Researchers gain new insights into the formation of non-pathological amyloids

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A team of scientists from the VIB lab of Han Remaut (VIB-VUB) and the lab of Yves Dufrêne at UCL Louvain-La-Neuve collaborated on a study of functional amyloids –protein aggregates with the typical amyloid structure that do not lead to disease but rather serve a dedicated biological function. Led by Mike Sleutel (VIB-VUB), the team used a novel microscopy method to examine the formation of functional amyloids by bacteria in real time, observing key growth and regulatory characteristics that could lead to new biomaterials as well as insights into the development and progression of human diseases caused by pathological amyloid plaques. Their research is published in the renowned scientific journal *Nature Chemical Biology*.

In humans, amyloids are associated with neurodegenerative illnesses such as Alzheimer's, Parkinson's and Huntington's disease, and prion diseases like bovine spongiform encephalopathy (BSE) and Creutzfeldt-Jakob disease. In these pathological amyloids, proteins are trapped in a toxic form that causes cell death, and leading to brain and organ damage and eventually death.

Proteins with purpose

Amyloid plaques are composed of proteins or protein fragments that organize into spiraling fibers that continuously grow by attracting new molecules. Previous research has indicated that the resulting tissue damage in human disease is mainly caused by small protein aggregates

generated during the early stages of amyloid formation. These molecular predecessors to amyloids are composed of the same subunits, but differ in structure. Bacteria, however, have the remarkable ability to make 'functional amyloids' through a deliberate pathway that does not involve the formation of toxic intermediates.

Prof. Dr. Han Remaut (VIB-VUB): "The goal of this research was to learn more about the process by which bacteria are able to circumvent the development of these harmful toxic intermediates. To do so, we relied on high-speed atomic force microscopy, which allowed us to observe the growth individual amyloid fibers 100 times faster than conventional atomic force microscopes can."

New pathways create non-toxic amyloids

The scientists found that curli, a type of functional amyloids created by E. coli to form biofilms, follow a different developmental process than pathological amyloids. They watched curli fibers spawn and grow under the atomic force microscope. During the nucleus-forming process of amyloid development, curli subunits collect into minimally sized fibers that immediately have the same properties as mature curli.

Dr. Mike Sleutel (VIB-VUB): "Curli fibers are formed in such a way that the subunits readily organize into a minimal amyloid fragment without forming any of the toxic intermediate states that are involved in amyloid diseases. Also, we found that bacteria have the capability to regulate the growth of these curli fibers by producing proteins that can block the sites where incoming subunits would bind."

Fascinating future avenues

Curli are an ideal model system to use in uncovering the differences

between functional and pathological amyloids, and to understand how bacteria are able to deal with potentially toxic types of amyloids without being damaged. Even more, functional amyloids could serve as the future building blocks of new biomaterials.

PhD student and co-author Imke Van Den Broeck (VIB-VUB): "An interesting research avenue that we are pursuing is the production of genetically modified amyloid fibers to display functional groups of interest, such as antibodies, enzymes, etc. Using this approach, we envisage the formation of self-assembling nanowires with programmable functions to create a novel class of biomaterials."

More information: Mike Sleutel et al. Nucleation and growth of a bacterial functional amyloid at single-fiber resolution, *Nature Chemical Biology* (2017). DOI: 10.1038/nchembio.2413

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