|----------------------------------------|-------------------------------------|------------------------|--------|
| | | coliform | <i>P. aeruginosa</i> non mucoid | <i>P. aeruginosa</i> mucoid | <i>Pseudomonas</i> sp. | <i>S. maltophilia</i> | <i>S. aureus</i> (MSSA ³) | <i>Staphylococcus</i> sp. | <i>Streptococcus</i> Group F | oral flora | unidentified | <i>Aspergillus</i> <i>fumigatus</i> | <i>Aspergillus</i> <i>flavus</i> | <i>Aspergillus</i> sp. | yeasts |
| 1 | 1 | | | | | | | | | | | | | | |
| | 2 | | | | 1 | | 1 | | | | | 1 | | | |
| | 3 | | | | | | | | | | 1 | | | | |
| | 4 | | | | | | | | | | | | | | |
| | 5 | | | 1 | 2 | | | | | | | | 1 | | |
| | 6 | | | | 1 | 1 | | | | | 1 | | | | |
| | 7 | | | | | | 1 | | | | 1 | | | | |
| | 8 | | 1 | | | | 1 | | | | 1 | | | | |
| | 9 | | 1 | | | | | | | | 1 | | | | |
| | 10 | | | | | 1 | | | | | | 1 | | 1 | |
| | 11 | | | | | 1 | | | 1 | | | 1 | | | |
| | 12 | | | | | | 1 | | | | 1 | | | | |
| 2 | 1 | | 1 | 1 | | | | | | | | | | | |
| | 2 | | 1 | | | | | | | 1 | | 1 | | | |
| | 3 | | | | 2 | | | | | | | | | | |
| | 4 | | | | | | | | | | | | | | |
| | 5 | | | | | | | | | | | | | | |
| | 6 | | | | | | | | | | | | | | |
| | 7 | | | | | | | | | | | | | | |
| | 8 | | 1 | 1 | 1 | | | | | 1 | | | | 1 | 1 |
| | 9 | | | | | | | | | | | | | | |
| | 10 | | | | 2 | | | | | 1 | | 1 | | | |
| | 11 | | 1 | 1 | | | 1 | | | | | 1 | | | |
| | 12 | | 1 | | 2 | | 1 | | | | 1 | 1 | | | |
| 3 | 1 | | | 1 | 1 | | | | | 1 | | | | | |
| | 2 | | | 1 | 1 | | | | | 1 | | | | | |
| | 3 | | | 1 | 1 | | | | | 1 | | | | | |
| | 4 | | | 1 | 2 | | | | | | | | | | |
| | 5 | | | | 2 | | | | | 1 | | | | | |
| | 6 | | | | | | | | | | | | | | |
| | 7 | | | | | | | | | | | | | | |
| | 8 | | | | 2 | | | | | | | | | | |
| | 9 | | | | | | | | | | | | | | |
| | 10 | | | | 2 | | | | | 2 | | | | | |
| | 11 | | | | 2 | | | | | 1 | | | | | 1 |
| | 12 | | | | 3 | | | | | 1 | | | | | |
| 4 | 1 | | | | | | | | | 1 | | | | | |
| | 2 | | | | | | 1 | | | 1 | | | | | |
| | 3 | | | | | | | | | | | | | | |
| | 4 | | | | 1 | | | | | | | | | | |
| | 5 | | | | | | | | | | | | | | |
| | 6 | | | | 1 | | | | | | | | | | |
| | 7 | | | | 1 | | 1 | | | | 1 | | | | |
| | 8 | | | | | | | | | | 1 | | | | |

