

## Blood Test for Alzheimer's Disease



### Features

- early detection of Alzheimer's disease in blood sample, long before clinical symptoms become visible
- analyzed morphological properties of pathological proteins linked to memory and cognition impairment
- quantification of morphological properties of protein aggregates from oligomers to fibrils on red blood cells by analysis with AFM
- study with patients and healthy controls published in Science journal (Science Advances, 2021)

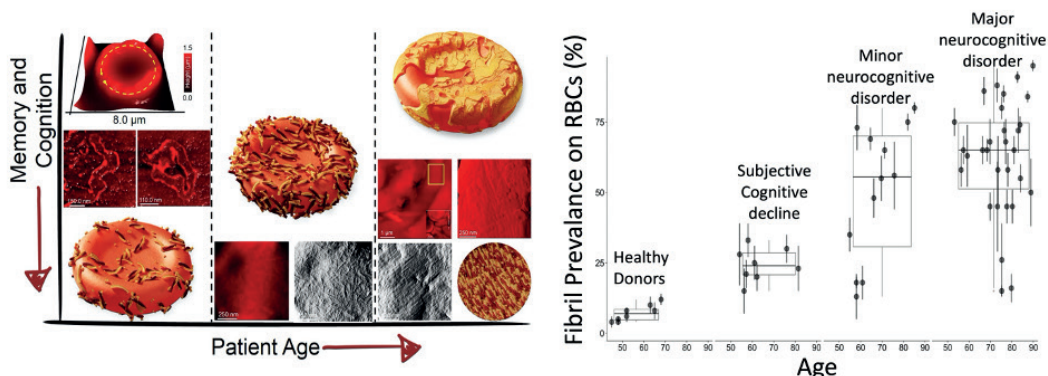
### Background

Alzheimer's disease, like other neurodegenerative diseases, leads to clinical symptoms only at an advanced stage, and currently no effective therapy is available. Experts believe that the chances of a successful medical treatment would increase dramatically by a much earlier onset of the therapy. This requires a reliable diagnosis by specific biomarkers long before the first clinical symptoms using a minimally invasive and cost-effective approach.

Alzheimer's disease is associated with deposits of misfolded amyloid and tau proteins, so-called plaques, in the affected regions of the brain. Such proteins are known to spill into the blood after crossing the blood brain barrier, hence highlighting blood as a rich source for screening such pathological proteins. Currently, available techniques can quantify the total amount of pathological amyloid and tau proteins, but information on the physical aspects of the proteins (structure), remains unknown in blood and hence unavailable to clinicians. Specific data on protein structure, however, provides important clues for diagnosis and disease stage.

## Invention

The invention relates to a method to determine morphological data of protein aggregates deposited on red blood cells present within a blood smear with nanometer scale spatial resolution. The cell surface is scanned using an Atomic Force Microscope. The so generated images are analyzed and morphological aspects of the protein aggregates on red blood cells are determined, such as size, shape, prevalence and assembly. The morphological parameters are physical biomarkers and serve to diagnose neurodegenerative diseases in human blood under standard laboratory conditions.



## Advantages

The present method requires just a blood sample taken from the patient's peripheral veins. The blood sample is directly analyzed under standard laboratory conditions, without chemical fixation, labelling, dyeing and no custom-made or expensive equipment is needed. The entire process can be largely automated. On a technical level, the invention can spatially map protein aggregates in blood/on red blood cells and resolve the full spectrum of aggregates from oligomers to mature fibrils. The technique can also differentiate between spherical and annular oligomers, which are known to be more cytotoxic species in certain neurodegenerative diseases. The method was validated in a study with patients and healthy controls (see reference below).

## Applications

- early blood-based detection of neurodegenerative disorders such as Alzheimer's disease.
- monitor disease relevant size, shape and morphology of protein aggregates in blood on red blood cells
- generate structural data to complement biochemical markers
- evaluate disease progression and efficiency of prescribed treatment.
- evaluate efficiency of novel therapies in clinical studies

## Ownership

Empa, Swiss Federal Laboratories for Materials Science and Technology, Überlandstrasse 129, CH-8600 Dübendorf; Patent pending

## References

Spatial organisation of protein aggregates on red blood cells as physical biomarkers of Alzheimer's disease. P.N. Nirmalraj, T. Schneider and A. Felbecker. Science Advances, 2021, 7, 39, eabj2137.

## Keywords

Protein imaging in blood, Alzheimer's disease pathology, atomic force microscopy

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