

# Intra and interspecies interaction between mass confined animals and their handlers – an ideal reservoir for Coronavirus evolution

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Multiple variants of the virus responsible for COVID-19 have been detected since the pandemic started, however a minuscule minority succeed in persisting and successfully promulgating infection in humans. A research group in Basel, Switzerland has detected a persistent mutant designated as 20A.EU1 of COVID-19, which has spread extensively in the European Continent [1]. The initial stages of the variant appear to have originated in the North East region of Spain and two outbreaks of infection with this variant were detected in farmers coming from the provinces of Aragon and Catalonia in late June 2020. Later in July, more than 100,000 minks in the Spanish North East were culled as they were found to be infected by SARS-CoV-2 [2]. There is the possibility that the mass confinement of infected animals resulted in high viral reproduction rates increasing the risk for the development of mutants, which through crossing-over and natural selection persisted to become pathogenic in humans.

Spain, following Italy, was one of the first European countries to have witnessed a significant impact of the coronavirus pandemic. The first Italian residents noted to have contracted SARS-CoV-2 infection were in a small town near Milan on February 21, 2020. It was suggested that a super spreader event occurred when a well-attended (about 50,000 spectators) football match between the Spanish team of Valencia and the Italian team of Atalanta was played in the stadium of Bergamo on February 19, 2020. Unknowingly in February, Bergamo was already the focus for seeding COVID-19 throughout the Lombardy region of Northern Italy. Following Italy, not unexpectedly, coronavirus made its appearance in Valencia and the rest of Spain was plunged into lockdown as the pandemic engulfed the whole nation, leading to high mortality rates in the elderly and other vulnerable populations [3].

By July 2020, the COVID-19 mutant Clade G (D614G) was already displacing the original Wuhan1 (Clade D) in most countries, and was prevalent in Spain [4]. This variant may have originally infected the Aragonese and Catalan farmers who possibly transmitted the virus to the mink population in the North Eastern regions of Spain. Similar to humans, where population density is a risk factor for high COVID-19 infection rates, the mass confinement of minks led to widespread

infection of the caged animals. This undoubtedly led to a high reproduction number ( $R_0$ ) in the confined animal population due to the exponential infection rate. High reproduction rates are a prerequisite for the occurrence of mutations, which eventually may thrive due to adapting to natural selective pressures [5]. In the event of the high reproduction rate and elevated viral counts, the possibility of viable mutations transmissible to humans could be more probable in the infected confined mink population. The risk is further exacerbated, similar to a multiplier effect, as repeated interspecies' infection may occur between the confined animals and their human handlers.

Following high mortality rates, national lockdown was enforced in mid-March 2020 in both Italy and Spain [6], and social distancing efforts helped in reducing the  $R_0$  by May 2020, which subsequently caused the diminution of restrictions in June. From the month of June 2020, with travel restrictions relaxed, tourists in their thousands crowded the Spanish coastal resorts. The holiday mood may have caused the relaxation of restriction on social distancing and the requirement of mandatory face protection. It should be noted that particulate matter and aerosol exhalation have been suggested as vectors for SARS-CoV-2 [7, 8], and the presence of vaping-derived particulate matter commonly performed in Spain [9] as a practice to reduce tobacco smoking, may have enhanced the transmission of the 20A.EU1 variant throughout the Spanish peninsula, and later to the European Continent. Due to the paucity of transatlantic travel, the 20A.EU1 variant has not yet been detected in the Americas.

Finally, the notion that some animals are reservoirs for coronaviruses is not a novel one. Bats and the Formosan pangolin were thought to have harboured the SARS-CoV-2 virus, which was transmitted to humans and further genetic studies indicate that SARS-CoV-2 shares 91.02% genomic concurrence with the Pangolin-CoV and Pangolin-CoV shares 90.55% genetic similarities with the BatCoV RaTG13 [10]. Although bats are increasingly recognized as the primary reservoir of coronaviruses due to the similarity in the crucial receptor binding domain between the Pangolin-CoV and SARS-CoV-2, other reports suggest the Formosan Pangolin

could be the principal reservoir [11]. The risk of transmission is elevated when animals are caged in large numbers. The forced confinement encourages high viral reproduction rates which may then increase the probability of viable pathogenic mutations.

