

Molecular Evidence for a Relationship between Human's Microbiome and Alzheimer's Disease

Ahmad Najar, Andrew Stein and Sara Goldberg
Mentor: Itzik Engelberg (MSc)
In the laboratory of Prof. Meytal Landau

Faculty of Biology , Technion

INTRODUCTION

Probiotic bacteria secrete Antimicrobial Peptides (AMPs) as first line of defence against pathogens (Hassan et al.,2012). We hypothesise that AMPs secreted from bacteria, including probiotics, interact with human amyloids and alter the appearance of Alzheimer's diseases. The sequence below describes the biological pathway in which amyloids fibrillate.

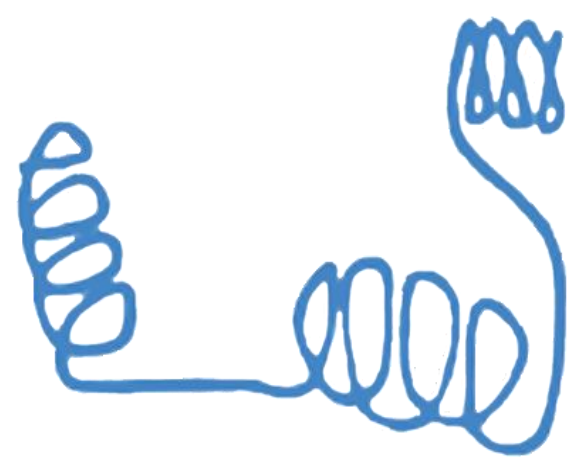
STATES OF AMYLOID FIBRILLATION

1. Monomers

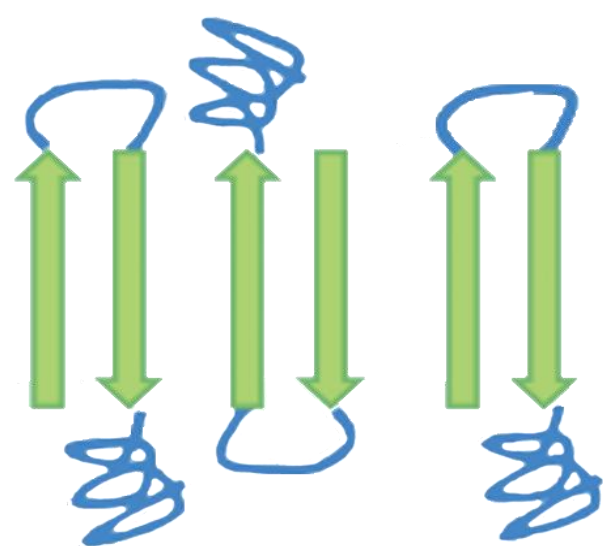


Clemens et al.,2016

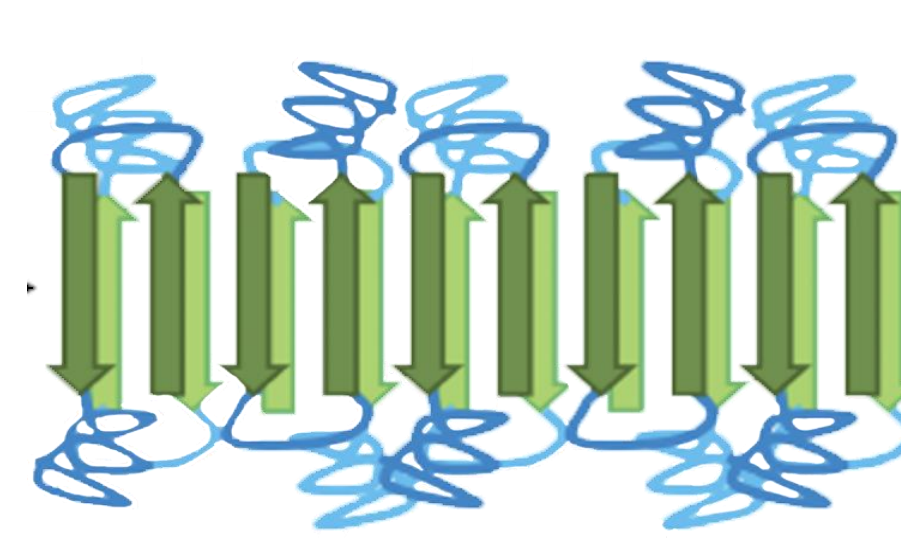
2. Misfolded Protein



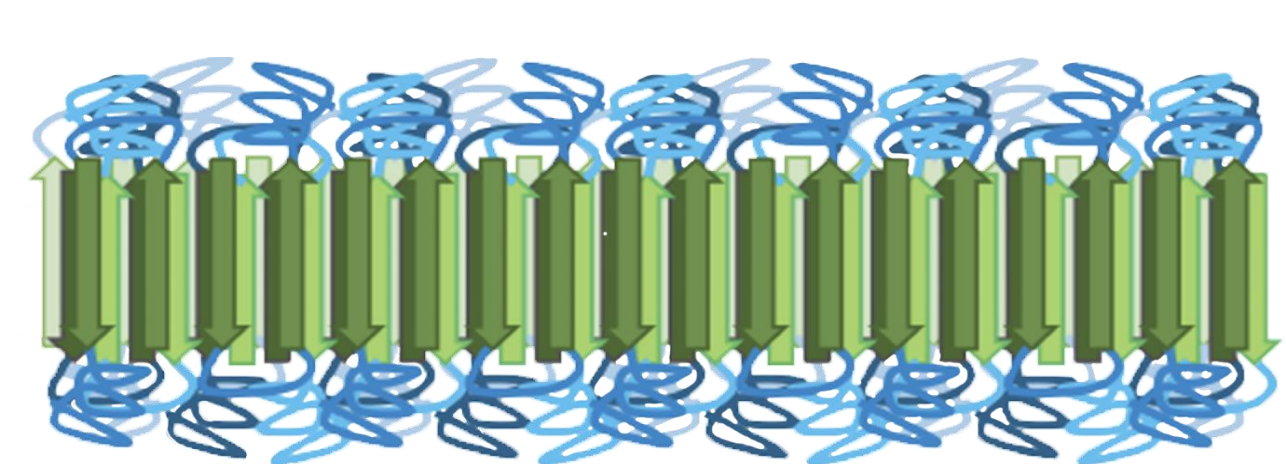
3. Soluble Oligomers



4. Protofibrils



5. Fibrils



RESULTS

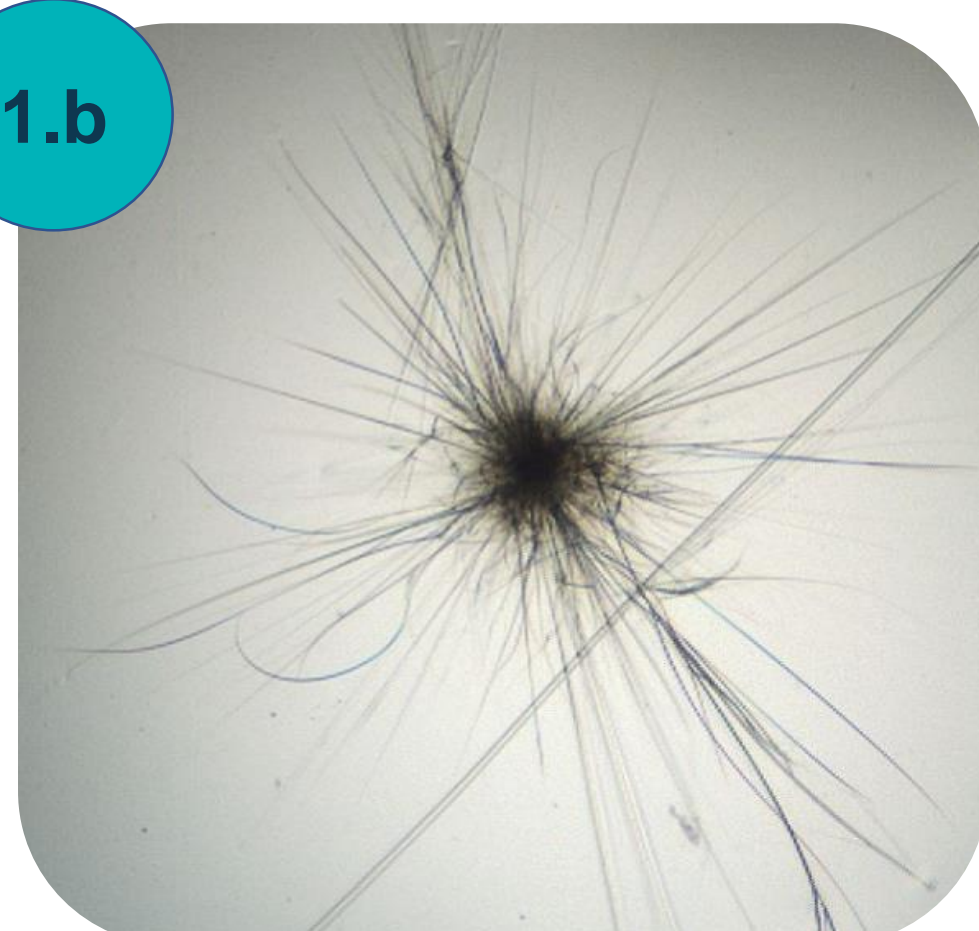
1. CO – CRYSTALLIZATION of gFK13 & PSMa3

