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► To cite this version:

Aurélie Hennebique, Yvan Caspar, Max Maurin, Sandrine Boisset, Isabelle Pelloux, et al.. Ulceroglandular Infection and Bacteremia Caused by *Francisella salinarina* in Immunocompromised Patient, France. *Emerging Infectious Diseases*, 2022, 28 (2), pp.465-467. 10.3201/eid2802.211380 . hal-03549298

HAL Id: hal-03549298

<https://hal.science/hal-03549298v1>

Submitted on 31 Jan 2022

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2. Karlinsky A, Kobak D. Tracking excess mortality across countries during the COVID-19 pandemic with the World Mortality Dataset. *eLife*. 2021;10:10. <https://doi.org/10.7554/eLife.69336>
3. Barchuk A, Skougarevskiy D, Titaev K, Shirokov D, Raskina Y, Novkunkskaya A, et al. Seroprevalence of SARS-CoV-2 antibodies in Saint Petersburg, Russia: a population-based study. *Sci Rep*. 2021;11:12930. <https://doi.org/10.1038/s41598-021-92206-y>
4. Zurochka A, Dobrinina M, Zurochka V, Hu D, Solovyev A, Ryabova L, et al. Seroprevalence of SARS-CoV-2 antibodies in symptomatic individuals is higher than in persons who are at increased risk exposure: the results of the single-center, prospective, cross-sectional study. *Vaccines (Basel)*. 2021;9:627. <https://doi.org/10.3390/vaccines9060627>
5. Cook S, Malyutina S, Kudryavtsev A, et al. Know Your Heart: rationale, design and conduct of a cross-sectional study of cardiovascular structure, function, and risk factors in 4,500 men and women aged 35–69 years from two Russian cities, 2015–18. *Wellcome Open Research* 2018;3:67. <https://doi.org/10.12688/wellcomeopenres.14619.3>
6. Kuvshinova IN, Nekrasov BG, Livitskaya NI, Molodykh SV, Rukavishnikov M. Sensitivity and specificity of reagent kits of JSC “Vector-Best” for the detection of immunoglobulins of different classes to SARS-CoV-2 [in Russian]. *Spravochnik Zaveduyushchego KDL*. 2021;10:27–32.
7. Barchuk A, Shirokov D, Sergeeva M, Tursunzade R, Dudkina O, Tychkova V, et al. Evaluation of the performance of SARS-CoV-2 antibody assays for a longitudinal population-based study of COVID-19 spread in St. Petersburg, Russia. *J Med Virol*. 2021;93:5846–52. <https://doi.org/10.1002/jmv.27126>
8. Sempos CT, Tian L. Adjusting coronavirus prevalence estimates for laboratory test kit error. *Am J Epidemiol*. 2021;190:109–15. <https://doi.org/10.1093/aje/kwaa174>
9. Government of Russia. The number of people vaccinated against coronavirus in Arkhangelsk [in Russian]. 2021 [cited 2021 Sep 20]. <https://gogov.ru/covid-v-stats/arkhangelsk>
10. European Centre for Disease Prevention and Control. Overview of the implementation of COVID-19 vaccination strategies and deployment plans in the EU/EEA, 14 June 2021. 2021 [cited 2021 Sep 20]. <https://www.ecdc.europa.eu/en/publications-data/overview-implementation-covid-19-vaccination-strategies-and-deployment-plans>

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Ulceroglandular Infection and Bacteremia Caused by *Francisella salimarina* in Immunocompromised Patient, France

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DOI: <https://doi.org/10.3201/eid2802.211380>

Although *Francisella tularensis* is a well-known, highly virulent bacterium that causes tularemia in humans, other *Francisella* species have been associated with sporadic human infections. We describe a human cutaneous infection with bacteremia caused by *F. salimarina*, a *Francisella* species recently identified from seawater and fishes, in an immunocompromised patient in France.

Although the taxonomy of the genus *Francisella* includes a wide diversity of species, only *F. tularensis* subspecies *tularensis* and *F. tularensis* subsp. *holarctica* cause the potentially life-threatening disease tularemia (1). Several *Francisella* spp., including *F. philomiragia*, *F. novicida*, *F. opportunistica*, and *F. hispaniensis*, are occasional opportunistic human pathogens; the other *Francisella* spp. are not associated with human infections (1). We describe a human infection caused by *F. salimarina*, recently identified from aquatic environments and fishes.

