

1 **SARS-CoV-2 variant from India to Marseille: the still active role of ports in**  
2 **the introduction of epidemics**

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14 A recent variant of SARS-CoV-2 named B.1.617 has recently spread to several  
15 countries from India (Cherian et al., 2021). The mutations found in the Indian variant in its  
16 spike are identified as E484Q, L452R, E154K and P681R. They involve amino acid 484 that  
17 is changed in the South African variant B.1.351 and in the Brazilian variant P1. Another  
18 mutation, L452R, was already detected in a Californian variant. It is therefore the association  
19 in a single variant of these mutations supposed to reduce recognition by antibodies and impact  
20 on attachment to the ACE2 receptor that has caused this strain to be classified as a variant of  
21 interest by the WHO due to a strong potential to cause epidemics and escape antibodies,  
22 especially those generated by vaccination (Starr et al., 2021; Zhou et al., 2021).

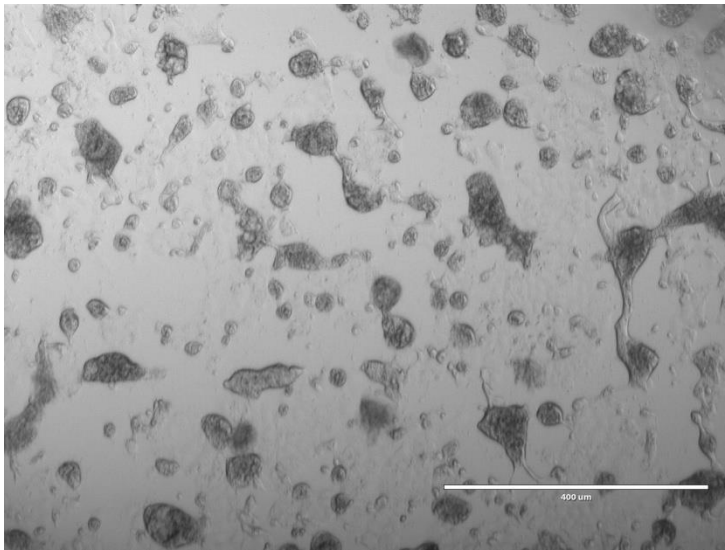
23 The case we report here is that of an Indian sailor coming to Marseille to embark on a  
24 ship as a crew member who illustrates the role of ports like that of Marseille in the historical  
25 introduction of epidemics. This patient from Goa, India, embarked at New Delhi airport,

26 passed through Amsterdam airport and landed at Marseille airport on April 26, 2021. Tested  
27 SARS-CoV-2-negative 72 hours before boarding, he was detected positive when he left the  
28 plane by an antigen test carried out by the civil security firefighters. The patient was  
29 quarantined in a city hotel. A new nasopharyngeal swab was performed for confirmation of  
30 the diagnosis and isolation of virus on April 27 and sent to our institute (Amrane et al., 2020).  
31 qRT-PCR was positive at Ct 17 and direct sequencing (Colson et al., 2021) confirmed the  
32 "Indian Variant" nature of this strain. The genomic sequence has been deposited in GISAID  
33 (No. XXXXX). On April 28, characteristic CPEs were seen in culture (Figure 1a) and the  
34 strain sub-cultured for subsequent sero-neutralization analysis on the sera of local patients  
35 carrying antibodies (vaccinated and convalescent).

36 This case perfectly illustrates the role played by ports such as Marseille in the entry of  
37 epidemics of distant origin. Indeed, for 2000 years this port has faced the arrival of epidemic  
38 agents, in particular plague, cholera, yellow fever. The history of these epidemics and the  
39 strategies put in place to fight them, including creation of our institute, have been recently  
40 reviewed (Barbieri et al., 2021). For many years, merchant navy crews have mainly come  
41 from countries with low labor costs, in particular the Indian subcontinent, and the case of this  
42 sailor continues to illustrate this historical characteristic by the fact that it is an area of mixing  
43 of populations. It also raises the question of the lack of real control over transfers of people  
44 from areas where variants of concern are circulating. This patient had been tested before  
45 boarding and was able to transit unchecked to Marseille where, fortunately, civil security  
46 checks as many travelers as possible but without being exhaustive. It is very probable that  
47 similar situations will occur, illustrating the extreme difficulty of controlling the introduction  
48 of new epidemic variants in countries or regions which are traditionally areas of intense  
49 transit. Ensuring effective detection of these cases is however critical, especially for crew

50 members destined, as was the case with this sailor, to embark on cruise ships in order to avoid  
51 a repetition of the Diamond Princess episode (Yamagishi et al., 2020).