³ Methicillin sensitive *Staphylococcus aureus*

| | | | | | | | | | |
|----|----|--|---|---|---|---|---|---|---|
| | 5 | | 1 | | | 1 | | | |
| | 6 | | | 2 | | 1 | | | |
| | 7 | | | | | | | | |
| | 8 | | | | | | | | |
| | 9 | | 1 | | | 1 | | | |
| | 10 | | 1 | 1 | | 1 | | | |
| | 11 | | | | | | | | |
| | 12 | | 1 | 1 | | | | | |
| 10 | 1 | | 1 | 1 | | 1 | | 1 | |
| | 2 | | | 1 | | 1 | | 1 | |
| | 3 | | | 1 | | 1 | | 1 | |
| | 4 | | | | | 1 | | 1 | |
| | 5 | | | 1 | | | | | |
| | 6 | | 1 | | | 1 | | 1 | |
| | 7 | | | | | | | | |
| | 8 | | | | | | | | |
| | 9 | | | | 3 | | 1 | | 1 |
| | 10 | | 1 | | | | 1 | | 1 |
| | 11 | | | | | | | | |
| | 12 | | | | | | 1 | | 1 |
| 11 | 1 | | 1 | 1 | | | 1 | 1 | |
| | 2 | | | | | | | | |
| | 3 | | | 2 | | 1 | | 1 | |
| | 4 | | | | | | | | |
| | 5 | | | 2 | | 1 | | 1 | |
| | 6 | | | 1 | | 1 | | 1 | |
| | 7 | | | | | | | | |
| | 8 | | | | 2 | | | 1 | |
| | 9 | | | | 2 | | 1 | | 1 |
| | 10 | | | | 1 | | 1 | | |
| | 11 | | | | | | | | |
| | 12 | | | 1 | 1 | | 1 | | 1 |
| 12 | 1 | | | 2 | | 1 | | | |
| | 2 | | | | | | | | |
| | 3 | | | | | | | | |
| | 4 | | | 2 | | 1 | | | |
| | 5 | | 1 | 1 | | 1 | | | |
| | 6 | | | | | | | | |
| | 7 | | | | | | | | |
| | 8 | | | 1 | 2 | | 1 | | |
| | 9 | | | 1 | 2 | | | | |
| | 10 | | | 1 | 1 | | 1 | | |
| | 11 | | | | 2 | | 1 | | |
| | 12 | | | 1 | 3 | | 1 | | |
| 13 | 1 | | 1 | 1 | | | | | |
| | 2 | | | 1 | | | | 1 | |
| | 3 | | 1 | 1 | 1 | | 1 | | |
| | 4 | | | | 2 | | | | |
| | 5 | | 1 | 1 | 1 | | | | |
| | 6 | | | | | | | | |
| | 7 | | 1 | | 1 | | | | |
| | 8 | | | 1 | 2 | | 1 | | 1 |
| | 9 | | 1 | 1 | 1 | | 1 | | 1 |
| | 10 | | 1 | 2 | | | 1 | | |
| | 11 | | | 1 | 1 | | 1 | | 1 |
| | 12 | | | 1 | 1 | | 1 | | 1 |

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Supplementary Table 4. Overall change in community composition.

| subject | overall (mean %) change of the bacterial community over year⁴ | standard deviation (%) |
|----------------|---------------------------------------------------------------------------------|-------------------------------|
| 1 | 52.9 | 15.0 |
| 2 | 4.3 | 3.3 |
| 3 | 18.1 | 16.5 |
| 4 | 70.0 | 16.4 |
| 5 | 18.7 | 11.2 |
| 6 | 24.8 | 13.4 |
| 7 | 31.7 | 19.7 |
| 8 | 25.0 | 24.7 |
| 9 | 39.5 | 22.2 |
| 10 | 38.9 | 18.4 |
| 11 | 45.7 | 26.4 |
| 12 | 27.4 | 21.9 |
| 13 | 35.8 | 19.6 |
| 14 | 64.3 | 18.2 |

