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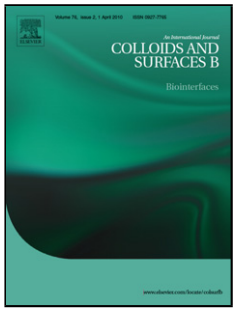

Title: Insulin amyloid structures and their influence on neural cells

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Insulin amyloid structures and their influence on neural cells

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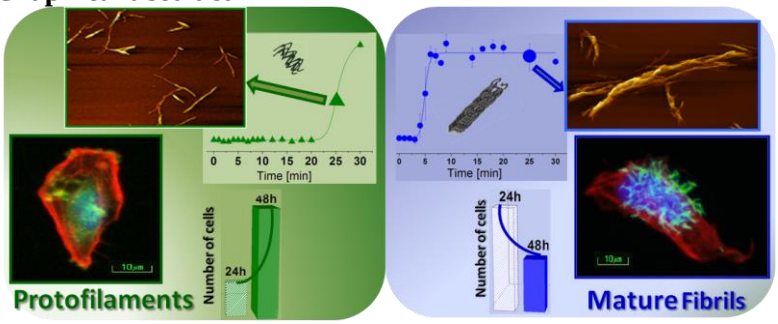
Graphical abstract



Highlights

- The effect of insulin amyloids on the human neuroblastoma cell line *in vitro* is explored.
- The aggregates deposited on cell cultures decreased their number depending on the degree of fibrillization.
- The cell growth and proliferation was affected by fibrils presence on the substrates.
- Amyloid fibrils interfere with cell adhesion machinery and prevent adhesion of the cells.

1. Abstract

Peptide aggregation into oligomers and fibrillar architectures is a hallmark of severe neurodegenerative pathologies, diabetes mellitus or systemic amyloidoses. The polymorphism of amyloid forms and their distribution are both effectors that potentially modulate the disease, thus it is important to understand the molecular basis of protein amyloid disorders through the interaction of the different amyloid forms with neural cells and tissues. Here we explore the effect of amyloid fibrils on the human neuroblastoma (SH-SY5Y) cell line *in vitro*. We control the kinetic of fibrillization of insulin at low pH and higher temperature. We use a multiscale characterization via fluorescence microscopy and multimodal scanning probe microscopy to correlate the number of cells and their morphology, with the finer details of the insulin deposits. Our results show that insulin aggregates deposited on neuroblastoma cell cultures lead to a progressive modification and decreased number of cells that correlates with the degree of fibrillization. SPM unravels that the aggregates strongly interact with the cell membrane, forming a stiff encase that possibly leads to an increased cell membrane stiffness and deficit in the metabolic exchanges between the cells and their environment. The presence of fibrils does not affect the number of cells at 24 hours whereas drop down to 60% is observed after 48 hours of incubation.

Keywords: Amyloid, amyloid diseases, protein aggregation, neural cells, microscopy