52 **Figure 1.** Indian variant isolated in Marseille at IHU Méditerranée Infection. Cytopathic  
53 effect observed on Vero E6 cells after 24 hours of incubation.



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## 56 **References**

57 Amrane S, Tissot-Dupont H, Doudier B, Eldin C, Hocquart M, Mailhe M, Dudouet P,  
58 Ormières E, Ailhaud L, Parola P, Lagier JC, Brouqui P, Zandotti C, Ninove L, Luciani L,  
59 Boschi C, La Scola B, Raoult D, Million M, Colson P, Gautret P. Rapid viral diagnosis and  
60 ambulatory management of suspected COVID-19 cases presenting at the infectious  
61 diseases referral hospital in Marseille, France, - January 31st to March 1st, 2020: A  
62 respiratory virus snapshot. *Travel Med Infect Dis* 2020;36:101632. doi:  
63 10.1016/j.tmaid.2020.101632.

64 Barbieri R, Colson P, Raoult D, Drancourt M. Two-millennia fighting against port-imported  
65 epidemics, Marseille. *IHU Preprint* 2021; doi: <https://doi.org/10.35088/84a4-me41>.

66 Cherian S, Potdar V, Jadhav S, Yadav P, Gupta N, Das M, Das S, Agarwal A, Singh S,  
67 Abraham P, Panda S, Mande S, Swarup R, Bhargava B, Bhushan R, NIC team, INSACOG  
68 Consortium. Convergent evolution of SARS-CoV-2 spike mutations, L452R, E484Q and  
69 P681R, in the second wave of COVID-19 in Maharashtra, India. *MedRxiv* 2021; doi:  
70 <https://doi.org/10.1101/2021.04.22.440932>.

71 Colson P, Levasseur A, Gautret P, Fenollar F, Thuan Hoang V, Delerce J, Bitam I, Saile R,  
72 Maaloum M, Padane A, Bedotto M, Brechard L, Bossi V, Ben Khedher M, Chaudet H,  
73 Million M, Tissot-Dupont H, Lagier JC, Mboup S, Fournier PE, Raoult D. Introduction  
74 into the Marseille geographical area of a mild SARS-CoV-2 variant originating from sub-  
75 Saharan Africa: An investigational study. *Travel Med Infect Dis* 2021;40:101980. doi:  
76 10.1016/j.tmaid.2021.101980. Epub 2021 Jan 31.

77 Starr TN, Greaney AJ, Dingens AS, Bloom JD. Complete map of SARS-CoV-2 RBD  
78 mutations that escape the monoclonal antibody LY-CoV555 and its cocktail with LY-  
79 CoV016. *Cell Rep Med* 2021;2(4):100255. doi: 10.1016/j.xcrm.2021.100255. Epub 2021  
80 Apr 5.

81 Yamagishi T, Kamiya H, Kakimoto K, Suzuki M, Wakita T. Descriptive study of COVID-19  
82 outbreak among passengers and crew on Diamond Princess cruise ship, Yokohama Port,  
83 Japan, 20 January to 9 February 2020. *Euro Surveill* 2020;25(23):2000272. doi:  
84 10.2807/1560-7917.ES.2020.25.23.2000272.

85 Zhou D, Dejnirattisai W, Supasa P, Liu C, Mentzer AJ, Ginn HM, Zhao Y, Duyvesteyn HME,  
86 Tuekprakhon A, Nutalai R, Wang B, Paesen GC, Lopez-Camacho C, Slon-Campos J,  
87 Hallis B, Coombes N, Bewley K, Charlton S, Walter TS, Skelly D, Lumley SF, Dold C,  
88 Levin R, Dong T, Pollard AJ, Knight JC, Crook D, Lambe T, Clutterbuck E, Bibi S,  
89 Flaxman A, Bittaye M, Belij-Rammerstorfer S, Gilbert S, James W, Carroll MW,  
90 Klenerman P, Barnes E, Dunachie SJ, Fry EE, Mongkolsapaya J, Ren J, Stuart DI,  
91 Screaton GR. Evidence of escape of SARS-CoV-2 variant B.1.351 from natural and  
92 vaccine-induced sera. *Cell* 2021;184(9):2348–2361.e6. doi: 10.1016/j.cell.2021.02.037.  
93 Epub ahead of print.

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