Belgian National Reference Laboratory for rabies

Rabies Laboratory of Sciensano, Brussels

The Rabies Laboratory of Sciensano (Brussels, former Scientific Institute of Public Health WIV-ISP) is officially recognized as the Belgian National Reference Centre for Human Rabies (NRC Rabies: financed by the National Institute for health and Invalidity Insurance, RIZIV-INAMI) and the National Reference Laboratory for Animal Rabies (NRL Rabies: recognized by the Federal Agency for the Safety of the Food Chain, FAVV-AFSCA). The lab is also recognized by the European Commission to perform rabies serology in pets in the frame of travel. The rabies laboratory is embedded within the Service of Viral Diseases that performs diagnosis and surveillance of emerging viruses, influenza and other respiratory viruses and vaccine-preventable viral diseases of humans.

Both human and animal rabies diagnosis and surveillance are thus centralized in the same laboratory. The laboratory also works in close collaboration with the Institute of Tropical Medicine in Antwerp (ITG), which is responsible for anti-rabies prophylaxis in humans.

Our rabies lab has been around for more than hundred years and was always closely involved in the history of rabies in Belgium. We were implicated in the oral vaccination campaigns in foxes in the eighties and nineties, which led to the official elimination of fox rabies in Belgium in 2001.

History of rabies in Belgium	
1922	Last local human case
1930	Elimination canine rabies
1966-99	Epidemic in foxes (33 years)
1989-2001	Oral vaccination campaigns foxes
1990	Last human import case
1998	Last fox case (Bastogne)
1999	Last case cow (Bastogne)
2001	OIE declares Belgium rabies-free
2007	1 import case dog (Morocco)
2008	1 import case dog (Gambia)
2010	1 import case bat (Spain)
2016	First detection of European Bat Lyssavirus-1 in a serotine bat (Bertrix)
2017	Second case of European Bat Lyssavirus-1 in a serotine bat (Etalle)

Our lab performs serological tests by the virus-neutralisation method (RFFIT) in both humans (to validate the efficacy of preventive vaccination and post exposure treatment) and pets (in the framework of pet travel). Our diagnosis and serology methods are accredited according to ISO17025 and ISO15189 standards.

A passive surveillance system for domestic animals and wildlife is maintained in Belgium. Each year, we analyse about 300-400 suspected domestic animals (dogs, cats and cattle) and 50-100 suspected wild animals in the frame of rabies surveillance and to guarantee the country's rabies-free status.

Our laboratory is involved in several projects concerning prevention, treatment and pathogenesis of rabies:

- *Use of the rabies model to study the impact of cell death (caspases, RIPK) and inflammation (NF-κB) signalling pathways on the outcome of viral brain infection*
- *Assessment of the efficacy of abbreviated intradermal vaccination schedules (one-day and two-day treatments): several clinical trials are running in collaboration with the Military Hospital Queen Astrid (Brussels) and the Institute of Tropical Medicine (Antwerp). This work contributed to the adaptation of the WHO rabies vaccination recommendations in 2018.*
- *Exploring and expanding therapeutic uses and applicability of therapeutic heavy-chain derived single variable domains: Nanobodies® (VHH) as a new strategy for prevention and treatment of rabies*

The rabies team is composed of Dr. Sanne Terryn (Ir, PhD), Dr. Bernard Brochier (DVM, PhD), Dr. Steven Van Gucht (DVM, PhD, also head of the Viral Disease Service) and 2 laboratory technicians: Marie-Louise Blondiau, and Aurélie Francart. Véronique Verhocht and Fabien Berger assist in the administration and call centre.

Current interests involve rabies (surveillance in bats, pathogenesis and vaccine development) and emerging zoonoses in wildlife, including tick-borne encephalitis virus and other rodent-borne viruses.

Some of our recent rabies publications:

De Pijper *et al.* 2018. Rabies antibody response after two intradermal pre-exposure prophylaxis immunizations: An observational cohort study. Travel Medicine and Infectious Disease 2018 April 6

Kip *et al.* 2018. MALT1 Controls Attenuated Rabies Virus by Inducing Early Inflammation and T Cell Activation in the Brain. J Virol. 2018 Mar 28;92(8).

Kip *et al.* 2017. Impact of caspase-1/11, -3, -7, or IL-1β/Il-18 deficiency on rabies virus-induced macrophage cell death and onset of disease. Cell Death Discov. 2017 Mar 6;3:17012.

Terryn *et al.* 2016. Post-exposure treatment with anti-rabies VHH and Vaccine significantly improves protection of mice from lethal rabies infection. PLoS Negl Trop Dis. 2016 Aug 2;10(8):e0004902.

Pastoret *et al*. 2014. Eradicating rabies at the source. Rev. Sci. Tech. Aug;33(2):509-19, 497-508.

Terryn *et al*. 2014. Protective effect of different anti-rabies virus VHH constructs against rabies disease in mice. PLOS ONE. Oct 7;9(10):e109367. doi: 10.1371/journal.pone.0109367. eCollection 2014.

Suin *et al*. 2014. A two-step lyssavirus real-time polymerase chain reaction using degenerate primers with superior sensitivity to the fluorescent antigen test. Biomed Res Int. 2014:256175. doi: 10.1155/2014/256175. Epub 2014 Apr 15.

Soentjens *et al*. 2013. Low cost intradermal rabies vaccination is indeed very promising. Clin Infect Dis. 2013 May;56(10):1509-10. doi: 10.1093/cid/cit080. Epub 2013 Feb 14.

Van Gucht *et al*. 2013. Favourable outcome in a patient bitten by a rabid bat infected with the European bat lyssavirus-1. Acta Clinica Belgica, 68, 1, 54-58. Doi: 10.2143/ACB.68.1.2062721.

Nazé *et al*. 2012. Infectivity of rabies virus-exposed macrophages. Microbes and Infection, Nov 14. doi:pii: S1286-4579(12)00272-9. 10.1016/j.micinf.2012.10.018.

Rosseels *et al*. 2011. A non-invasive intranasal inoculation technique using isoflurane anesthesia to infect the brain of mice with rabies virus. J Virol Methods. 173(1):127-36. Epub 2011 Feb 3.

Hultberg *et al*. 2011. Llama-derived single domain antibodies to build multivalent, superpotent and broadened neutralizing anti-viral molecules. PLoS One.Apr 1;6(4):e17665.