**Supplemental Table 5a.** Composition of training set for IMX-BVN-1.

|  |  |  |  |
| --- | --- | --- | --- |
| **Data** | **Bacterial Subjects** | **Viral Subjects** | **Non-infected Subjects** |
| Training | 607 | 266 | 196 |

The IMX-BVN-1 development data sets have been previously described1 and did not use a validation set.

1. Mayhew MB, Buturovic L, Luethy R, et al. A generalizable 29-mRNA neural-network classifier for acute bacterial and viral infections. *Nat Commun.* 2020;11(1):1177.

**Supplemental Table 5b.** Patient characteristics and composition of training studies for IMX-BVN-2

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study identifier | First author | Study description | N | Age | Female (%) | Platform | Country | Bacterial (%) | Viral (%) | Non-infected (%) |
| [E-MEXP-3589](https://www.ebi.ac.uk/arrayexpress/experiments/E-MEXP-3589/) | Almansa | Patients hospitalized with COPD exacerbation | 23 | 70.1a | 5 (22) | Agilent | Spain | 4 (17) | 5 (22) | 14 (61) |
| [E-MTAB-1548](https://www.ebi.ac.uk/arrayexpress/experiments/E-MTAB-1548/) | Almansa | Surgical patients with sepsis (EXPRESS) | 140 | Median 72 (IQR 61-78) | 44 (31) | Agilent | Spain | 82 (59) | 0 | 58 (41) |
| [E-MTAB-3162](https://www.ebi.ac.uk/arrayexpress/experiments/E-MTAB-3162/) | van de Weg | Patients with dengue | 21 | Median 20 (IQR 17-28) | 10 (48) | Affymetrix | Indonesia | 0 | 21 (100) | 0 |
| [E-MTAB-5273](https://www.ebi.ac.uk/arrayexpress/experiments/E-MTAB-5273/) / 5274 | Burnham | Sepsis due to faecal peritonitis or pneumonia | 227 | Median 69 (IQR 54-77) | 99 (44) | Illumina | UK | 227(100) | 0 | 0 |
| [E-MTAB-5638](https://www.ebi.ac.uk/arrayexpress/experiments/E-MTAB-5638/) | Almansa | ICU patients with ventilator-associated pneumonia | 17 | Median 68 (± 26) | 7 (41) | Agilent | Spain | 0 | 0 | 17 (100) |
| GlueBuffyHCSS | Multiple | Trauma patients | 119 | Median 33 (IQR 25-43) | 43 (36) | Affymetrix | USA | 45 (38) | 0 | 74 (62) |
| [GSE13015 (GPL6102)](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE13015) | Pankla | Sepsis, many cases from burkholderia | 45 | Median 54 (IQR 48-61) | 19 (42) | Illumina | Thailand | 45 (100) | 0 | 0 |
| [GSE13015 (GPL6947)](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE13015) | Pankla | Sepsis, many cases from burkholderia | 15 | Median 49 (IQR 43.5-59.5) | 9 (60) | Illumina | Thailand | 15 (100) | 0 | 0 |
| [GSE21802](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi) | Bermejo-Martin | Pandemic H1N1 in ICU | 10 | unknown | unknown | Illumina | Canada | 0 | 10 (100) | 0 |
| Study identifier | First author | Study description | N | Age | Female (%) | Platform | Country | Bacterial (%) | Viral (%) | Non-infected (%) |
| [GSE22098](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE22098) | Berry | Patients with active TB and other IDs | 193 | Median 16 (IQR 11-26) | 134 (69) | Illumina | UK | 52 (27) | 0 | 141 (73) |
| [GSE25504 (GPL13667)](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE25504) | Smith | Neonatal sepsis | 12 | Median 0 (IQR 0-0) | 4 (33) | Affymetrix | UK | 9 (75) | 3 (25) | 0 |
| [GSE25504 (GPL6947)](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE25504) | Smith | Neonatal sepsis | 21 | Median 0 (IQR 0-0) | 10 (48) | Illumina | UK | 20 (95) | 1 (5) | 0 |
| [GSE27131](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE27131) | Berdal | Severe H1N1 | 7 | Median 38 (IQR 33-50) | 1 (14) | Affymetrix | Norway | 0 | 7 (100) | 0 |
| [GSE28750](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE28750) | Sutherland | Sepsis or post-surgical SIRS | 21 | unknown | 10 (48) | Affymetrix | Australia | 10 (48) | 0 | 11 (52) |
| [GSE28991](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE28991) | Naim | Acute dengue | 11 | unknown | unknown | Illumina | unknown | 0 | 11 (100) | 0 |
| [GSE29385](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE29385) | Naim | Patients with influenza and other respiratory infections | 80 | Median 25 (IQR 22-40) | 23 (29)b | Illumina | unknown | 0 | 80 (100) | 0 |
| [GSE30119](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE30119) | Banchereau | Patients with active TB and other IDs | 59 | Median 6.5 (IQR 1.92-11) | 25 (42) | Illumina | USA | 59 (100) | 0 | 0 |
| [GSE32707](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE32707) | Dolinay | Critically ill patients in Brigham \& Women's ICU | 44 | Median 56 (IQR 45-59) | 8 (18)b | Illumina | USA | 0 | 0 | 44 (100) |
| [GSE40012](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE40012) | Parnell | Bacterial or influenza A pneumonia or SIRS | 36 | Median 59 (IQR 46.5-67) | 16 (44) | Illumina | Australia | 16 (45) | 8 (22) | 12 (33) |
| [GSE40165](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE40165) | Nguyen | Children and adolescents with dengue | 123 | Median 12 (IQR 10-14) | 38 (31) | Illumina | Vietnam | 0 | 123 (100) | 0 |
| [GSE40396](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE40396) | Hu | Febrile young children | 30 | Median 0.92 (IQR 0.33-1.6) | 13 (43) | Illumina | USA | 8 (27) | 22 (73) | 0 |
