Molecular Modeling Study for Interaction between *Bacillus subtilis* Obg and Nucleotides

Yuno Lee¹, Woo Young Bang¹,², Songmi Kim¹, Prettina Lazar¹, Chul Wook Kim², Jeong Dong Bahk¹, Keun Woo Lee³*

¹ Division of Applied Life Science, Environmental Biotechnology National Core Research Center, Plant Molecular Biology and Biotechnology Research Center, Gyeongsang National University, Jinju, Gyeongsangnam-do, Republic of Korea, ² Swine Science and Technology Center, Jinju National University, Jinju, Gyeongsangnam-do, Republic of Korea

Abstract

The bacterial Obg proteins (SpoOB-associated GTP-binding protein) belong to the subfamily of P-loop GTPase proteins that contain two equally and highly conserved domains, a C-terminal GTP binding domain and an N-terminal glycine-rich domain which is referred as the “Obg fold” and now it is considered as one of the new targets for antibacterial drug. When the Obg protein is associated with GTP, it becomes activated, because conformation of Obg fold changes due to the structural changes of GTPase switch elements in GTP binding site. In order to investigate the effects and structural changes in GTP bound to Obg and GTPase switch elements for activation, four different molecular dynamics (MD) simulations were performed with/without the three different nucleotides (GTP, GDP, and GDP + Pi) using the *Bacillus subtilis* Obg (BsObg) structure. The protein structures generated from the four different systems were compared using their representative structures. The pattern of Cα-Cα distance plot and angle between the two Obg fold domains of simulated apo form and each system (GTP, GDP, and GDP+Pi) were significantly different in the GTP-bound system from the others. The switch 2 element was significantly changed in GTP-bound system. Also mean-square fluctuation (MSF) analysis revealed that the flexibility of the switch 2 element region was much higher than the others. This was caused by the characteristic binding mode of the nucleotides. When GTP was bound to Obg, its γ-phosphate oxygen was found to interact with the key residue (D212) of the switch 2 element, on the contrary there was no such interaction found in other systems. Based on the results, we were able to predict the possible binding conformation of the activated form of Obg with L13, which is essential for the assembly with ribosome.

Citation: Lee Y, Bang WY, Kim S, Lazar P, Kim CW, et al. (2010) Molecular Modeling Study for Interaction between *Bacillus subtilis* Obg and Nucleotides. PLoS ONE 5(9): e12597. doi:10.1371/journal.pone.0012597

Editor: Claudine Mayer, University Paris 7, France

Received: March 15, 2010; Accepted: August 16, 2010; Published: September 7, 2010

Copyright: © 2010 Lee et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: This research was supported by Basic Science Research Program (2009-0073267), Pioneer Research Center Program (2009-0081539), Priority Research Centers Program (2009-0093813), and Environmental Biotechnology National Core Research Center program (20090091489) through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (MEST). All students were recipients of fellowship from the BK21 Program of MEST. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

