# 第 1509 回生物科学セミナー

日時: 8 月 29 日(木) 16:00-17:00 理学部 1 号館 337A

演者: **Peter Mombaerts, M.D., Ph.D.**
(Director, Max Planck Research Unit for Neurogenetics)

演題: **Visualizing how SARS-CoV-2 attacks the olfactory system in COVID-19 patients**

Anosmia, the loss of smell, is a common and often the sole symptom of COVID-19. The onset of the sequence of pathobiological events leading to olfactory dysfunction remains obscure. We reasoned that the neurotropic or neuroinvasive capacity of SARS-CoV-2, if it exists, should be most easily detectable in individuals who died in the acute phase of the infection. Procuring high-quality fresh tissue samples from the human olfactory mucosa and olfactory bulb has proved challenging, either from living patients or during an autopsy. We developed a protocol for rapid postmortem bedside sampling of these structures, using an endoscopic endonasal surgical technique adapted from skull base surgery. The procedure leaves no visible incisions and enables a rapid response and logistic flexibility in a variety of hospital settings including a ward. Compared to a typical autopsy, the protocol drastically reduces the postmortem interval — in our experience, the median was 89 minutes — thereby contributing to preserving the tissue samples in pristine condition. Our cohort included 115 COVID-19 patients who died a few days after diagnosis of SARS-CoV-2 infection, enabling us to catch the virus while it was still replicating. We found that sustentacular cells are the major target cell type in the olfactory mucosa. We failed to find evidence for infection of olfactory sensory neurons. We postulate that transient insufficient support from sustentacular cells triggers transient olfactory dysfunction in COVID-19 and that olfactory sensory neurons get affected without getting infected. Confocal imaging of sections stained with fluorescence RNAscope and immunohistochemistry afforded the light-microscopic visualization of extracellular SARS-CoV-2 virions in tissues. We failed to find evidence for viral invasion of the parenchyma of the olfactory bulb and of the frontal lobe of the brain. Instead, we identified anatomical barriers at vulnerable interfaces, such as by perineurial olfactory nerve fibroblasts that enwrap olfactory axon fascicles in the lamina propria of the olfactory mucosa. This poorly characterized cell type appears to seal olfactory axon fascicles hermetically from invasion by SARS-CoV-2 virions. We speculate that this barrier may also be effective against some of the many other pathogens that infect the nasal mucosa and could threaten the brain.

参考文献:

Khan, Mona et al. “Visualizing in deceased COVID-19 patients how SARS-CoV-2 attacks the respiratory and olfactory mucosae but spares the olfactory bulb.” ***Cell*** vol. 184,24 (2021): 5932-5949.e15. doi:10.1016/j.cell.2021.10.027

Khan, Mona et al. “Anatomical barriers against SARS-CoV-2 neuroinvasion at vulnerable interfaces visualized in deceased COVID-19 patients.” ***Neuron*** vol. 110,23 (2022): 3919-3935.e6. doi:10.1016/j.neuron.2022.11.007

担当: 東京大学大学院理学系研究科・生物科学専攻・ 竹内研究室