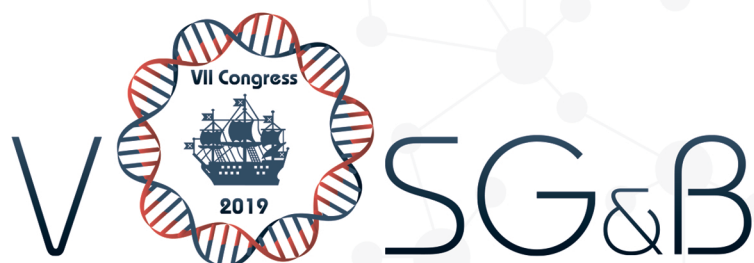




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and Associate Symposiums

VII Съезд Вавиловского общества  
генетиков и селекционеров (ВОГиС)

# СБОРНИК ТЕЗИСОВ BOOK OF ABSTRACTS

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## HUMAN NUCLEOPORIN NUP58 IS A NEW AMYLOID WHICH IS COLOCALIZED WITH 103QP PROTEIN IN YEAST MODEL

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Amyloids are a group of protein aggregates possessing a set of unusual features including resistance to detergent or protease treatment and their ability to induce the transition of some proteins from soluble to aggregated form. Numerous investigations of amyloids are of much interest due to increasing frequency of amyloid-associated disorders. One of such diseases is Huntington's disease, which is an inherited disorder accompanied by the encephalopathy and the accumulation of amyloid aggregates of the Huntingtin protein (Htt). Several proteins interacting with these aggregates are supposed to be amyloidogenic. Coaggregation of these proteins with Htt may cause or accelerate development of the disease.

To identify such proteins we have screened human proteome, focusing on proteins physically interacting with Htt according to the BioGRID database. These proteins were analyzed with ArchCandy and IUPred programs to identify amyloidogenic regions within unstructured part of the protein. This allowed to find a set of potential amyloids, including Nup58, a component of a midplane ring of nuclear pore complex. This protein is implicated in regulation of nucleocytoplasmic traffic of different RNA's.

To check amyloid properties of Nup58 we used the well-known C-DAG (curli-dependent amyloid generator) system. We found that overproduction of Nup58 in *Escherichia coli* leads to staining of the bacterial cells with Congo Red dye. Using transmission electronic microscopy we have shown that Nup58 forms fibrils on the cell surface. We also tested the ability of the Nup58 to form amyloid aggregates *in vitro*. We incubated the protein in the buffer for aggregation at 37°C degrees during 96 hours. Obtained Nup58 aggregates were resistant to SDS treatment according to results of SDS-PAGE and SDD-AGE analysis and stained by Thiofavin T and Congo Red dyes.

Finally, we demonstrated, that Nup58p fused to EGFP formed fluorescent foci when overproduced in the yeast cells. Nup58 aggregates from cellular lysates were resistant to SDS treatment according to the results of SDD-AGE analyses. Also, we demonstrated that aggregates of Nup58 colocalized with aggregates of 103QP, but not with 25QP. These constructionsconstuctins correspond to glutamine (Q) and proline (P) rich regions of Htt, andthey are often used to model Htt aggregation in yeasts.

All these results allowed us to suggest that Nup58 is a candidate for new human amyloid, which can coaggregate with Htt. The research was supported by the Russian Science Foundation (17-74-10159) and by RRC MCT SPbSU.