

Structure of an Inter-ring Allosteric GroEL Mutant (E461K) at 3.3Å Resolution

Aintzane Cabo^a, S. Spinelli^b, B. Sot^a, J. Agirre^a, A. Mechaly^a, C. Cambillau^b, A. Muga^a, Diego M.A. Guérin^{a,c}, ^a*Unidad de Biofísica (UPV/EHU-CSIC). Bilbao, Spain.* ^b*AFMB-UMR 6098-CNRS-IFR1, Marseille, France.* ^c*UNSur, Bahía Blanca, Argentine.* E-mail: gbxguxxd@lg.ehu.es

The chaperonin GroEL in complex with its co-chaperonin GroES helps unfolded polypeptides to gain the active conformation through a nucleotide-regulated cyclic reaction. GroEL is an homo-oligomeric double heptameric toroid of 800 KDa with positive intra-ring and negative inter-ring cooperativity in ATP binding and hydrolysis. GroES is a dome-like 70kDa homo-heptamer that binds to the same GroEL ring where the other ligands (non-native polypeptide and nucleotide) are already bound. In this way, the complex GroES-GroEL forms a hydrophobic cavity where the peptide search for the productive structure in an isolated environment within the Anfinsen cage, and afterwards is delivered back to the medium. GroEL inter-ring communication is a temperature dependent interaction and salt-bridges E461-R452 and E434-K105 at the inter-ring interface regulate the 'thermostat' of GroEL. Disruption upon mutation of any of the two ionic contacts allows GroEL mutants to weaken the inter-ring negative cooperativity. Inter-ring communication disappears in wt GroEL at 42°C whereas for E461K mutant this temperature is 37°C. In order to understand how the thermostat of GroEL is programmed we have solved the structure of E461K mutant. Here we report the characteristics of this structure and give an explanation for the quaternary structural changes induced by this mutation.

Keywords: GroEL, E461K mutant, inter-ring communication