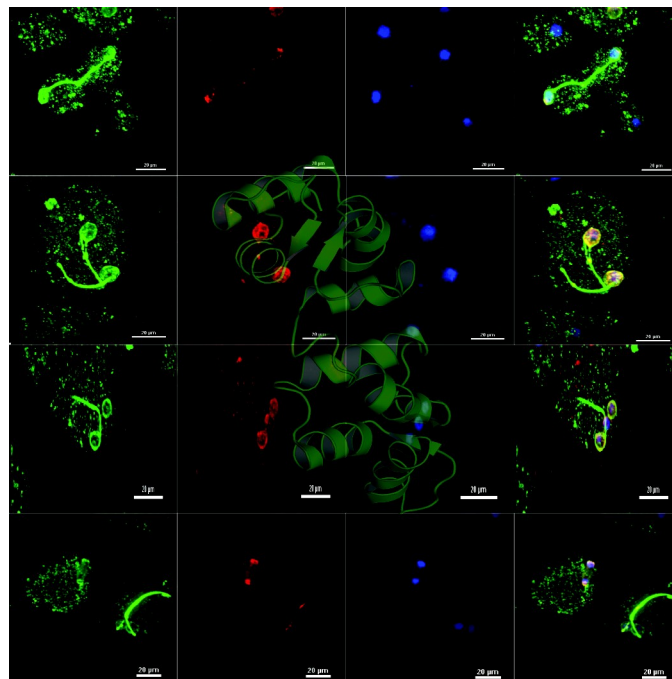


## Structure of Ca<sup>2+</sup>-binding protein-6 from *Entamoeba histolytica* and its involvement in trophozoite proliferation regulation

Deepshikha Verma<sup>1#</sup>, Aruna Murmu<sup>2#</sup>, Samudrala Gourinath<sup>2</sup>, Alok Bhattacharya<sup>2</sup> and Kandala V. R. Chary<sup>1\*</sup>

<sup>1</sup>Department of Chemical Sciences, Tata Institute of Fundamental Research, Mumbai, 400005, India and Tata Institute of Fundamental Research, Center for Interdisciplinary Sciences, Hyderabad, 500075, India

<sup>2</sup>School of Life Sciences, Jawaharlal Nehru University, New Delhi, 110067, India



### Abstract

Cell cycle of *Entamoeba histolytica*, the etiological agent of amoebiasis, follows a novel pathway, which includes nuclear division without the nuclear membrane disassembly. We report a nuclear localized Ca<sup>2+</sup>-binding protein from *E. histolytica* (abbreviated hereafter as EhCaBP6), which is associated with microtubules. We determined the 3D solution NMR structure of EhCaBP6, and identified one unusual, one canonical and two non-canonical cryptic EF-hand motifs. The cryptic EF-II and EF-IV pair with the Ca<sup>2+</sup>-binding EF-I and EF-III, respectively, to form a two-domain structure similar to Calmodulin and Centrin proteins. Downregulation of EhCaBP6 affects cell proliferation by causing delays in transition from G1 to S phase, and inhibition of DNA synthesis and cytokinesis. We also demonstrate that EhCaBP6 modulates microtubule dynamics by increasing the rate of tubulin polymerization. Our results, including structural inferences, suggest that EhCaBP6 is an unusual CaBP involved in regulating cell proliferation in *E. histolytica* similar to nuclear Calmodulin.