Table S1. non-CNS infection patients with mNGS positive

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| case | Organism and unique reads | Organism number | Additional Testing | Diagnosis | Possible explanation |
| Case 6 | Epstein-Barr Virus (EBV), 3 | 1 | anti-MOG antibody positive | Autoimmune encephalitis | Prodromic inflammation |
| Case 10 | Mycobacterium tuberculosis complex, 1 | 1 | anti-MOG antibody positive | Autoimmune encephalitis | Prodromic inflammation |
| Case 11 | Epstein-Barr Virus (EBV), 7; human herpesvirus 6B (HHV-6B), 3 | 2 | anti-MOG antibody positive | Autoimmune encephalitis | Prodromic inflammation |
| Case 13 | Epstein-Barr Virus (EBV), 3; Streptococcus pneumoniae, 2 | 2 | anti-NMDAR antibody positive | Autoimmune encephalitis | Prodromic inflammation |
| Case 20 | Human herpesvirus 1 (HSV1), 1; Pseudomonas aeruginosa, 5 | 2 | anti-MOG antibody positive | Autoimmune encephalitis | Prodromic inflammation |
| Case 21 | Acinetobacter baumannii, 3 | 1 | anti-MOG antibody positive | Autoimmune encephalitis | Prodromic inflammation |
| Case 56 | Human cytomegalovirus-human herpesvirus 5 (CMV), 3; human herpesvirus 7 (HHV 7), 3; Lactobacillus rhamnosus GG, 246; Actinomyces viscosus, 28; Actinomyces naeslundii 10 | 4 | anti-MOG antibody positive | Autoimmune encephalitis | Prodromic inflammation |

Table S2. CNS Infection case with only clinically irrelevant organism

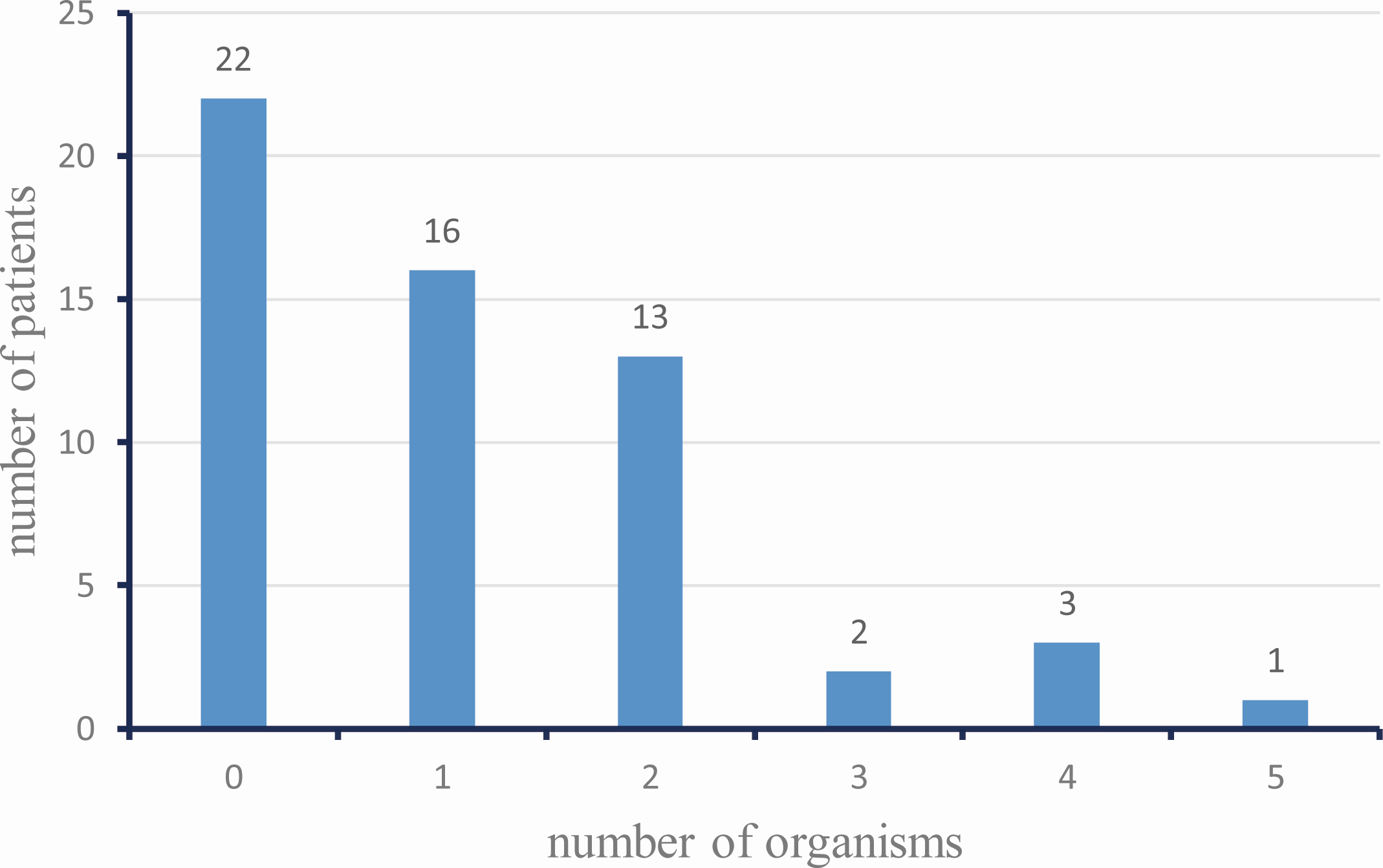
|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| case | Organism and unique reads | Organism number | Diagnosis | Possible explanation |
| Case 28 | varicella zoster virus (VZV), 6 | 1 | Suspected CNS infections (bacteria) | CSF herpes simplex virus and varicella zoster PCR were negative.  Anti-bacterial treatment had an effect. |

