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BLOOD-DERIVED VESICLES LIKELY TO HELP DETECT BRAIN DISEASE

To monitor the onset and progression of diseases or the effectiveness of treatment it is essential to rely on indicators that reflect actual tissue damage and are easily accessible. Scientists from the Institute of Animal Physiology and Genetics CAS have succeeded in isolating small blood particles that are able to carry information about the neurodegenerative Huntington's disease. Further research into the composition of these particles may help detect damage to otherwise inaccessible organs, including the brain.

The brain acts as the control unit of the entire nervous system and its damage is usually associated with grave consequences. At the same time, it is rather difficult to directly observe the composition of brain tissue during an individual's lifetime, as it is a fundamentally inaccessible organ for biopsy purposes. Scientists from the PIGMOD Center of the Institute of Animal Physiology and Genetics CAS in Liběchov, who have long been involved in serious brain disease research, have succeeded in isolating and describing small vesicles that can be easily derived from blood and may carry information about brain tissue damage.

Small vesicles derived from blood may carry information about the condition of remote organs

"We found out that the small vesicles derived from blood, so-called extracellular vesicles or exosomes, bear huntingtin, a protein, whose mutation is the cause of Huntington's disease," says the team leader Helena Kupcová Skalníková from the Institute of Animal Physiology and Genetics CAS. *"The overall amount of huntingtin in these vesicles is higher in porcine models and patients with Huntington's disease compared to healthy control subjects. Besides that, even specific forms of mutant huntingtin were detected that were not found in the healthy individuals,"* the scientist adds.

In recent years, extracellular vesicles have become an object of great interest to researchers – precisely due to the fact that they are relatively easy to derive from blood or other body fluids and contain various molecules, including RNA or proteins, that could be used to diagnose a variety of disease.

"We can imagine this as if tiny portions of diseased tissue from remote and hard-to-reach organs got into the blood and, without the need for biopsies of the relevant organs, a blood sample could serve to examine the diseased tissue as well as to detect or monitor the course and effectiveness of treatment of diseases such as neurodegenerative disorders or tumours," Helena Kupcová Skalníková explains the potential role of vesicles.

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A long road to true biomarkers

However, the work of THE PIGMOD Center scientists is just beginning. The role of extracellular vesicles as a source of biomarkers for neurodegenerative disorders is still a long way off. One of the prerequisites is successful basic research regarding the molecular composition of these particles. By implementing the methods for isolating and characterising blood-derived vesicles within the laboratory, scientists can continue to use them in their search for other molecules (besides huntingtin itself) that could reflect disease progression and monitor treatment effectiveness. However, in the course of working with extracellular vesicles, scientists have had to deal with the fact that only a handful of vesicles can be derived from blood and that they are difficult to manipulate, since they are not visible and conventional technologies are not able to detect them.

"It may sound simple, but technically, manipulation of vesicles is particularly challenging. Imagine working with something for ten hours and at the end of it you do not really know if your samples actually carry the particles you are observing. That is because the particles are virtually so small that they cannot be seen even in a light microscope and there are so few of them that the test-tube appears completely empty," Helena Kupcová Skalníková describes the pitfalls of working with extracellular vesicles. *"Thanks to the collaboration with the Institute of Experimental Medicine CAS and the University of Chemistry and Technology, we had access to specialised technologies for nanoparticles detection, which allowed us to determine the number and size of the isolated vesicles,"* adds the scientist.

Scientists are now analysing the molecular composition of the vesicles and comparing the content of the vesicles between the minipigs carrying the gene for mutant huntingtin responsible for Huntington's disease and the control subjects. In collaboration with the Department of Neurology and Centre for Clinical Neuroscience at the 1st Faculty of Medicine of Charles University and the General University Hospital they are also analysing the composition of vesicles isolated from the blood plasma of patients with Huntington's disease as well as control subjects.

"Our results have proven that extracellular vesicles carry information about Huntington's disease. If we manage to find other molecules that reflect tissue damage in a specific manner, it could speed up the development of new therapies and facilitate the monitoring of their effectiveness," says Helena Kupcová Skalníková, highlighting the potential of extracellular vesicles.

Huntington's disease is a rare genetic neurodegenerative brain disease that is currently still untreatable and affects 8 out of 100,000 people. It is characterised by jerky movements of the limbs and entire body that may gradually progress into complete paralysis. Impaired mobility is usually accompanied by behavioural disturbances and cognitive decline. The insidious nature of the disease lies in its gradual and irreversible adult-onset, typically around the age of 40. At the same time, it is an autosomal inherited disease, which means that when it first "appears" in a family, it is not only the patient who faces the diagnosis, but also their children, who have a 50% chance of inheriting the disease.

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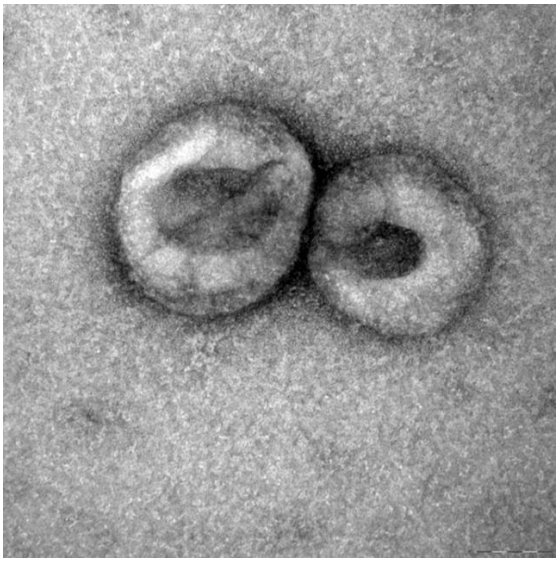
We offer the media the option to film at the minipig breeding facilities and in the laboratories of IAPG CAS in Liběchov.

Photo gallery

Liběchov minipigs – Huntington's research model
PHOTO: Helena Kupcová Skalníková



Extracellular vesicles derived from blood plasma, reaching a size of approximately 30-150 nm, can be observed in an electron microscope after being magnified multiple times (shown magnified 200,000x). For visualisation purposes, it is like magnifying a 5 mm drop of blood to the size of 1 km and then observing the vesicles with the naked eye. Originally, the vesicles have a spherical shape, but during sample preparation and drying, their top falls off, so they look like little cups under a microscope.
PHOTO: Helena Kupcová Skalníková