GÖTEBORGS UNIVERSITET

A tale of two songs: oligomeric and monomeric roles of the molecular chaperone CCT

Carmen Maria Córdoba Beldad
Institutionen för kemi och molekylärbiologi
Naturvetenskapliga fakulteten

Akademisk avhandling för filosofie doktorsexamen i Naturvetenskap med inriktning Biologi, som med tillstånd från Naturvetenskapliga fakulteten kommer att offentligt försvaras fredagen den 6 december 2024 kl. 09:00 i Sal Korallrevet, Institutionen för kemi och molekylärbiologi, Medicinaregatan 7, Göteborg.

ISBN: 978-91-8069-945-7

GÖTEBORGS UNIVERSITET

Abstract

The chaperonin-containing tailless complex polypeptide 1 (CCT) is a 1 MDa barrel shaped molecular chaperone present in the cytoplasm of all eukaryotes. Eight different subunits, located in a fixed position, form CCT, which is mostly studied as the folding machinery of the cytoskeletal proteins actin and tubulin. Roles beyond folding have been reported for the CCT oligomer and together with the increasing evidence of monomeric CCT subunit functions, have elevated the importance of studying the chaperone CCT. Here, we show that the transcription factor STAT3, a previously reported oligomeric binding partner of CCT, does not behave as an obligate folding substate but rather is sequestered by CCT. To expand our knowledge of the monomeric roles of the CCT subunits, we have studied the interaction between CCTδ and $p150^{Glued}$, a component of the dynactin complex involved in crucial biological processes such as mitosis. We show that monomeric CCTδ is required for the correct localisation of $p150^{Glued}$ at spindle poles and for accurate chromosome segregation. Furthermore, we explore interactions between two other CCT subunits and two regulatory components of mitosis, the centromeric protein Mis18BP1 and the outer kinetochore component KNL1. Taken together the work in this thesis extends the understanding of both oligomeric and monomeric functions of CCT beyond folding.

Keywords: CCT, mitosis, oligomer, monomer, CCTα, CCTε, CCTδ, STAT3, $p150^{Glued}$, Mis18BP1, KNL1