* E-mail: kwlee@gnu.ac.kr

Introduction

GTP-binding proteins have been found in all living organisms and are involved in various essential cellular processes such as signal transduction, protein synthesis, membrane trafficking and, cell proliferation [1,2]. These proteins belong to the GTPase superfamily whose sequence motifs are conserved in diverse species ranging from prokaryotes to eukaryotes [3]. Binding and hydrolysis of GTP effect the conformation of the GTP-binding proteins. The GTP and GDP-bound forms define the active and inactive states, respectively. Subfamilies of widely distributed bacterial GTP-binding proteins were discovered by the *Escherichia coli* (E.coli) Era and the *Bacillus subtilis* (B.subtilis) Obg (BsObg) proteins [1,2,4]. The Obg protein was originally identified in *B. subtilis* as a gene with GTP binding domain located downstream of spoOB. Consequently, Obg name originated from SpoOB-associated GTP-binding protein [5-7]. This protein was the first to be recognized as a member of a subfamily of GTP binding proteins that are conserved in both prokaryotic and eukaryotic cells [1,2,4,8]. The Obg family GTPase implicated in the following diverse cellular processes including cell growth such as morphological differentiation and DNA replication [9–11], early steps of sporulation and for stress-dependent activation of the σ⁷ factor that controls a cellular response to environmental stress [12,13]. Moreover, ObgE, an Obg homolog in *Escherichia coli*, has also been reported to be involved in chromosome partitioning, the regulation of DNA replication as well as DNA repair process [14,15]. Although the basic functions of the Obg subfamily proteins are not clearly established, the majority of bacterial Obgs have been commonly found to be associated with ribosome, in specific binding of Obg with ribosomal protein L13 was proved through an affinity blot assay method, implying that those proteins fundamentally could play a role in ribosome assembly or maturation [12,16–22]. The Obg subfamily proteins such as Era, Obg, YjeQ, and YlqF which are also known as translation factor T. thermophilus (T. thermophilus) Obg proteins were determined at 2.6 Å and 2.07 Å resolutions, respectively. The Obg protein contains three domains. The N-terminal glycine-rich domain (residues 1–158) which is...
referred as the “Obg fold” includes a sequence highly conserved among other members of the Obg family, but it doesn’t identify any structural similarity with the other known proteins. The GTPase domain (residues 159–342) is a conserved GTP-binding domain similar to that found in small Ras-like GTPases [24,25] (see Figure 1). The members of the Obg family share significant conservation along the switch 1 and switch 2 domains. These regions are also involved in protein-protein interactions [26–28]. The C-terminal domain (residues 343–428) which is called TGS domain is structurally similar to a domain found in bacterial stress response proteins. But TGS domain which was missing from BsObg structure is not widely conserved between Obg family members. The BsObg structure showed slightly different domain orientations between the molecules in the asymmetric unit [25], and the comparison between nucleotide-free *T. thermophilus* Obg and BsObg structures also revealed a dramatic domain rearrangement of Obg with significant conformational changes in the switch 1 and switch 2 regions [25]. However, no structural differences were observed between apo form and GDP-bound configurations of BsObg, implying that conformational changes associated with GDP binding are not sufficient to affect the Obg domain movement [24]. Altogether, these suggest that the orientation of N-terminal domain (Obg fold) of Obg proteins may be regulated by guanine nucleotides and further that the switch element recognition of GTP-bound configurations can trigger a conformational rearrangement between the domains [24,25]. Thus, in order to fully understand the molecular switch of Obg [24,25,29].

Here, we studied the structural change in switch element of BsObg due to GTP binding using molecular dynamics (MD) simulations. To investigate the effects and structural changes of GTP bound to Obg and GTPase switch elements for activation, four different molecular dynamics (MD) simulations were performed with/without the three different nucleotides (GTP, GDP, and GDP + Pi) using the currently available BsObg structure.

**Results**

1. **Stability of Obg protein structure during MD simulations**

Four 10 ns MD simulations were successfully performed and analyzed. The details of the MD simulation environments and the size of the systems are listed in Table 1. In order to compare the protein structures from the four different systems, their representative structures were selected from each simulation and those are the most closed conformation to the average structure for the last 2 ns snapshots. The calculated average Ca root-mean-square deviations (RMSDs) of each system (apo, GTP, GDP, and GDP + Pi) during the last 2 ns are 0.417, 0.415, 0.375, and 0.434 nm, respectively. The RMSD values of all the systems are slightly high because the structure has elongated N-terminal domain (Obg fold) (see Figure 2).

2. **Comparison of entire structures (Obg fold, GTPase domain)**

During intra-domain comparison no significant structural differences were noticed in each Obg fold and GTPase domain (see Figure 3 and 4). However, we found a major change in the entire protein structure comparison. The angle between the Obg fold and GTPase domain in the GTP-bound system was significantly different from the others (see Figure 5). Hereafter,
in our analysis apo form will be used as standard structure for the comparison with other systems. When the apo form was superimposed with other systems (GTP, GDP, and GDP+Pi) focusing on the Obg fold domain (residues 1–158), the RMSDs were 0.23, 0.29, and 0.29 nm, respectively (see Figure 3). Another superimposition using the GTPase domain (residues 159–342) resulted that the RMSDs were 0.26, 0.29, and 0.30 nm, respectively (see Figure 4). In order to study global motion of the protein for the systems, the bending angle of GTPase domain was compared. The angles between the apo form and each system (GTP, GDP, and GDP+Pi) were 21.24, 32.58, and 30.34°, respectively (see Figure 5). The GTP-bound form showed about 10 degrees difference compared to the other systems. The Cα-Cα distance plot also shows that the GTP-bound form only has different pattern from the rests. The average distances in the GTP-bound form were about 1 nm less than the rests (see Figure 5).