In June 2017, a 76-year-old man received a diagnosis of acute myelomonocytic leukemia and was admitted to Poitiers University Hospital (Poitiers, France). The patient lived in a small town 30 km from the Atlantic Ocean, had not travelled abroad recently, and had no pets. The day after admission, first-line chemotherapy of subcutaneous azacitidine was started for 7 days. After 3 days of chemotherapy, piperacillin/tazobactam was introduced for 5 days because of febrile aplasia. The patient was then discharged with

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an antibiotic prophylaxis (sulfamethoxazole/trimethoprim at 800 mg/160 mg 3×/wk). On July 26, the second azacitidine treatment was not administered because the patient again experienced febrile aplasia. Physical examination revealed skin lesions on 2 left-hand fingers that had appeared 3 weeks earlier. These lesions were erythematous and crusty but not purulent (Figure, panel A). They were associated with a left axillary lymphadenopathy. Antibiotic treatment with piperacillin/tazobactam and teicoplanin was started but was changed to imipenem/cilastatin and daptomycin after 5 days because of poor clinical response. Aerobic blood cultures performed at admission tested positive on July 31 and Gram stain showed a small gram-negative coccobacillus (Figure, panel B). Antibiotic treatment was changed to cefepime, administered for 3 days. No identification could be obtained by MALDI-TOF (matrix-assisted laser desorption/ionization time-of-flight) mass spectrometry (Vitek MS; bioMérieux, <https://www.biomerieux.com>). The strain was identified as a *Francisella* spp. by 16s rDNA amplification and sequencing. A cutaneous biopsy was performed because of persistent fever and worsening skin lesions in the patient; the same *Francisella* spp. strain was isolated. Doxycycline (100 mg 2×/d) was administered for 8 days, followed by sulfamethoxazole/trimethoprim, which led to apyrexia.

The *Francisella* spp. strain (referred to as CHUGA-F75) was sent to the French National Reference Centre for *Francisella* for further characterization. The strain was strictly aerobic and grew well on chocolate agar supplemented with IsoVitaleX (bioMérieux), blood agar, and tryptic soy agar, yielding gray mucoid colonies after 24 h of incubation at 35°C in 5% CO₂, but not on Drigalski agar (Figure, panels C, D). Biochemical testing revealed a positive oxidase, a weakly positive catalase, and a negative urease test. The strain was also halotolerant; it could grow in modified Mueller-Hinton broth with up to 8% NaCl. ISFtu2, Tul4, and type

B real-time PCR tests, which detected most *Francisella* spp., *F. tularensis*, and *F. tularensis* subsp. *holarctica*, were all negative for DNA extracted from this strain (2,3). Species identification could not be obtained by using MALDI-TOF mass spectrometry, either with the routine database (MBT IVD Library DB-7171), the Biotox database (MBT SR Library; both from Bruker, <https://www.bruker.com>), or the French National Reference Centre for *Francisella* database containing *F. tularensis*, *F. novicida*, and *F. philomiragia* (4). Therefore, we performed whole-genome sequencing by using second and third next-generation sequencing platforms MiSeq (Illumina, <https://www.illumina.com>) and MinION (Oxford Nanopore Technologies, <https://nanoporetech.com>). Hybrid assembly of the sequencing data using Unicycler software on the Galaxy web platform (<https://usegalaxy.org>) enabled circularization of a 1,940,863 bp bacterial chromosome (Genbank accession no. CP076680). Whole-genome-based identification of the strain was assessed by using the Type Strain Genome Server (<https://tygs.dsmz.de>) (5). The CHUGA-F75 strain clustered in the same branch as the *F. salinarina* SYSU SYW-1, the *F. marina* E95-16, and the *F. salina* TX07-7308 strains (Appendix Figure, <https://wwwnc.cdc.gov/EID/article/28/2/21-1380-App1.pdf>), probably representing the same species because of high genetic homology, although different species names have been published (6–8). Digital DNA-DNA hybridization >70%, average nucleotide identity >95%, and difference in percent guanine-cytosine content <1 percent between the CHUGA-F75 strain and the 3 *F. salinarina*, *F. marina*, and *F. salina* strains confirmed the CHUGA-F75 isolate belonged to the same species. Because the only validly published species name according to the International Code of Nomenclature of prokaryotes is *F. salinarina*, we identified CHUGA-F75 as *F. salinarina*. Using the broth microdilution method in cation-adjusted Mueller-Hinton broth as recommended by the Clinical and Laboratory Standards