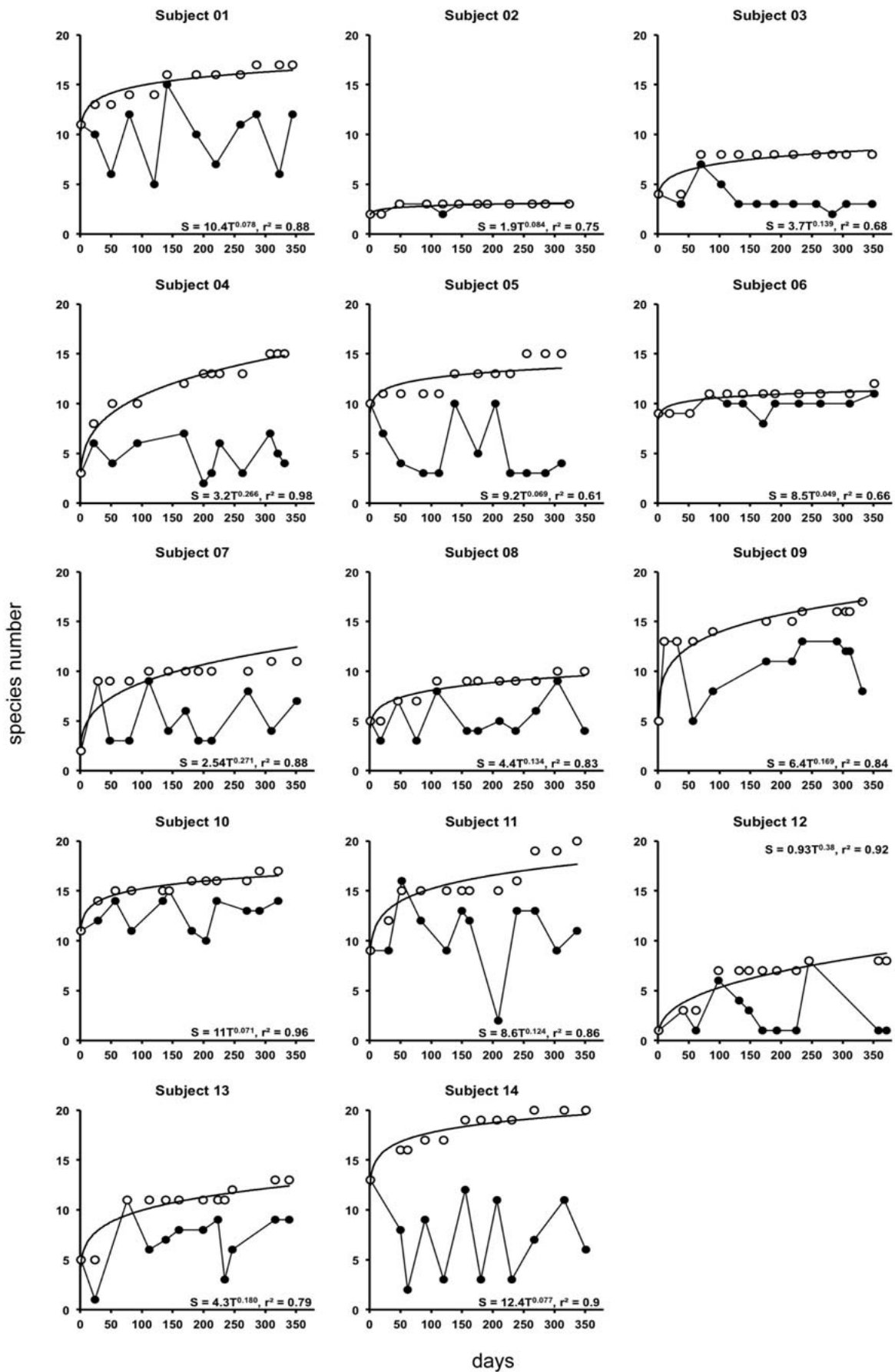
mean inverse of the Bray-Curtis similarity index

