Commentary: SLAM- and Nectin-4-Independent Noncytolytic Spread of Canine Distemper Virus in Astrocytes

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Keywords: Canine Distemper Virus, Cetacean morbillivirus, Measles Virus, brain, astrocytes, viral neuropathogenesis, comparative neuropathology

A commentary on

SLAM- and Nectin-4-Independent Noncytolytic Spread of Canine Distemper Virus in Astrocytes
by Alves, L., Khosravi, M., Avila, M., Ader-Ebert, N., Bringolf, F., Zurbriggen, A., et al. (2015). J. Virol. 89, 5724–5733. doi: 10.1128/JVI.00004-15

As in the case of the small subset (8–20 per 1 million) of Measles Virus (MeV)-infected humans developing a peculiar neurological disease condition known as “subacute sclerosing panencephalitis” (SSPE) (Garg, 2008; Kweder et al., 2015), Canine Distemper Virus (CDV) may also give rise to a persistent, “brain-only” form of disease in dogs, known as “old dog encephalitis” (ODE) (Reuter and Schneider-Schaulies, 2010; Sato et al., 2012). Interestingly, peculiar forms of morbilliviral disease resembling those reported in MeV-infected patients and CDV-infected dogs have also been described among Cetacean Morbillivirus (CeMV)-infected striped dolphins (Stenella coeruleoalba) after the two major morbilliviral epidemics occurred in 1990–92 and 2006–08 in the Western Mediterranean. In a similar manner to what seen in CDV-affected canines and MeV-affected humans, dolphins hit by this form of infection harbor morbilliviral genome and/or antigens exclusively in their brain parenchyma (Domingo et al., 1995; Di Guardo et al., 2013).

Is this enough to conclude that the aforementioned cases of “brain-only,” Morbillivirus infection in striped dolphins could/should be regarded as reliable, comparative neuropathology and viral neuropathogenesis models in relation to their canine and human “counterparts”?

We don’t know, although “yes and no” seems to be the best possible answer at the moment, provided that the agent- and host-related factors and mechanisms driving CeMV colonization and persistence inside the brain of chronically infected dolphins are unknown (Di Guardo et al., 2013; Di Guardo and Mazzariol, 2016). In this respect, Signaling Lymphocyte Activation Molecule (SLAM/CD150), the cell receptor involved in the well-documented lymphotropic behavior of Morbillivirus genus members, is not expressed by neurons, similarly to nectin-4, another receptor molecule accounting for morbilliviral epitheliotropism (Sato et al., 2012). Nevertheless, it has also been suggested that nectin-4 expression could be related to CDV neurovirulence, with nectin-4-immunoreactive neurons of the canine brain representing a preferential virus target (Pratakpiriya et al., 2012). Worthy to be mentioned, the long-lasting persistence of CDV in the brain tissue from ODE-affected dogs could have been recently described as the result of a non-cytolytic, astrocyte-to-astrocyte viral spread through a putative, hitherto unknown glial cell receptor, different from SLAM and nectin-4, which has been provisionally termed “GliaR” (Alves et al., 2015). This is of special concern in relation to “canine demyelinating leukoencephalitis,” one of the various disease conditions suffered by CDV-infected dogs, a peculiar feature of which is...
Di Guardo, G., Giacominelli-Stuffler, R., Baffoni, M., Pietroluongo, G., Di Guardo, G., and Mazzariol, S. (2016). Cetacean Morbillivirus Infection in Cetacean Brain: Pathological, Immunohistochemical and Biomolecular Findings. *J. Neurol.* 243, 1326–1332. doi: 10.1007/s00415-016-3010-2

Reference to the original manuscript: Alves, L., Khosravi, M., Avila, M., Ader-Ebert, N., Bringolf, F., Zurbriggen, A., et al. (2015). Characterization of Measles Virus Strains Causing Subacute Sclerosing Panencephalitis in France in 1977 and 2007. *J. Med. Virol.* 87, 1614–1623. doi: 10.1002/jmv.24257

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