As seen in figure 1, Co-Crystallization of gFK13 (an AMP) with PSMa3 (an amyloid) demonstrates the feasibility of molecular interaction between AMPs and amyloids.

1.a

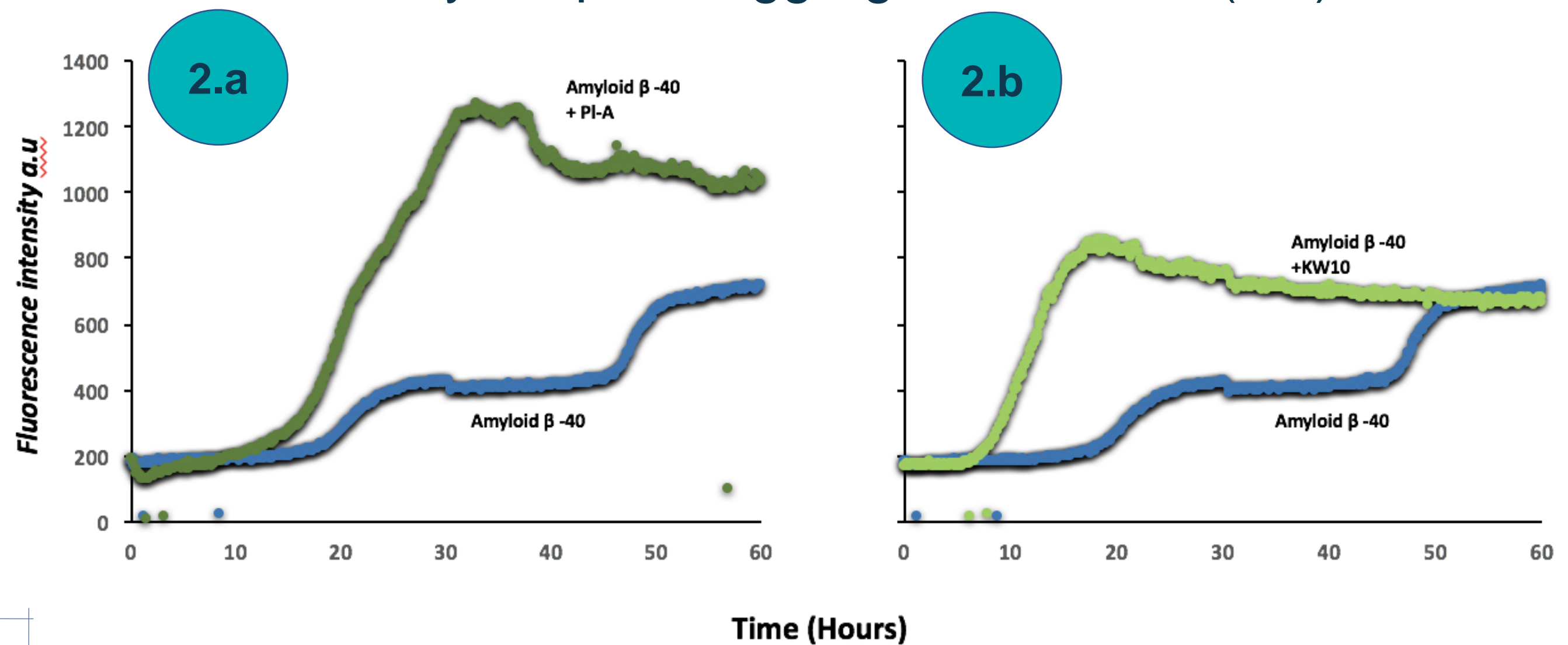


1.b



2. THIOFLAVIN T (ThT)

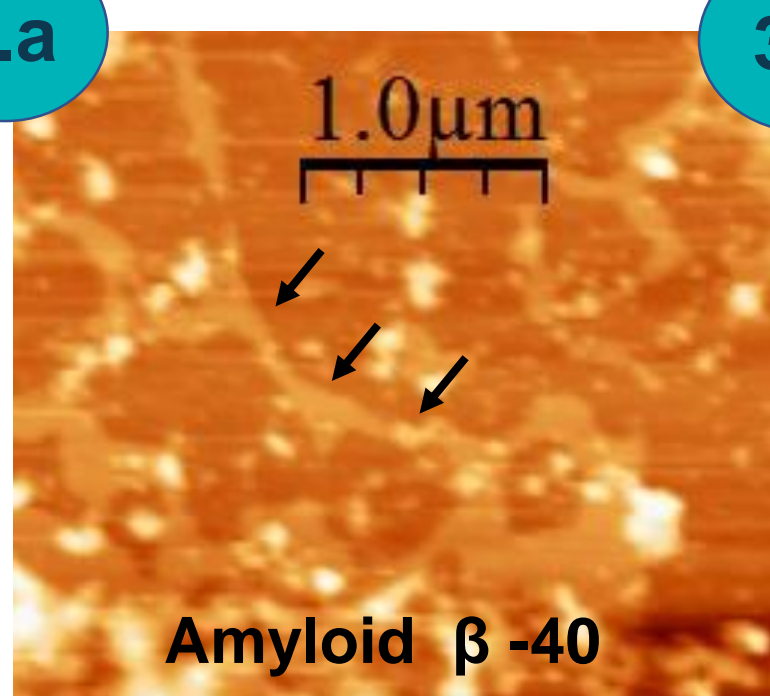
PI-A and KW10 added to amyloid β -40 in molar ratios of 2:1 increase the aggregation rate of amyloid β -40 (2.a and 2.b respectively) in