ABSTRACT

Visualizing Temperature Mediated Activation of Gelsolin and Its Deactivation by PIP_2: A SAXS Based Study

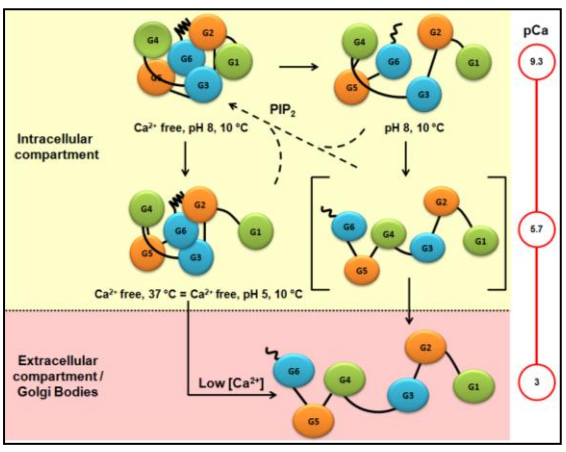
Maulik D. Badmalia, Shikha Singh, Renu Garg and Ashish
CSIR-Institute of Microbial Technology, Chandigarh India

Keywords: Gelsolin; Small Angle X-ray Scattering; Temperature; Shape Changes; PIP_2

I. Abstract Body

The present study is the first report describing temperature based initiation of gelsolin's F-actin depolymerization activity, even in absence of free Ca^{2+} or low pH. Small angle X-ray scattering (SAXS) and circular dichroism (CD) studies revealed that temperature in the range of 30-40°C is capable of opening the G1 domain alone, as remaining domains are held together by the Ca^{2+}-sensitive C-tail latch without any loss in the secondary structural content. Full opening of all domains of tail-less gelsolin, and retention of closed shape for G2-G6 gelsolin merely by heating, further substantiated our findings. The Ca^{2+}/pH independent activity of gelsolin near physiological temperature brought out a query: whether gelsolin is always active, and if not, what might deactivate it? Earlier, PIP_2 has been reported to render gelsolin inactive with no structural insight. Reduction in shape parameters and modelling revealed that PIP_2 reverses the temperature induced extension of g1-g2 linker leading to a compact shape seen for Ca^{2+}-free gelsolin. Similar results for partially activated gelsolin (by low pH or Ca^{2+} ions below 0.1 μM) imply that inside cells, depolymerization, capping, and nucleation of F-actin by gelsolin is regulated by the culmination of local Ca^{2+} ion concentration, pH, temperature and PIP_2 levels.

II. *Image*



III. References:

Maulik D. Badmalia, Shikha Singh, Renu Garg and Ashish. Visual insights into temperature based activation of Gelsolin under Ca^{2+} free condition Scientific Report, 2017, 7 (1):p. 4670 doi:10.1038/s41598-017-04975-0

Peddada, N. et al. Global shapes of F-actin depolymerization-competent minimal gelsolins: insight into the role of g2-g3 linker in pH/Ca^{2+} insensitivity of the first half. The Journal of Biological Chemistry 288, 28266-28282, doi:10.1074/jbc.M113.463224 (2013)

Ashish et al. Global structure changes associated with Ca^{2+} activation of full-length human plasma gelsolin. The Journal of Biological Chemistry 282, 25884-25892, doi:10.1074/jbc.M702446200 (2007)

IV. Biography:

Maulik Badmalia has completed his PhD from Jawaharlal Nehru University. Currently he is working as a Research Associate with Dr. Ashish, at Institute of Microbial Technology, Chandigarh, India. He has exhaustive experience in recombinant protein expression and biophysical characterization using techniques such as SAXS, XRD, CD, SEC, DLS etc.

V. Presenting author details



Maulik Dinesh Badmalia
+91 828 302 4878
maulik.badmalia@gmail.com
Category: Poster presentation