Title:	Single- droplet vibrational raman spectroscopy illuminates the inner workings of phase- separated biomolecular condensates.
Authors:	Avni, Anamika (/jspui/browse?type=author&value=Avni%2C+Anamika) Agarwal, Aishwarya (/jspui/browse?type=author&value=Agarwal%2C+Aishwarya) Rai, Sandeep K. (/jspui/browse?type=author&value=Rai%2C+Sandeep+K.) Joshi, Ashish (/jspui/browse?type=author&value=Joshi%2C+Ashish) Walimbe, Anuja (/jspui/browse?type=author&value=Walimbe%2C+Anuja) Pattanashetty, Swastik G. (/jspui/browse?type=author&value=Pattanashetty%2C+Swastik+G.) Mukhopadhyay, Samrat (/jspui/browse?type=author&value=Mukhopadhyay%2C+Samrat)
Keywords:	Single-droplet vibrational raman spectroscopy phase-separated biomolecular condensates
Issue Date:	2022
Publisher:	Elsevier
Citation:	Biophysical Journal, 121(3), 307-308.
Abstract:	Eukaryotic cells contain a host of non-canonical membrane-less organelles that are formed via liquid-liquid phase separation (LLPS) of intrinsically disordered proteins/regions (IDPs/IDRs) along with nucleic acids and other biomolecules. These biomolecular condensates are involved in a myriad of critical cellular functions and neurodegenerative diseases. Unmasking the role of intrinsic disorder and conformational heterogeneity of IDPs/IDRs in promoting promiscuous and ephemeral interactions resulting in liquid-like behavior of these condensates is crucial to understand the molecular drivers of LLPS. While a host of existing microscopic and spectroscopic tools are immensely useful to study LLPS, most of these methodologies are inadequate in illuminating the conformational heterogeneity and distribution within individual droplets. In order to overcome these limitations, we have developed and adapted a novel, highly sensitive, single-droplet structural tool involving dispersive laser Raman spectroscopy in a microscopy format that offers a wealth of fundamental molecular information within the mesoscopic liquid condensed phase. This design allows us to focus the laser beam into the protein-rich dense phase of individual droplets to capture Raman scattering bands associated with a range of molecular vibrational modes from protein-rich single droplets. Using our studies, we have been able to capture unique conformational characteristics that govern LLPS of an intrinsically disordered pathological stop codon variant of the prion protein namely, Y145Stop that is associated with Gerstmann-Stráussler-Scheinker syndrome and familial cerebral amyloid angiopathy. These single-droplet vibrations studies illuminate the conformational disorder, heterogeneity, and distribution in Y145Stop liquid droplets and their maturation into ordered, beta-rich, autocatalytic, amyloid-like aggregates formed via liquid-to-solid phase transitions. I will also discuss new results from our ongoing Raman spectroscopic investigation on the phase transition of FUS that is modulated by the RNA-protein stoichiometry.
Description:	Only IISERM authors are available in the record
URI:	https://doi.org/10.1016/j.bpj.2021.11.1216 (https://doi.org/10.1016/j.bpj.2021.11.1216) http://hdl.handle.net/123456789/4800 (http://hdl.handle.net/123456789/4800)
Appears in Collections:	Research Articles (/jspui/handle/123456789/9)

Files in This Item:

File	Description	Size	Format	
Need To Add…Full Text_PDF. (/jspui/bitstream/123456789/4800/1/Need%20To%20Add%e2%80%a6Full%20Text_PDF.)		15.36 kB	Unknown	View/Open (/jspui/I

Show full item record (/jspui/handle/123456789/4800?mode=full)

(/jspui/handle/123456789/4800/statistics)