

## Loss of sense of smell: SARS-CoV-2 does not seem to infect the olfactory nerves

**Anosmia – or loss of sense of smell – is one of the symptoms commonly encountered in COVID-19 patients, and healthcare personnel include this parameter when diagnosing patients infected with SARS-CoV-2. Very recent studies<sup>1</sup> have put forward the hypothesis that the virus infects the olfactory nerves in the nose. However, INRAE researchers, working closely with ANSES, have shown with an experimental hamster model that the virus infects other cells of the nasal mucosa, but not the olfactory nerves. Their work was published on 3 July in the journal *Brain, Behaviour, and Immunity*.**

Loss of sense of smell is one of the most common symptoms of a SARS-CoV-2 infection. Although rarer in the case of respiratory viruses such as influenza, this type of symptom is in fact well known and is related to the ability of these viruses to infect olfactory neurons. These neurons are exposed to the environment and connect directly to the central nervous system (CNS). A virus capable of infecting them could therefore find it easier to pass into the CNS through this "olfactory pathway". Many patients have neurological symptoms, especially in the most severe cases of COVID-19, suggesting that SARS-CoV-2 may invade the CNS. In this context, it is important to understand the interactions between olfactory neurons and this virus.

SARS-CoV-2 enters cells through a specific receptor called ACE2. The olfactory neurons in the nose are surrounded by supporting cells known as sustentacular cells that have this specific ACE2 receptor, while the neurons themselves do not express it. The researchers showed that in hamsters, SARS-CoV-2 massively infected these sustentacular cells but not the olfactory neurons. They found that in addition to the infection of the supporting cells, there was desquamation of the nasal mucosa, which could explain this loss of the sense of smell. Indeed, this desquamation led to a loss of the olfactory neurons responsible for detecting odours. If this mechanism in infected hamsters also occurs in humans, it could be the cause of the observed anosmia and may prevent the virus from entering the CNS via the olfactory pathway as recently suggested<sup>2</sup>.

Fortunately, the nasal mucosa is able to regenerate itself throughout life thanks to pluripotent cells<sup>3</sup>. In their experiments, the researchers observed a 50% recovery of the initial structure of the nasal mucosa, 14 days after the onset of infection.

<sup>1</sup>Sia, S.F., Yan, L.M., Chin, A.W.H., Fung, K., Choy, K.T., Wong, A.Y.L., Kaewpreedee, P., Perera, R., Poon, L.L.M., Nicholls, J.M., Peiris, M., Yen, H.L., 2020. Pathogenesis and transmission of SARS-CoV-2 in golden hamsters. *Nature*.

<sup>2</sup> Romoli, M., Jelcic, I., Bernard-Valnet, R., Garcia Azorin, D., Mancinelli, L., Akhvlediani, T., Monaco, S., Taba, P., Sellner, J., 2020. A systematic review of neurological manifestations of SARS-CoV-2 infection: the devil is hidden in the details. *European Journal of Neurology*.

<sup>3</sup> Cells capable of dividing throughout an individual's lifetime in order to renew different types of cells, including the olfactory epithelium with its neurons and sustentacular cells.

#### Reference:

Bertrand Bryche, Audrey St Albin, Severine Murri, Sandra Lacôte, Coralie Pulido, Meriadeg Ar Gouilh, Sandrine Lesellier, Alexandre Servat, Marine Wasniewski, Evelyne Picard-Meyer, Elodie Monchatre-Leroy, Romain Volmer, Olivier Rampin, Ronan Le Goffic, Philippe Marianneau, Nicolas Meunier, Massive transient damage of the olfactory epithelium associated with infection of sustentacular cells by SARS-CoV-2 in golden Syrian hamsters, **Brain, Behavior, and Immunity**, 2020, <https://doi.org/10.1016/j.bbi.2020.06.032>.

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