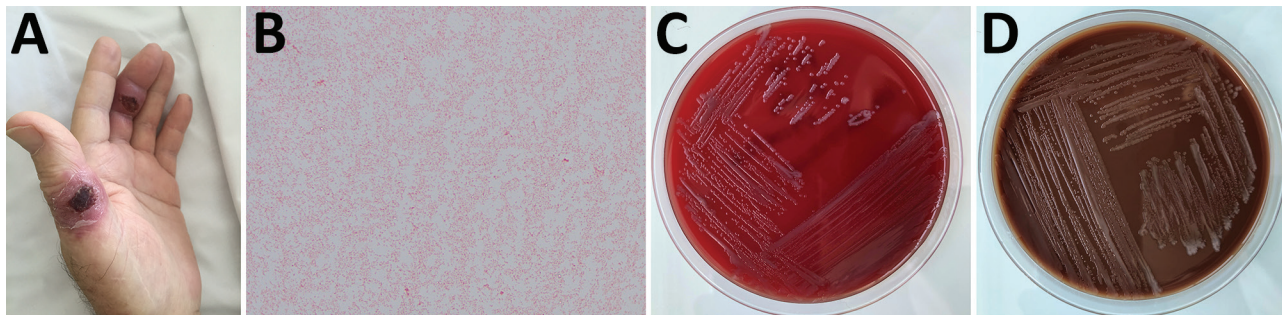


Figure. Skin ulcers and bacteremia caused by *Francisella salinarina* in an immunocompromised patient and isolated bacteria morphology, France. A) Skin lesion on 2 left-hand fingers. B) Small gram-negative coccobacillus isolated from blood and skin lesions (original magnification ×1,000). C) Growth on blood agar after 2 days of incubation at 35°C in 5% CO₂. D) Growth on chocolate agar after 2 days of incubation at 35°C in 5% CO₂.

Institute, we found that the CHUGA-F75 strain was sensitive to gentamicin (MIC = 0.125 mg/L), doxycycline (MIC = 1 mg/L), and ciprofloxacin (MIC = 0.016 mg/L) and resistant to sulfamethoxazole/trimethoprim (MIC = 32 mg/L).

F. marina was described as responsible for systemic disease in fishes (*Lutjanus guttatus*, the cultured spotted rose snapper) in Central America, whereas 4 *F. salinarum* strains have been isolated from coastal seawater in Guangdong Province, China, and 1 strain of *F. salina* has been grown from brackish seawater and seaweed off the coast of Galveston, Texas, USA (6–8). To our knowledge, these *Francisella* spp. were not responsible for human infection so far. This report, like previous descriptions of human infections caused by emergent *Francisella* spp., highlights that environmental or fish-related *Francisella* spp. could be responsible for opportunistic human infections resembling tularemia.

The Direction Générale de l'Armement of France funded this research (ANR-17-ASTR-0024).

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References

- Hennebique A, Boisset S, Maurin M. Tularemia as a waterborne disease: a review. *Emerg Microbes Infect.* 2019; 8:1027–42. <https://doi.org/10.1080/22221751.2019.1638734>
- Versage JL, Severin DDM, Chu MC, Petersen JM. Development of a multitarget real-time TaqMan PCR assay for enhanced detection of *Francisella tularensis* in complex specimens. *J Clin Microbiol.* 2003;41:5492–9. <https://doi.org/10.1128/JCM.41.12.5492-5499.2003>
- Kugeler KJ, Pappert R, Zhou Y, Petersen JM. Real-time PCR for *Francisella tularensis* types A and B. *Emerg Infect Dis.* 2006;12:1799–801. <https://doi.org/10.3201/eid1211.060629>
- Regoui S, Hennebique A, Girard T, Boisset S, Caspar Y, Maurin M. Optimized MALDI TOF mass spectrometry identification of *Francisella tularensis* subsp. *holarctica*. *Microorganisms.* 2020;8:E1143. <https://doi.org/10.3390/microorganisms8081143>
- Meier-Kolthoff JP, Göker M. TYGS is an automated high-throughput platform for state-of-the-art genome-based taxonomy. *Nat Commun.* 2019;10:2182. <https://doi.org/10.1038/s41467-019-10210-3>
- Challacombe JF, Petersen JM, Gallegos-Graves LV, Hodge D, Pillai S, Kuske CR. Whole-genome relationships among *Francisella* bacteria of diverse origins define new species and provide specific regions for detection. *Appl Environ Microbiol.* 2017;83:e02589-16.
- Li L-H, Luo H-M, Feng J-H, Ming Y-Z, Zheng M-L, Deng G-Y, et al. *Francisella salinarum* sp. nov., isolated from coastal seawater. *Int J Syst Evol Microbiol.* 2020;70:3264–72. <https://doi.org/10.1099/ijsem.0.004164>
- Soto E, Griffin MJ, Morales JA, Calvo EB, de Alexandre Sebastião F, Porras AL, et al. *Francisella marina* sp. nov., etiologic agent of systemic disease in cultured Spotted Rose Snapper (*Lutjanus guttatus*) in Central America. *Appl Environ Microbiol.* 2018;84:e00144-18. <https://doi.org/10.1128/AEM.00144-18>

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Surveillance of Rodent Pests for SARS-CoV-2 and Other Coronaviruses, Hong Kong

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DOI: <https://doi.org/10.3201/eid2802.211586>

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