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Atomic view of the histidine environment stabilizing higher-pH conformations of pH-dependent proteins

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External stimuli are powerful tools that naturally control protein assemblies and functions. For example, during viral entry and exit changes in pH are known to trigger large protein conformational changes. However, the molecular features stabilizing the higher pH structures remain unclear. Here we elucidate the conformational change of a self-assembling peptide that forms either small or large nanotubes dependent on the pH. The sub-angstrom high-pH peptide structure reveals a globular conformation stabilized through a strong histidine-serine H-bond and a tight histidine-aromatic packing. Lowering the pH induces histidine protonation, disrupts these interactions and triggers a large change to an extended β-sheet-based conformation. Re-visiting available structures of proteins with pH-dependent conformations reveals both histidine-containing aromatic pockets and histidine-serine proximity as key motifs in higher pH structures. The mechanism discovered in this study may thus be generally used by pH-dependent proteins and opens new prospects in the field of nanomaterials.. This work is based on three complementary x-ray techniques: Single crystal solving at 0.85 Å, Fiber diffraction at wide angles that gives insight into the molecular structures, and, SAXS, Small Angle X-ray Scattering that illuminates the packing and the radial electron density profiles of the nanotubes. The full x-ray analysis that reveals both nanostructures at the molecular scale will be detailed. *Céline Valéry, Stéphanie Deville-Foillard, Christelle Lefebvre, Nuria Taberner, Pierre Legrand, Florian Meneau, Cristelle Meriadec, Camille Delvaux, Thomas Bizien, Emmanouil Kasotakis, Carmen Lopez-Iglesias, Andrew Gall, Stéphane Bressanelli, Marie-Hélène Le Du, Maïté Paternostre, Franck Artzner*, Nature Communications 6: 7771 (2015). https://www.nature.com/articles/ncomms8771.

Biography

The Franck Artzner's bio-inspired self-assemblies group addresses materials issues from fibrillation of pharmaceutical peptides to the colloids crystallization by fibrillar proteins. The group has an expertise in technical development as well as crystallographic characterization of structures by unconventional X-ray scattering techniques, SAXS, Fiber Diffraction. A Joint Laboratory with IPSEN and Maïté Paternostre is headed by Franck Artzner and investigates commercial formulation of self-assembled peptides. FA was the chairman of the National brain storming group on Bio-inspired Nanotechnologies at OMNT. He is involved in the review committees of synchrotons : SOLEIL, ESRF, NSLS I. He received the Young Investigator Award of the Physical Chemistry Division of the French Chemical Society (SFC) and the French Physical Society (SFP) in 2015, and the Delalande prize from the French Pharmaceutical academy in 2016.

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