Supplementary Table 5. Summary of bacterial community characteristics.⁵

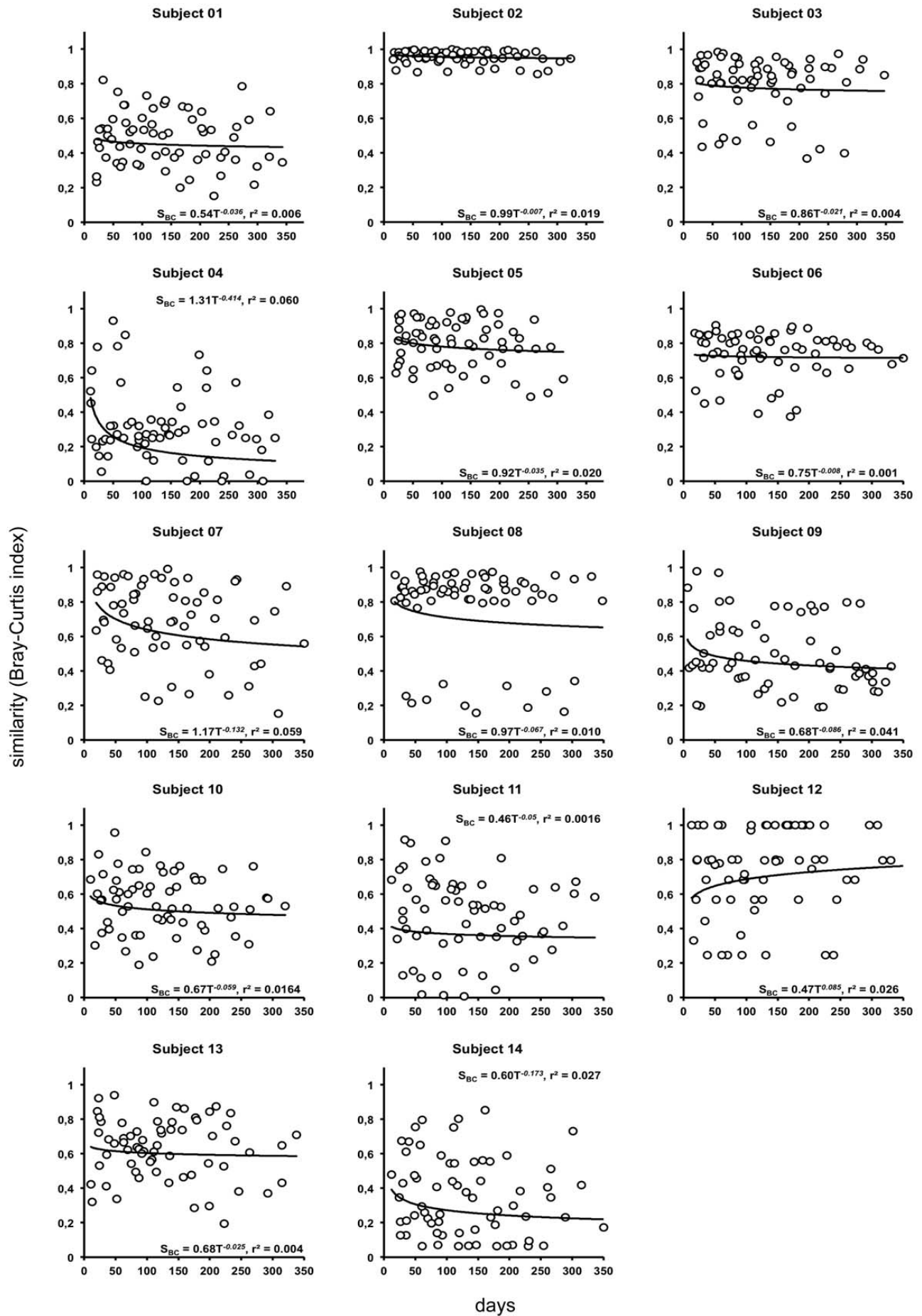
| Subject | mean FEV ₁ (L) | mean species number | mean <i>P. aeruginosa</i> T-RF band % | TTR scaling component (w) | significance of TTR scaling component (<i>P</i>) | DDR scaling component | significance of DDR scaling component (<i>P</i>) |
|---------|---------------------------|---------------------|---------------------------------------|---------------------------|----------------------------------------------------|-----------------------|----------------------------------------------------|
| 1 | 2.13 | 9.8 | 4.65 | 0.078 | 0.0001 | -0.036 | 0.533 |
| 2 | 0.95 | 2.8 | 93.59 | 0.084 | 0.0001 | -0.007 | 0.275 |
| 3 | 1.08 | 3.5 | 77.22 | 0.139 | 0.001 | -0.021 | 0.624 |
| 4 | 1.15 | 4.7 | 12.31 | 0.266 | 0.0001 | -0.414 | 0.040 |
| 5 | 1.15 | 5.4 | 78.63 | 0.069 | 0.003 | -0.035 | 0.254 |
| 6 | 1.71 | 9.8 | 17.49 | 0.049 | 0.001 | -0.008 | 0.810 |
| 7 | 1.82 | 5.1 | 64.66 | 0.271 | 0.0001 | -0.132 | 0.040 |
| 8 | 1.68 | 5.2 | 64.27 | 0.134 | 0.0001 | -0.067 | 0.422 |
| 9 | 0.62 | 10.3 | 26.48 | 0.169 | 0.0001 | -0.086 | 0.102 |
| 10 | 2.81 | 12.7 | 21.96 | 0.071 | 0.0001 | -0.059 | 0.306 |
| 11 | 2.14 | 10.7 | 25.62 | 0.124 | 0.0001 | -0.05 | 0.750 |
| 12 | 1.06 | 2.6 | 84.11 | 0.38 | 0.0001 | -0.846 | 0.197 |
| 13 | 1.87 | 6.8 | 51.83 | 0.18 | 0.0001 | -0.025 | 0.607 |
| 14 | 2.40 | 7.3 | 34.63 | 0.077 | 0.001 | -0.173 | 0.186 |