| [GSE40586](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE40586) | Lill | Community-acquired bacterial meningitis | 15 | Median 57 (IQR 53-70.5) | unknown | Affymetrix | Estonia | 15 (100) | 0 | 0 |
| [GSE42026](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE42026) | Herberg | Children with H1N1/09, RSV or bacterial infection | 59 | Median 1.25 (IQR 0.38-4) | 26 (44) | Illumina | UK | 18 (31) | 41 (69) | 0 |
| [GSE42834](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE42834) | Bloom | Bacterial pneumonia or sarcoidosis | 82 | unknown | 40 (49) | Illumina | UK, France | 14 (17) | 0 | 68 (83) |
| [GSE47655](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE47655) | Stone | Acute anaphylaxis | 6 | unknown | unknown | Affymetrix | Australia | 0 | 0 | 6 (100) |
| [GSE51808](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE51808) | Kwissa | Dengue patients | 28 | unknown | unknown | Affymetrix | Thailand | 0 | 28 (100) | 0 |
| [GSE57065](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE57065) | Cazalis | Septic shock | 28 | Median 62 (IQR 54.25-76) | 9 (32) | Affymetrix | France | 28 (100) | 0 | 0 |
| [GSE57183](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE57183) | Senoi | SJIA patients | 11 | Median 3.6 (IQR 3.3-7.3) | 6 (55) | Illumina | USA | 0 | 0 | 11 (100) |
| [GSE60244](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE60244) | Suarez | Lower respiratory tract infections | 93 | Median 63 (IQR 50-77) | 56 (60) | Illumina | USA | 22 (24) | 71 (76) | 0 |
| **Study identifier** | **First author** | **Study description** | **N** | **Age** | **Female (%)** | **Platform** | **Country** | **Bacterial (%)** | **Viral (%)** | **Non-infected (%)** |
| [GSE61821](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE61821) | Hoang | Febrile patients positive for H1N1, H3N2 | 48 | Median 40 (IQR 19.75-51) | 24 (50) | Illumina | Vietnam | 0 | 48 (100) | 0 |
| [GSE63881](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE63881) | Hoang | Kawasaki disease | 171 | Median 2.75 (IQR 1.42-4.25) | 69 (40) | Illumina | USA | 0 | 0 | 171 (100) |
| [GSE64456](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE64456) | Mahajan | Febrile infants (60 days of age and younger) | 200 | Median 0.10 (IQR 0.06-0.13) | 94 (47) | Illumina | USA | 89 (44) | 111 (56) | 0 |
| [GSE65682](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE65682) | Scicluna | Suspected but negative for CAP | 33 | Median 59 (IQR 48-67) | 11 (33) | Affymetrix | Netherlands | 0 | 0 | 33 (100) |
| [GSE66099](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE66099) | Sweeney | Pediatric ICU (sepsis, septic shock, or SIRS) | 150 | Median 2.45 (IQR 1-5.88) | 56 (37) | Affymetrix | USA | 109 (73) | 11 (7) | 30 (20) |
| [GSE67059](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE67059) | Heinonen | Children with HRV infection | 80 | Median 0.83 (IQR 0.3-1.29) | 27 (34) | Illumina | USA | 0 | 80 (100) | 0 |
| [GSE68310](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE68310) | Zhai | Outpatients with acute respiratory viral infections | 104 | Median 20.96 (IQR 20.09-22.77) | 54 (52) | Illumina | USA | 0 | 104 (100) | 0 |
| [GSE69528](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE69528) | Khaenam | Sepsis, many cases from burkholderia | 83 | unknown | 44 (53) | Illumina | Thailand | 83 (100) | 0 | 0 |
| [GSE72810](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE72810) | Herberg | Children with H1N1/09, RSV or bacterial infection | 15 | Median 1.83 (IQR 0.88-3.29) | 7 (47) | Illumina | UK | 5 (33) | 10 (67) | 0 |
| [GSE73461](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE73461) | Wright | Children with various IDs | 308 | Median 2.79 (IQR 0.92-8.81) | 143 (46) | Illumina | UK | 52 (17) | 94 (31) | 162 (52) |
| [GSE77087](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE77087) | de Steenhuijsen Piters | Children with RSV infection | 41 | Median 0.45 (IQR 0.14-0.69) | 16 (39) | Illumina | USA | 0 | 41 (100) | 0 |
| [GSE77791](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE77791) | Plassais | Severe burn shock | 30 | Median 48 (IQR 40.25-55) | 9 (30) | Affymetrix | France | 0 | 0 | 30 (100) |
| [GSE82050](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE82050) | Tang | Moderate and severe influenza infection | 24 | Median 64.5 (IQR 48.5-74.25) | 10 (42) | Agilent | Germany | 0 | 24 (100) | 0 |
| [GSE103842](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE103842) | Rodriguez-Fernandez | Children with RSV infection | 62 | Median 0.25 (IQR 0.17-0.44) | 23 (37) | Illumina | USA | 0 | 62 (100) | 0 |
| [GSE111368](https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE111368) | Dunning | Adults hospitalised with influenza | 33 | Median 38 (IQR 29-49) | 18 (55) | Illumina | UK | 0 | 33 (100) | 0 |
| AUS-NS | Tang | Patients with infections; primarily influenza | 254 | Median 54 (IQR 35-68) | 139 (55) | NanoString | Australia | 59 (23) | 195 (77) | 0 |