Our hypothesis that mass confinement of minks in Spain is associated with the development and spread of the 20A.EU1 variant in the European continent needs to be investigated further. Besides the risk of coronavirus mutation and the potential low efficacy to vaccines, there is also the element of animal cruelty associated with mass confinement.

## REFERENCES

- Hodcroft, E., Zuber, M., Nadeau, S., Crawford, K. H. D., Bloom, J.D., Velesler, D., Vaughan, T. G., Coma, I., Candelas, F. G., Stadler, T., Neher, R. A. (2020) Emergence and spread of a SARS-CoV-2 variant through Europe in the summer of 2020. medRxiv [Preprint]. 2020.10.25.20219063. doi: 10.1101/2020.10.25.20219063. PMID: 33269368; PMCID: PMC7709189.
- Girola, M. 100,000 mink to be culled in Spain after testing positive for coronavirus. Lifegate. 23rd July 2020
- Mas Romero, M., Avendaño Céspedes, A., Taberero Sahuquillo, M. T. COVID-19 outbreak in long-term care facilities from Spain. Many lessons to learn. *PLOS*, 27, 2020 <https://doi.org/10.1371/journal.pone.0241030>
- Korber, B., Fischer, W. M., Gnanakaran, S. et al. (2020). Tracking Changes in SARS-CoV-2 Spike: Evidence that D614G Increases Infectivity of the COVID-19 Virus. *Cell*, 182, 812–827.
- Domingo, E. (2016) Molecular Basis of Genetic Variation of Viruses: Error-Prone Replication. Editor(s): Esteban Domingo, *Virus as Populations*, Academic Press, Chapter 2 - Pages 35-71, ISBN 9780128008379, <https://doi.org/10.1016/B978-0-12-800837-9.00002-2>.
- Tobías, A. (2020). Evaluation of the lockdowns for the SARS-CoV-2 epidemic in Italy and Spain after one month follow up. *Sci Total Environ*.725:138539. doi: 10.1016/j.scitotenv.2020.138539. Epub 2020 Apr 6. PMID: 32304973; PMCID: PMC7195141.
- Muscat Baron, Y. 2020b. Covid-19 Pandemic in relation to PM2.5, and Ambient Salinity – An Environmental Wake-up Call. MedRXiv <https://doi.org/10.1101/2020.05.03.20087056>
- Setti, L., Passarini, F., de Gennaro G et al. (2020). Potential role of particulate matter in the spreading of COVID-19 in Northern Italy: first observational study based on initial epidemic diffusion. *BMJ Open*, 10(9):e039338 DOI: 10.1136/bmjopen-2020-039338.
- Font-Mayolas, S., Sullman, M. J. M., Gras, M. E. (2019). Sex and Polytobacco Use among Spanish and Turkish University Students. *Int J Environ Res Public Health*, 16(24):5038. doi: 10.3390/ijerph16245038. PMID: 31835705; PMCID: PMC6950255.
- Zhang, T., Wu, Q., Zhang, Z. (2020). Probable Pangolin Origin of SARS-CoV-2 Associated with the COVID-19 Outbreak. *Curr Biol*. 30(7):1346-1351.e2. doi: 10.1016/j.cub.2020.03.022. Epub. Erratum in: *Curr Biol*. 2020 Apr 20;30(8):1578. PMID: 32197085; PMCID: PMC7156161.
- Ye, Z.W., Yuan, S., Yuen, K.S., Fung, S.Y., Chan, C.P., Jin, D.Y. (2020). Zoonotic origins of human coronaviruses. *Int J Biol Sci*. 16(10):1686-1697. doi: 10.7150/ijbs.45472. PMID: 32226286; PMCID: PMC7098031. \*