Nanomechanical properties of steric zipper globular structures

The term amyloid defines a group of proteins that aggregate into plaques or fibers. Amyloid fibers are mostly related with neurodegenerative diseases in humans, however they play a functional role when secreted by bacteria and fungi. Originating either in humans or in microorganisms, the sequence of amyloid proteins in decorated with hexapeptides that bare a high propensity to form fibers, known as steric zippers. We have found that steric zippers form globular structures on route to making fibers and exhibit a characteristic Force (F)-Distance (D) fingerprint when pulled with an AFM tip. In particular, the F-D pulling curves showed a force-plateau behavior, suggesting that the globules were composed of chains that were unwound like a yarn ball. Force-plateau statistical analysis showed that the F-D characteristic parameters were sequence-sensitive, representing differences in the packing of the hexapeptides in the globules. These unprecedented findings reveal that, in addition to their characteristic crystal structure, steric zippers also exhibit a characteristic nanomechanical signature in solution. Getting to the fundamental interactions that govern the unzipping of amyloid fibers may contribute to the design of anti-amyloid drugs that target their physical-in addition to their structural-features.

Reference: