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How to detect signs of neurodegeneration earlier and more accurately

Signs of neurodegenerative diseases, visible years before the emergence of clinical manifestations, can be detected during the examination of medical samples by means of fluorescence microscopy. This is, however, on condition that suitably sensitive and selective dyes are used that bind to specific amyloid structures. The new dye, proposed by the Polish-American group of scientists, is a step towards the personalized neuromedical prophylaxis of the future.

From memory disorders to the notorious Creutzfeldt-Jakob disease or Alzheimer's disease – dozens of diseases are related to the formation of amyloid fibrils deposits of complex shapes. They are deposited as a result of proteins misfolding, to structures mainly known as amyloid beta. There are grounds to believe that soon the first signs of neurodegeneration will be identifiable in medical laboratories at an earlier stage of development of brain disease, and in a much more precise way than ever before. The new avenues of detection are being opened thanks to the achievements of a Polish-American team, which includes scientists from the Institute of Physical Chemistry of the Polish Academy of Sciences (IPC PAS) in Warsaw, Wroclaw University of Technology, the University of Michigan and the University of California, Santa Barbara.

With the aging of society, the importance of early detection of neurodegenerative diseases, usually manifesting in people at a later age, is growing. The stakes are high – just from looking at the data on Alzheimer's disease. While just 3% of people over 70 years of age suffer from the disease, as many as half of the population suffers after the age of 90. It is known, however, that this disease probably begins even 20 years before the onset of its first symptoms. In this situation, the early and precise detection of its harbingers takes on a particular significance.

“Before a lab technician examines a sample of a patient’s cerebrospinal fluid under a fluorescence microscope, he must somehow label the required chemicals with a fluorescent dye. Usually, small molecules are used for this purpose, selected so that they only bind with the molecules that are to be detected. We have proved that we can successfully use the polythiophene derivative PTEBS as the dye. This is a polymer, that is, quite a big atomic structure. In practice, it has turned out that the molecule size of PTEBS is not only not a disadvantage, but in fact quite a significant advantage,” says Dr. Piotr Hanczyc (IPC PAS, currently Faculty of Physics, University of Warsaw), the first author of the publication in the *Journal of Luminescence*.

The team’s research has made it possible to conclude that the presence of both the required chemical molecules as well as their aggregates can be recorded using the PTEBS dye, even when

they are present in the sample at significantly lower concentrations than detected by thioflavin T, currently one of the most popular fluorescent dyes used for labelling protein aggregates.

An important advantage of the new dye is related to the existence of polymorphic forms of amyloid, i.e. the fact that while one configuration of atoms in a molecule may be responsible for triggering neurodegenerative processes, the another can turn out to be harmless.

“Standard dyes are molecules of a small size. You cannot do too much with them, in addition they have been thoroughly tested and a lot is already known about them. The molecules of our dye are large, and many substituent groups are attached to the main chain. These groups can be modified and extended to a large extent, increasing the affinity of the dye not only to the selected form of amyloid, but also to its specific polymorph. This gives us a lot to work with,” emphasizes Dr. Hanczyc.

The new dye should help, among others, in the more precise determination of the polymorphic variations responsible for the course of neurodegenerative processes in patients. However, its applications in prophylactic examinations are particularly promising. They would allow for the selection of more effective treatment strategies, personalized for a particular patient. This sort of procedure would mean that it would be possible to significantly delay the development of neurodegenerative diseases and possibly even completely prevent them in the future.

On the Polish side, the research was financed from the International Brain Research Organization (IBRO) grant.

The Institute of Physical Chemistry of the Polish Academy of Sciences (http://www.ichf.edu.pl/) was established in 1955 as one of the first chemical institutes of the PAS. The Institute's scientific profile is strongly related to the newest global trends in the development of physical chemistry and chemical physics. Scientific research is conducted in nine scientific departments. CHEMIPAN R&D Laboratories, operating as part of the Institute, implement, produce and commercialise specialist chemicals to be used, in particular, in agriculture and pharmaceutical industry. The Institute publishes approximately 200 original research papers annually.

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SCIENTIFIC PAPERS:

1. “Surface patterns of insulin fibrils revealed by time-resolved spectroscopy measurements of fluorescent probes”
P. Hańczyc, A. Justyniarski, J. Kim, A. Mikhailovsky, M. Ivanova
Journal of luminescence, 201, 31-37, 2018
DOI: 10.1016/j.jlumin.2018.03.038

LINKS:

http://www.ichf.edu.pl/
The website of the Institute of Physical Chemistry of the Polish Academy of Sciences.

http://www.ichf.edu.pl/press/
Press releases of the Institute of Physical Chemistry of the Polish Academy of Sciences.

IMAGES:

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The new fluorescent dye can be tailored to bind with specific polymorphic forms of insulin amyloid complexes. (Source: IPC PAS, Grzegorz Krzyzewski)

IChF181129b_fot02s.jpg **HR:** http://ichf.edu.pl/press/2018/11/IChF181129b_fot02.jpg
The PTEBS dye should help in the earlier detection of neurodegenerative diseases. (Source: IPC PAS, Grzegorz Krzyzewski)