ID = Infectious Disease; COPD = Chronic Obstructive Pulmonary Disease; ICU = Intensive Care Unit, CAP = Community-Acquired Pneumonia; SIRS = Systemic Inflammatory Response Syndrome; TB = Tuberculosis; SJIA = Systemic Juvenile Idiopathic Arthritis; HRV = Human Rhinovirus; RSV = Respiratory Syncytial Virus. aStudy description is taken from the study’s corresponding publication and includes some patients that were excluded from the training set. bNumbers and percentages shown reflect the fact that some patients in the study had unknown/unreported sex.

**Supplemental Table 5c.** Patient characteristics and composition of validation studies for IMX-BVN-2..

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study identifier | Study description | N | Age | Female (%) | Country | Bacterial (%) | Viral (%) | Noninfected (%) |
| INF-03 | Patients with viral infection; collected by nasal swab | 27 | Median 28 (IQR 24-37) | 10 (37) | India | 0 | 27 (100) | 0 |
| INF-IIS-01 | ICU patients with various IDs | 109 | Median 66 (IQR 56-75) | 48 (44) | USA | 70 (64) | 14 (13) | 25 (23) |
| INF-IIS-04 | Bacterial-infected patients from ICU | 30 | Median 72 (IQR 56.5-76.75) | 12 (40) | Greece | 30 (100) | 0 | 0 |
| INF-IIS-10 | Bacterial-infected patients from ICU | 42 | Median 68.5 (IQR 60.25-79.75) | 24 (57) | USA | 42 (100) | 0 | 0 |
| [INF-IIS-19](https://www.ebi.ac.uk/arrayexpress/experiments/E-MTAB-3162/) | Emergency room patients bacterial infections or noninfected | 20 | Median 59 (IQR 41.5-66.25) | 6 (30) | USA | 11 (55) | 0 | 9 (45) |
| INF-IIS-21 | Outpatient viral infections | 65 | Median 81 (IQR 73-87) | 25 (38) | Spain | 0 | 65 (100) | 0 |

All samples were profiled on the NanoString platform