Abstract 815.09 Summary

Lead Author: Charlotte D'Hulst, PhD (212) 650-3169
Hunter College, City University of New York cdhulst@genectr.hunter.cuny.edu
New York, NY

Scientists Developing Mice Able to Detect Hidden Landmines

Genetic modification could increase capacity to smell TNT by 500 fold

Inspired by a widely acclaimed program that has deployed specially trained rats to sniff out landmines, scientists are now working to develop transgenic mice with the capacity to smell landmine explosives amplified by 500 fold. The results of the new effort, The MouSensor Project, to build a "biosensor" for landmine detection were presented today at Neuroscience 2012, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

Landmines affect 66 countries and 7 territories around the world, posing a structural barrier to development and economic growth. Landmine removal is costly and dangerous. Giant African pouched rats (HeroRats), with their acute sense of smell, have proven to be effective at detecting landmines, yet small enough not to detonate them.

"The rats are very effective but mice have some advantages as mine detectors because they are cheaper to manage and house, and easier to breed," said lead author Charlotte D'Hulst, Ph.D. in the laboratory of Dr. Paul Feinstein at Hunter College, City University of New York. "Most importantly, it is relatively easy to genetically manipulate odorant receptors in mice."

Odorant receptors give mammals the ability to distinguish one odor from another. A specific receptor for identifying a particular smell is typically found in 1 out of every 1,000 olfactory neurons, the cells in the nose that process activity from odorant receptors and transmit these signals to the brain. Recently, other U.S. scientists identified the specific rodent odorant receptor that detects a chemical known as 2,4-dinitrotoluene, or DNT, which is essentially the same as TNT. Feinstein and his colleagues were able to genetically modify a mouse so that the odorant receptor for DNT now occurs at much greater proportions in the mouse's nose. Follow-up imaging and behavioral tests will measure their sensitivity to DNT.

Research was supported with funds from the National Institutes of Health.

Scientific Presentation: Wednesday, Oct. 17, 8 –9 a.m., Hall F-J

815.09, Generating a biosensor for the detection of landmines
***C. D'HULST**, M. SAPARAUSKAITE, P. FEINSTEIN; Biol. Sci., Hunter College/Cuny, New York, NY

TECHNICAL ABSTRACT: Detection of landmines is difficult, dangerous, costly and time-consuming (http://www.apopo.org). Considering the critical need to develop a biosensor for the detection of explosives found in landmines, our goal is to generate a transgenic mouse strain that is hypersensitive to 2,4-dinitrotoluene (DNT), a mimic for the explosive TNT. Currently, a Belgian NGO, APOPO, trains giant African pouched rats (HeroRats) to identify the scent of explosives in landmines. The rats have an acute sense of smell and are small enough not to detonate the mines. Every time they detect TNT, the rats make a clicking sound and receive a bite of banana as a reward. Although this approach has proven to be effective (two of APOPO's mine detection rats, working with two human handlers, can cover 300 square meters of land in one hour. In comparison, two manual deminers using metal detectors, will need two full days to cover the same area), it takes nine months of painstaking on-and-off field training for a rat to be deployed for mine detection. Therefore, we engineered an innovative biological approach to challenge this global health problem. We generated a transgenic mouse model that over expresses a newly identified odorant receptor (OR) that can report the presence of 2,4-dinitrotoluene (DNT), an explosive residue mimic (Radhika et al., 2007 & Fukutami et al., 2011). Usually, a specific OR is expressed in 1/1000 neurons with a limited detection of the specific odorant as a consequence; our technique allows us to amplify the detection limit of a specific odor of interest 500-fold, which may be even further amplified by higher cortical areas of the brain. A first analysis of these transgenic animals showed that glomeruli (the first relay station in the brain, which allows for synaptic activity of an activated odorant receptor to be registered), which are tagged with a red fluorescent protein, are formed in the olfactory bulb. We are currently testing these genetically modified mice for their sensitivity to DNT using in vivo imaging techniques and behavioral tests such as the go/no go discrimination test. This is the first time that a mouse with a monoclonal nose', in which greater than 50% of the sensory neurons express a single odorant receptor gene, hypersensitive to a mimic for the explosive TNT has been created.