Trojan horse bacteria use nanobodies to conquer sleeping sickness

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Sleeping sickness, caused by the trypanosome *Trypanosoma brucei*, is transmitted to humans (and animals) via the bite of the tsetse fly. New research published in BioMed Central's open access journal *Microbial Cell Factories* uses a bacteria, which naturally lives in the fly, to release nanobodies (antibody fragments) against the trypanosome. These antibodies, which bind to the surface of the parasite, are the first stage in producing targeted nanobodies which could kill, or block, trypanosome development.

Sleeping sickness threatens millions of lives across sub-Saharan Africa. The first stage (haemolymphatic phase) of infection causes fever, headaches, aching joints and itching. The second stage (neurological phase), when the parasite crosses the blood brain barrier, results in confusion, poor co-ordination and the sleep disturbances which give the disease its name. Without treatment sleeping sickness is fatal. However diagnosis and treatment are difficult and require specially trained staff. Trypanosome infection in cattle causes anemia and weight loss, which can lead to death of the anima. Together these have a serious impact on public health and agricultural development across Africa.

The bacterium (*Sodalis glossinidius*) is an endosymbiont, similar to the 'good bacteria' which populate human intestines, found in tsetse fly midgut, muscle, fat and salivary glands. They are passed from a mother to her offspring - consequently genetically modified bacteria should be spread down generations of flies once females are released into the wild. Researchers from Belgium genetically altered S. glossinidius bacteria so

that they secreted a single domain antibody against a variant surface glycoprotein (VSG) of T. brucei. The growth of the mutated bacteria was unaltered, increasing their chances of survival once released.

Prof Van Den Abbeele, from the Institute of Tropical Medicine, Antwerp, explained, "When we looked at living trypanosomes under conditions that mimic the inside of the tsetse gut the Sodalis-expressed nanobodies were biologically active and bound all over the surface of the parasite. Now that we know this technique works we are looking at making nanobodies which will destroy or block development of the parasite in the tsetse fly gut."

The most recent epidemic occurred in 1970 and, despite continued efforts and falling numbers of new cases in that last decade, this disease has not yet gone away. This new technology provides hope against a devastating disease.

More information: Expression and extracellular release of a functional anti-trypanosome Nanobody(R) in Sodalis glossinidius, a bacterial symbiont of the tsetse fly. Linda De Vooght, Guy Caljon, Benoit Stijlemans, Patrick De Beatselier, Marc Coosemans and Jan Van Den Abbeele. *Microbial Cell Factories* (in press)

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