⁵ Shading denotes patients with a mean FEV₁ above the median (1.68 L) that shared at least 4 out of 5 of the following community characteristics: a mean species number > 7, a mean relative abundance of *P. aeruginosa* of < 35%, TTR and SDR values of < 0.1 with no statistical significance.

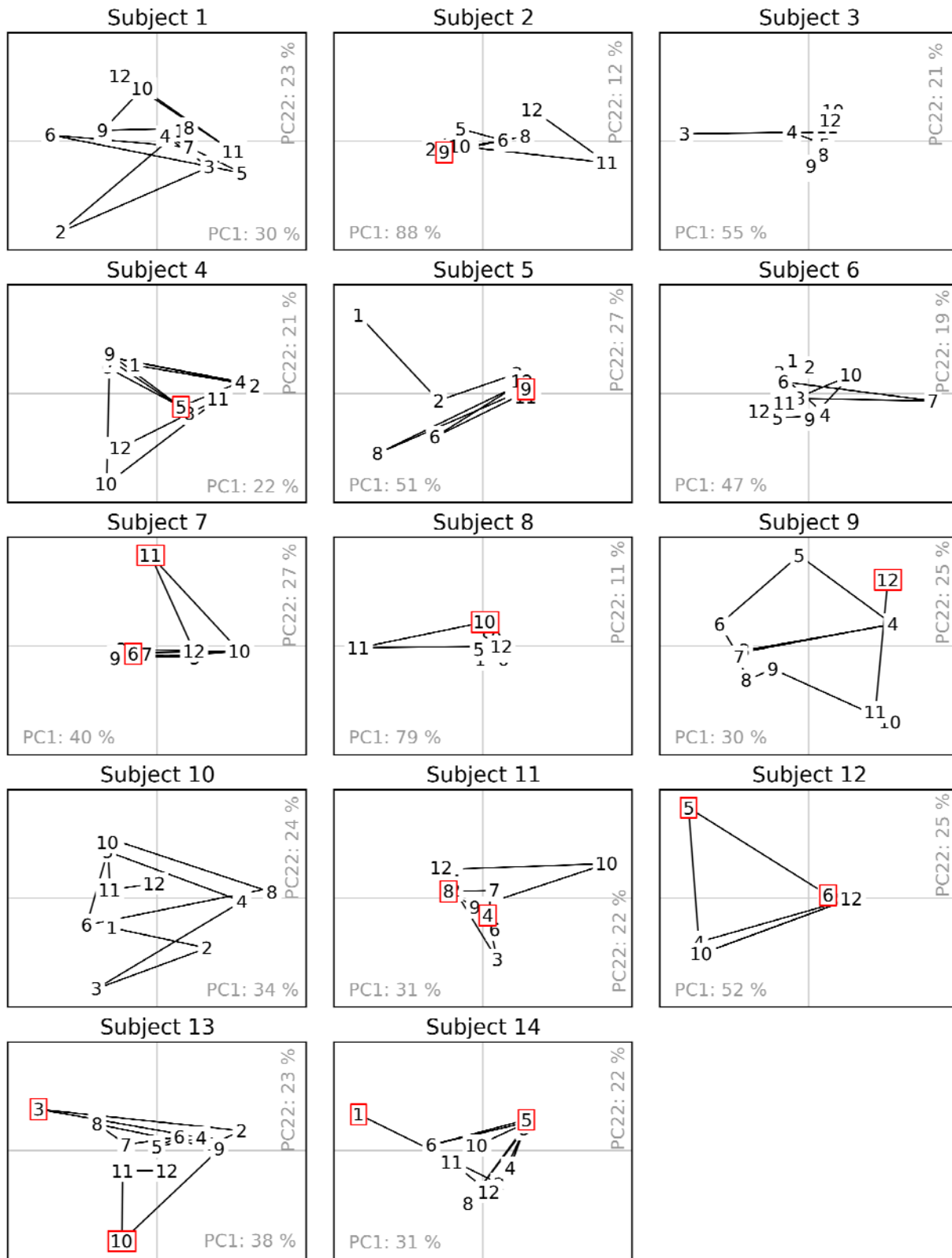
Supplementary Figure 1



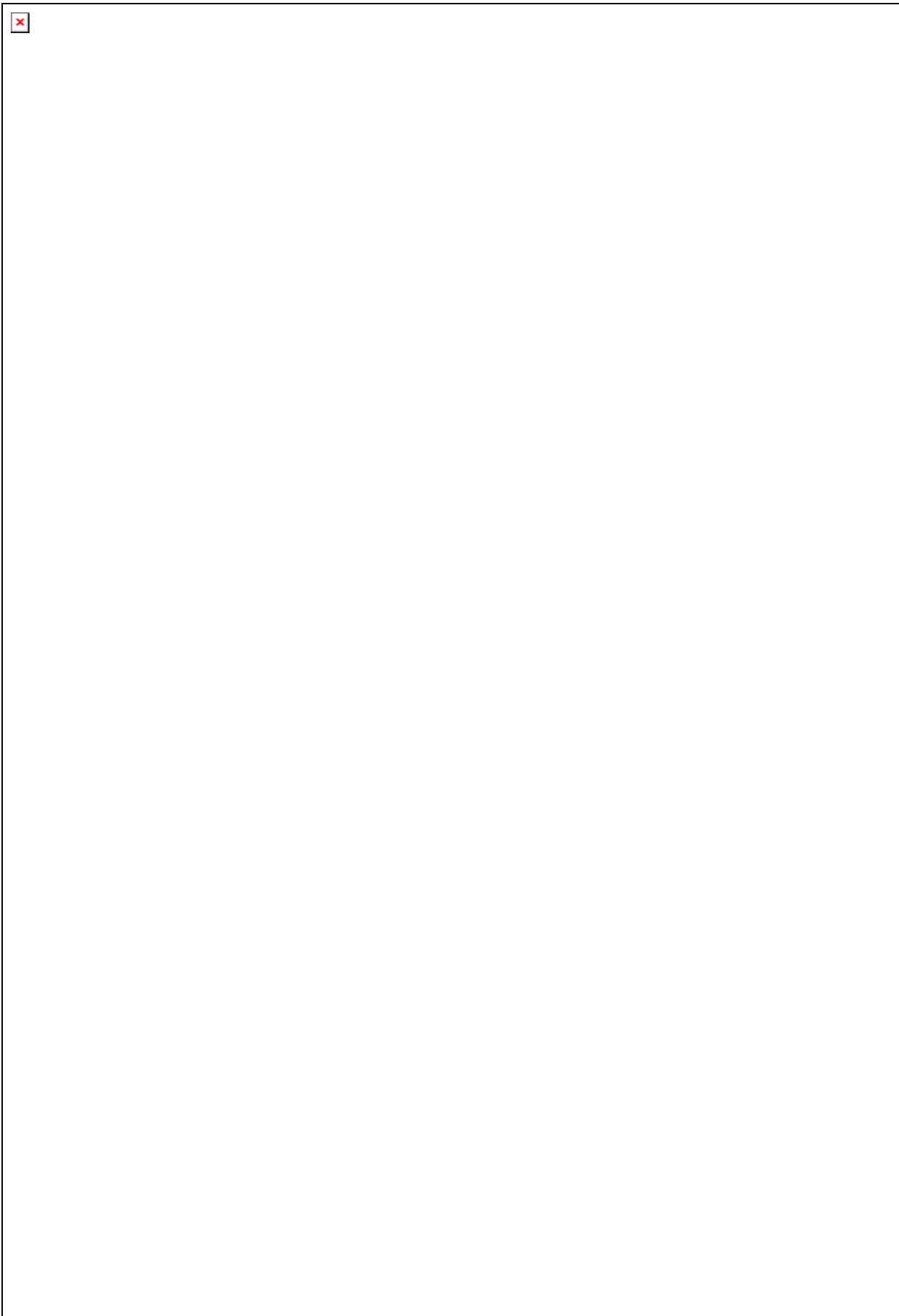
Supplementary Figure 2



Supplementary Figure 3



Supplementary Figure 4



Supplementary Figure 5

