Metagenome of SARS-Cov2 patients in Shenzhen with travel to Wuhan shows a wide range of species - *Lautropia*, *Cutibacterium*, *Haemophilus* being most abundant - and *Campylobacter* explaining diarrhea

Sandeep Chakraborty

Letter

The metagenome of patients infected with SARS-Cov2 [1] has shown *Prevotella* to be a key player in immune response [2] in one Chinese study [3], just starting in another [4] and a host of other opportunistic pathogens in a study from San Diego county [5]. The metagenome can also be queried to find host response genes [5], as was done in monkey cells infected with SARS-Cov2 [6]

Nanopore sequencing data from a familial cluster in Shenzhen

The patients were tested for 4 bacterial species - *Bordetella pertussis*, *Bordetella parapertussis*, *Chlamydophila pneumoniae*, and *Mycoplasma pneumoniae*. The sequencing data (Accid:SRR10948474, Nanopore) from five patients in a family cluster from Shenzhen who presented with unexplained pneumonia after returning from Wuhan (Table 1) shows a wide range of bacterial species - *Lautropia*, *Cutibacterium*, *Haemophilus* being most abundant. The presence of *Campylobacter* explains diarrhea seen in the patient [7,8]. Also, their tests should have detected *Mycoplasma*, since it is there in the data.

Significant bacterial load with some bacterial species predominating

The bacterial reads are about 20% (95K out of 500K reads). The viral load is also significant here (70K reads) [2]. They are in SI.familial/allsequences.fa. The number of bacterial species (with at least two reads) is 876 (SI.familial/list.allbacteria.txt). Thus, it is important to consider secondary infection, a possible reason why azithromycin (in addition to hydroxychloroquine) has given good initial results in a clinical trial [9].

References

1. Perlman S (2020). Another decade, another coronavirus.
2. Chakraborty S (2020). The 2019 Wuhan outbreak could be caused by the bacteria *Prevotella*, which is aided by the coronavirus, possibly to adhere to epithelial cells - *Prevotella* is present in huge amounts in patients from both China and Hong Kong. doi:10.31219/osf.io/usztn. URL osf.io/usztn.
3. Wu F, Zhao S, Yu B, Chen Y, Wang W, et al. (2020) Complete genome characterisation of a novel coronavirus associated with severe human respiratory disease in Wuhan. China bioRxiv 24.
4. Chen L, Liu W, Zhang Q, Xu K, Ye G, et al. (2020) RNA based mNGS approach identifies a novel human coronavirus from two individual pneumonia cases in 2019 Wuhan outbreak. *Emerging Microbes & Infections* 9: 313–319.
5. Chakraborty S (2020). San Diego county Nanopore SARS-Cov2 sequencing data shows metagenomic *Prevotella*, *Haemophilus parainfluenzae*, a lot of unknown species and chimeric reads. doi:10.31219/osf.io/cvbqf. URL osf.io/cvbqf.

6. Taiaroa G, Rawlinson D, Featherstone L, Pitt M, Caly L, et al. (2020) Direct RNA sequencing and early evolution of SARS-Cov-2. bioRxiv .
7. Lindblom GB, Sjögren E, Hansson-Westerberg J, Kaijser B (1995) *Campylobacter upsaliensis*, *C. sputorum sputorum* and *C. concisus* as common causes of diarrhoea in Swedish children. *Scandinavian journal of infectious diseases* 27: 187–188.
8. Nelson JM, Smith KE, Vugia DJ, Rabatsky-Ehr T, Segler SD, et al. (2004) Prolonged diarrhea due to ciprofloxacin-resistant *Campylobacter* infection. *The Journal of infectious diseases* 190: 1150–1157.
9. Gautret P, Lagier JC, Parola P, Meddeb L, Mailhe M, et al. (2020) Hydroxychloroquine and azithromycin as a treatment of covid-19: results of an open-label non-randomized clinical trial. *Inter-*

Table 1: **Bacterial secondary infections in a familial cluster of pneumonia indicating person-to-person transmission** [10] GN=Gram-negative, GP=GP, FAC-ANE=facultatively anaerobic (aerobic, but capable of switching to fermentation if oxygen is absent). Is there a link to anaerobic coinfection (like *Prevotella*, which is again present here)? Many more species, just listed top 30 here.