terms of rapidness and speed. PI-A induce amyloid β -40 aggregation as well (2.a).



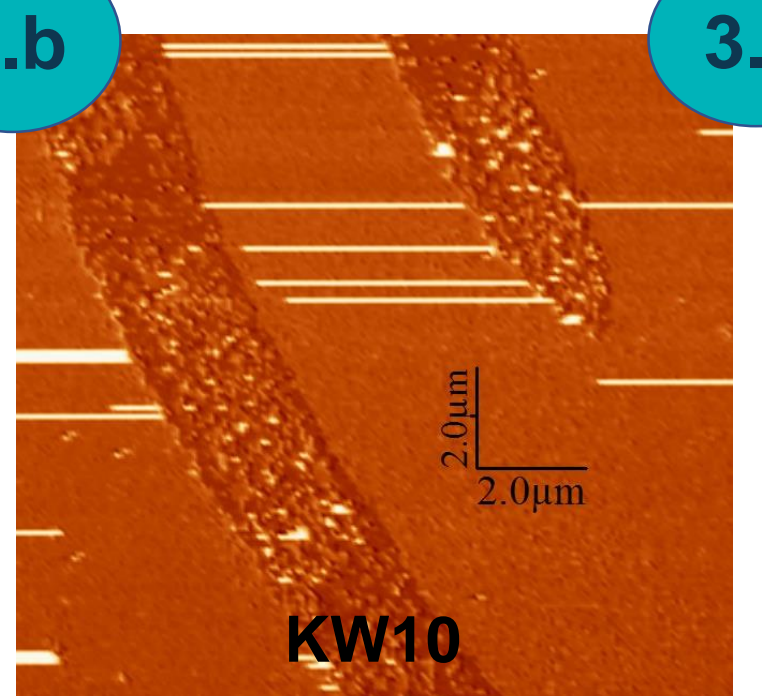
3. ATOMIC FORCE MICROSCOPY (AFM)

Nanoscale images taken from AFM demonstrate the fibrillation of amyloid β -40 alone (indicated by arrows in 3.a), while KW10 alone also fibrillate (3.b). No fibrils were seen when mixing KW10 with amyloid β -40 but a dense population of oligomers particles (3.c).

