InterDocSchool Project

Research Trip Summary Report

Task 2. Foreign mobility of WUST doctoral students

I. Data of the doctoral student

1.Full name: Jakub Wojciechowski

2.Year of studies: 4

3. Educational discipline: Biomedical Engineering

II. Foreign research trip (research visit)

1. Research institute in which the foreign research was implemented:

Max Planck Institute for Multidisciplinary Sciences

2. Name and surname of the host person (mentor): Johannes Soeding

3. Dates of the research trip: 15.08.2022 – 15.11.2022

4. Title and date of a seminar delivered during the research trip:

Functional amyloids and how to find them, 25.10.2022

5. Description of work carried out during the research trip:

The human gut microbiome composition can be directly related to the occurrence of severe diseases including amyloid related ones such as Parkinson's and Alzheimer's diseases or type II diabetes. Several possible mechanisms were proposed to explain this phenomenon including cross-interactions between microbial functional amyloids and human proteins. Unfortunately, despite two decades of study of functional amyloids from microorganisms only a small fraction of them were extensively studied.

The aim of this was to identify functional amyloids from the human microbiome assess possible interactions of newly identied functional amyloids with human proteins.

We analyzed homologs of CsgA, CsgB and PSM proteins identified in Unified Human Gastrointestinal Proteome identified during previous internship. We extracted amyloid prone regions and tested them for possible cross-interactions with human disease related amyloids including amyloid beta 40 and 42, islet amyloid polypeptide, p53, TDP-43, alpha-synuclein and Serum amyloid A. We analyzed interactions patterns using Principle Component Analysis and

performed cluster anaylsis. Based on that we selected representants for more detailed studies using molecular modeling methods. Selected pairs were modeled using coarse grained model CABS, and will be later subjected to experimental validation.

We tried to extend the data set of functional amyloids, by applying number of amyloid prediction tools, however we showed that they cannot be utilized in a genome wide research due to high false positive rate. We checked the possibility of identifying novel functional amyloids using tandem repeats enrichment, however obtained results were not conclusive due to lack of available data. We also tested number of other approaches including search for sequential motifs, or conserved aggregation prone regions. Finally we tested deep learning approach involving natural language processing models adopted for analysis of protein sequences including protBERT.

6. Description of the main results obtained:

We showed that functional amyloids from bacteria colonizing human gut can potentially interact with human disease related amyloids. We also identified number of interactions patterns of specific proteins and their homologs as well as identified potential regions involved in interactions. We characterized in more details structures of aggregates composed of interacting proteins and assessed their stability using coarse grain modeling.

We showed the capabilities of natural language processing deep learning models for identification of functional amyloids which will be further studied in greater details.

The visit allowed me to gather results for my doctoral dissertation and strengthen the collaboration with my second supervisor Dr Johannes Soeding. It was an opportunity to collaborate with a team which have great experience with development of high quality bioinformatic software.

7. Future collaborations (if applicable):

We are going to prepare manuscript describing obtained results and send it to a peer review journal. We are aiming at development of new tools for identification of functional amyloids based on protBERT deep learning model.

8. Title and date of a seminar presenting the results of the trip delivered at Wroclaw University of Science and Technology after returning from the research trip: Interaction patterns of bacterial functional amyloids with human disease related proteins – 17.11.2022

III. Doctoral student's signature

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     (Date)
(doctoral student's signature)

IV. Confirmation and information from the host

1. Confirmation of compliance of the information contained in the report: I CONFIRM / DO NOT CONFIRM. (*In justified cases, the confirmation of the host may be sent by e-mail to the Dean's Office of the Doctoral School email:* interdocschool@pwr.edu.pl*)*

2. Additional information and comments

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     (Date)
(signature(s) of Host)