NReads	Bacteria	Type	Diseases
16594	Lautropia	GN FAC-ANE	oral cavities of HIV-infected children [11]
14330	Cutibacterium	GP anaerobic	chronic blepharitis and endophthalmitis,
9618	Escherichia	GN FAC-ANE	
5558	Haemophilus	GN FAC-ANE	pneumonia, meningitis and bloodstream infection
4649	Scytonema	cyanobacteria	
3798	Hyphomicrobium	GN aerobic	
3289	Capnocytophaga	GN FAC-ANE	usually occur with dog or cat bites
2440	Burkholderia	GN aerobic	melioidosis [12]
2098	Variovorax	GN aerobic	
1811	Campylobacter	GN aerobic	diarrhoea [7]
1781	Pseudomonas	GN FAC-ANE	
1659	Staphylococcus	FAC-ANE	Boils, impetigo, food poisoning, cellulitis, and toxic shock syndrome
1604	Schaalia	GP aerobic	
1541	Streptococci	GP aerobic	pharyngitis, pneumonia, sepsis, endocarditis, etc
1174	Mycoplasma	Lack a cell wall	respiratory Mycoplasma pneumoniae [13]
1047	Phyllobacterium	GN aerobic	
997	Moraxella	GN aerobic	otitis media in infants and children [14]
940	Flavobacterium	GN aerobic	fish pathogens
931	Bacillus	GP FAC-ANE	Inhalation or respiratory anthrax
659	Neisseria	GN aerobic	infection and persistence in the upper respiratory tract [15]
493	Prevotella	GN anaerobic	aspiration pneumonia, lung abscess, pulmonary empyema, etc
463	Fusobacterium	GN anaerobic	periodontal, tonsillitis, peritonsillar abscess, etc
358	Veillonella	GN anaerobic	rare cases of meningitis, osteomyelitis, and periodontal disease
328	Cupriavidus	GN aerobic	Infection in 87 yr Chinese man [16]
325	Corynebacterium	GP aerobic	diphtheria toxin [17]
318	Sphingomonas	GN aerobic	
314	Micrococcus	GP aerobic	anaphylactoid [18]
307	Loriellopsis	cyanobacteria	
297	Calothrix	cyanobacteria	
281	Lysinibacillus	GP	Sepsis [19]
278	Methylobacterium	GN aerobic	opportunistic pathogens in immunocompromised patients
277	Treponema	?	syphilis, bejel, and yaws

national Journal of Antimicrobial Agents : 105949.

10. Chan JFW, Yuan S, Kok KH, To KKW, Chu H, et al. (2020) A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *The Lancet* .
11. Rossmann SN, Wilson PH, Hicks J, Carter B, Cron SG, et al. (1998) Isolation of *Lautropia mirabilis* from oral cavities of human immunodeficiency virus-infected children. *Journal of clinical microbiology* 36: 1756–1760.
12. Nieves W, Heang J, Asakrah S, Zu Bentrup KH, Roy CJ, et al. (2010) Immunospecific responses to bacterial elongation factor Tu during *Burkholderia* infection and immunization. *PloS one* 5.
13. Chu HW, Honour JM, Rawlinson CA, Harbeck RJ, Martin RJ (2003) Effects of respiratory *Mycoplasma pneumoniae* infection on allergen-induced bronchial hyperresponsiveness and lung inflammation in mice. *Infection and immunity* 71: 1520–1526.
14. Goldstein EJ, Murphy TF, Parameswaran GI (2009) *Moraxella catarrhalis*, a human respiratory tract pathogen. *Clinical Infectious Diseases* 49: 124–131.
15. Weyand NJ (2017) *Neisseria* models of infection and persistence in the upper respiratory tract. *Pathogens and disease* 75.
16. Zhang Z, Deng W, Wang S, Xu L, Yan L, et al. (2017) First case report of infection caused by *Cupriavidus gilardii* in a non-immunocompromised Chinese patient. *IDCases* 10: 127–129.
17. Murphy JR (1996) *Corynebacterium diphtheriae*. In: *Medical Microbiology*. 4th edition, University of Texas Medical Branch at Galveston.
18. Monodane T, Kawabata Y, Takada H (1997) *Micrococcus luteus* cells and cell walls induce anaphylactoid reactions accompanied by early death and serum cytokines in mice primed with muramyl dipeptide. *FEMS Immunology & Medical Microbiology* 17: 49–55.
19. Wenzler E, Kamboj K, Balada-Llasat JM (2015) Severe sepsis secondary to persistent *Lysinibacillus sphaericus*, *Lysinibacillus fusiformis* and *Paenibacillus amylolyticus* bacteremia. *International Journal of Infectious Diseases* 35: 93–95.