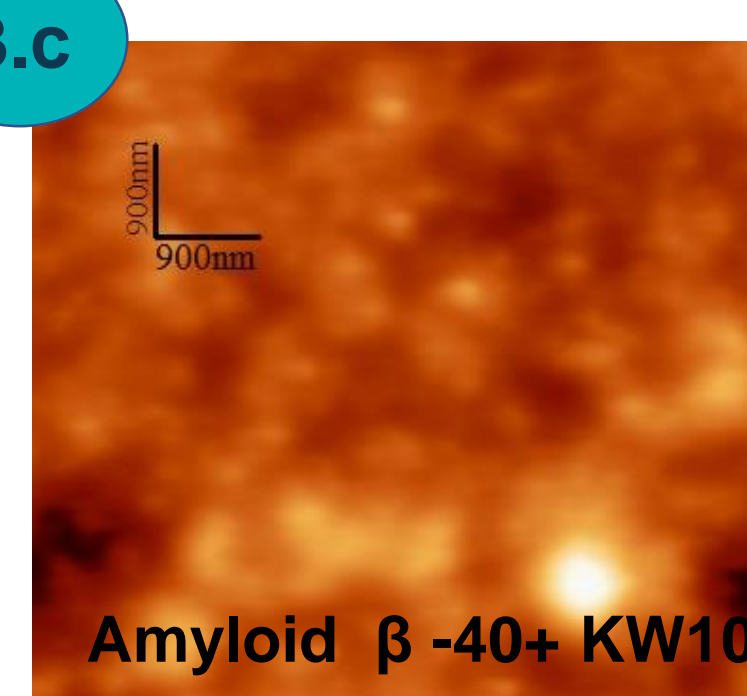
3.a



3.b

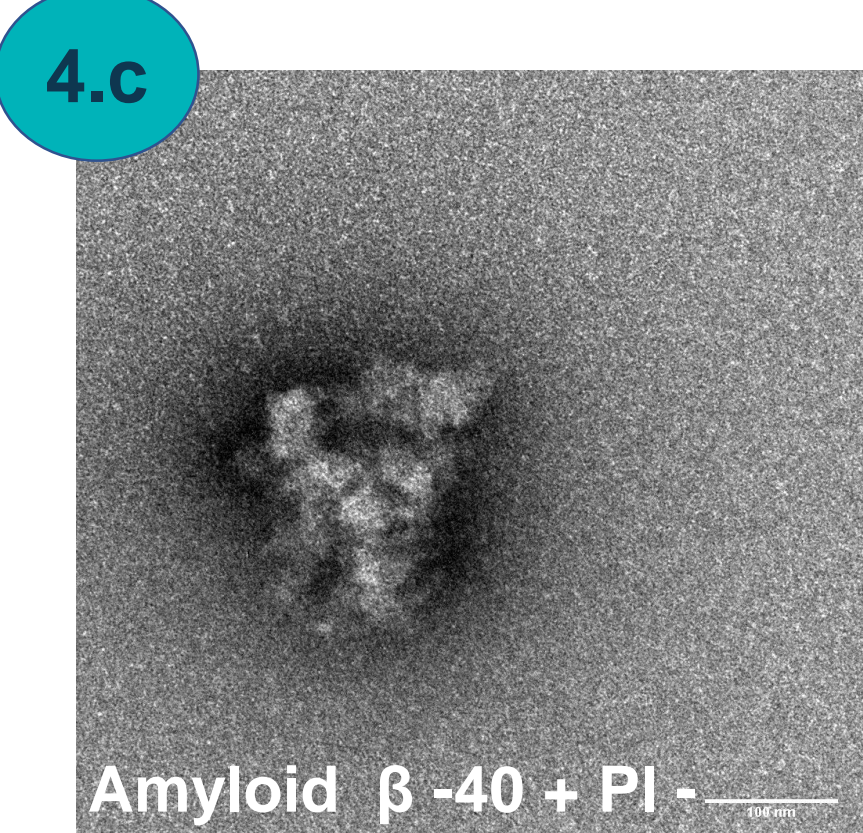
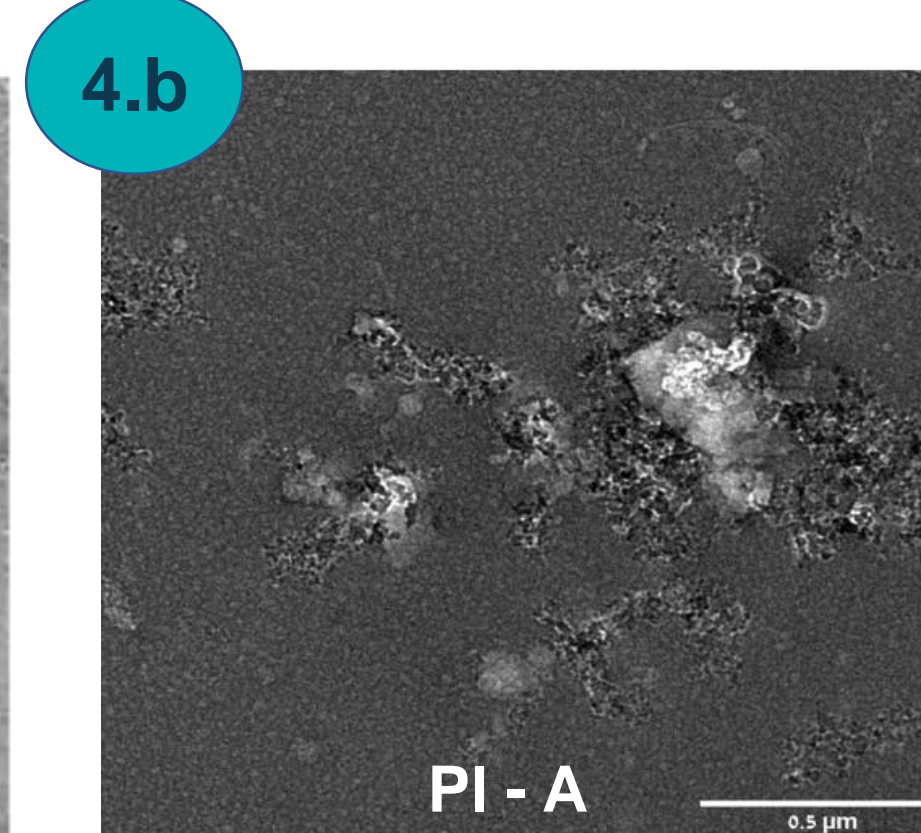
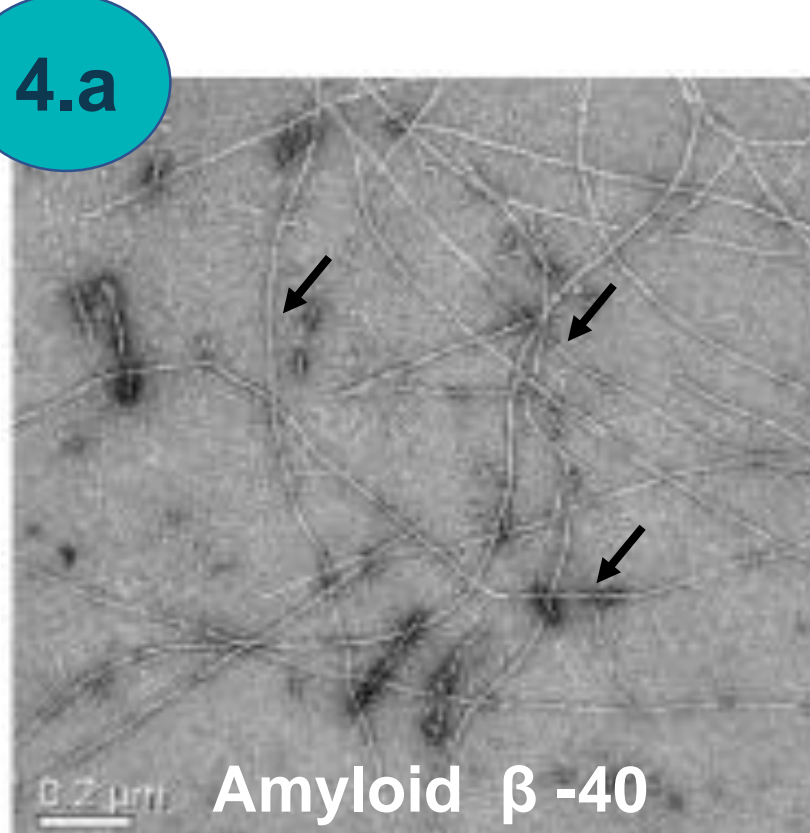


3.c



4. TRANSMISSION ELECTRON MICROSCOPY (TEM)

TEM images indicate that amyloid (indicated by arrows in 4.a), while PI-A alone create amorphous aggregates (4.b). No fibrils seen when mixing PI-A with amyloid β -40 but a dense population of oligomers particles (3.c).



CONCLUSIONS

Using PI-A and KW10, an AMPs from human's probiotic bacteria, we discovered alternations in amyloid β -40 aggregation, a human pathogenic amyloid. Those results have a great impact on the further studies gut – brain axis.

ACKNOWLEDGEMENTS

We would like to thank Itzik Engleberg (MSc) and Prof. Meytal Landau for hosting and guiding us through our research in her laboratory. We would also like to thank the foundation and donors for their generous support of the SciTech Program.



Technion
Israel Institute of Technology