Table S3. CNS infection cases with clinical irrelevant organisms (by each organism assessed)

|  |  |  |  |
| --- | --- | --- | --- |
| Patients | Organisms and unique reads | Diagnosis | Possible explanation |
| Case 18 | Human herpesvirus 1 (HSV1), 3 | Hemophilus influenzae meningitis | Hemophilus was co-detected. Anti-bacterial treatment had an effect. |
| Case 28 | varicella zoster virus (VZV), 6 | Suspected CNS infections | CSF herpes simplex virus and varicella zoster PCR were negative.  Anti-bacterial treatment had an effect. |
| Case 32 | Epstein-Barr Virus (EBV), 6 | Bacterial meningitis | Mycobacteroides abscessus was co-detected. Anti-bacterial treatment had an effect. |
| Case 38 | Epstein-Barr Virus (EBV),2 | Cryptococcal meningitis | Cryptococcus was co-detected. Anti-bacterial treatment had an effect. |

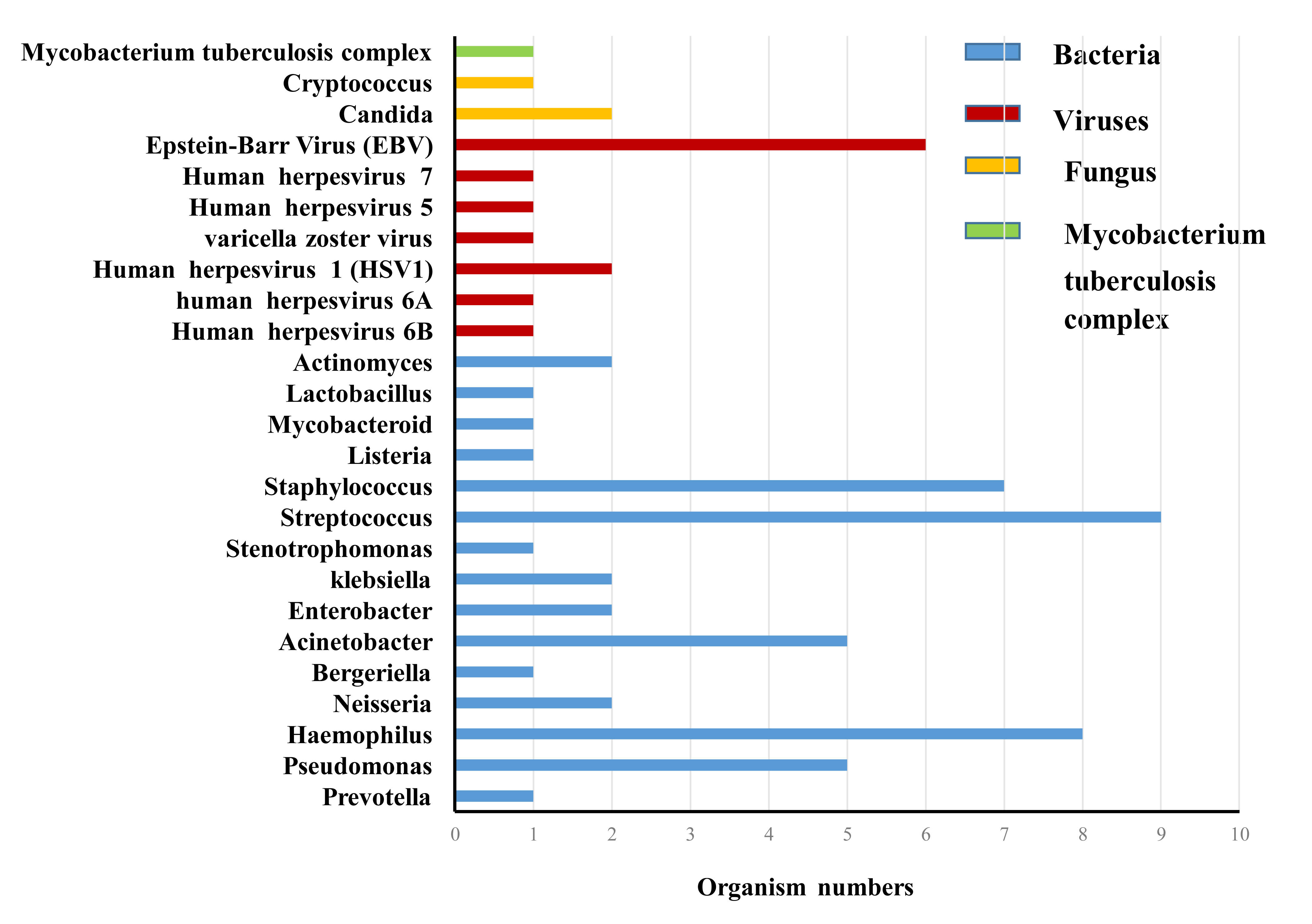
Table S4. Cases with clinically relevant and irrelevant organism in an mNGS test

|  |  |  |
| --- | --- | --- |
| Patients | Organisms | Diagnosis |
| Case 18 | Human herpesvirus 1 (HSV1),  Haemophiles | Hemophilus influenzae meningitis |
| Case 32 | Epstein-Barr Virus (EBV), Mycobacteroides abscessus | Bacterial meningitis |
| Case 38 | Epstein-Barr Virus (EBV), Cryptococcus | Cryptococcal meningitis |



**Fig. S1** The number of patients with a combination of different pathogens **identified by** mNGS

Patients were categorized based on the total number of organisms identified by each mNGS test. Each column represents a total number of patients: 22 patients with no organisms, 16 patients with one organism, 19 patients with multiple organisms.



**Fig. S2** Distribution of **organism** genus and species numbers identified by mNGS

Organisms were categorized under different genera. Each column depicts the total number of the organism under each genus.