3. Differences of switch elements

The structures of switch 1 (residues 180–195) and switch 2 (residues 211–237) elements in nucleotide binding site were compared. In switch 2 element, we identified one substantial change in the loop region between the two helices of the GTP-bound system (see Figure 6A). The loop of the GTP-bound system was significantly shifted to the right site in the figure 6A1 compared to the rest. It can be regarded as the main position of the loop is different from the other systems. It is also noticed that the conformation of switch 1 element is severely changed in the GTP-bound system comparing with the GDP and GDP+Pi-bound systems (see Figure 6B). The switch 1 element of the GTP-bound system was most shifted to the right side in the figure 6B1 and as a result the switch 1 element is the closest to the switch 2 element in the GTP-bound system (see Figure 6B2).

RMSF analysis result showed that the flexibility of the switch 2 element in GTP-bound system was much higher than the other systems, while there is no remarkable difference in the switch 1 element (see Figure 7). Since the switch 1 element is located between the switch 2 element and the Obg fold, the switch 1 element seems to be used as the signal transporter between the two structures. Therefore the signal caused by the nucleotide substrates such as GDP or GTP will flow through the switch 2 element and then the switch 1 element and finally will reach to the Obg fold. From our analysis it is proposed that the flexible nature of the switch 2 element of the GTP-bound system is preferred to interact with and/or to control the switch 1 element and Obg fold, and eventually the function of the protein.

4. Essential dynamics (ED) analysis

The essential dynamics analysis was carried out to support our MD results and to understand the correlated motion of the switch elements in the four different simulations, and which identifies the essential movement in Obg during the simulation. We observed maximum movement of switch 2 element in the GTP-bound system compared to the other systems (see Figure 8B). A significant movement was also observed in the Obg fold of the GDP and GDP+Pi-bound systems (see Figure 8C and D) but no such motions were noticed in apo form (see Figure 8A). From these results, it can be concluded that each system has its own characteristics.

5. Binding mode of nucleotides

When GTP was bound, its γ-phosphate oxygen was found to interact with the key residue (D212) of the switch 2 element, on the
contrary to no interaction in other systems (see Figure 9). The GTP-bound system has seven H-bonding interactions compared to two for GDP and none for GDP+Pi-bound system. One hydrophobic interaction was observed in the GTP-bound system whereas other systems have three (see Figure 9 and Table 2). The oxygen of guanine ring has stable H-bonding interaction with K283 in GTP and GDP-bound systems whereas no such H-bonding interaction can be noticed in GDP+Pi-bound system. Based on this observation, it is concluded that the H-bond interaction plays main role in the recognition for the GTP.

In order to understand the interaction energy between the protein and nucleotides, the number of intermolecular hydrogen bonds and the columbic energy were monitored and compared. It was shown that GTP is more stable with the Obg than others (see Figure 10).

**Discussion**

Upon binding of GTP, Obg protein becomes active. It is assumed that such a binding will lead to structural changes within the Obg fold, and subsequently, it triggers an important functional role. It is already suggested that the Obg fold may be the main platform for protein-protein interaction [24]. Our results also substantiate the importance of the Obg fold through its differential dynamic behavior in each system showing the possibility of Obg fold as the most favored part for protein-protein interaction.

![Figure 3. Structural comparison of Obg fold.](image)

Obg fold of each structure was superimposed for the comparison. The BsObg crystal structure in yellow was overlapped with the three model structures (A): apo (blue), GTP (red), GDP (green), and GDP+Pi-bound form (violet). And then the apo form was compared to the GTP (B), GDP (C), and GDP+Pi-bound form (D), respectively.

doi:10.1371/journal.pone.0012597.g003

![Figure 4. Structural comparison of GTPase domain.](image)

GTPase domain of each model structure was superimposed. Apo form (blue) was compared to the GTP in red (A), GDP in green (B), and GDP+Pi-bound form in violet (C), respectively.

doi:10.1371/journal.pone.0012597.g004


reported in the previous paper on the BsObg crystal structure that there is no conformational change between BsObg apo and GDP-bound form [24]. But according to our analysis of BsObg apo and GDP-bound form structures, we observed dramatic conformational changes in the Obg fold. In Figure 5, we showed the measured angle value of the Obg fold between simulated apo form and the representative structures of other nucleotide bound simulated systems. It clearly shows that apo form has more movement of the Obg fold during simulation, comparing to the other nucleotide bound systems, except GTP-bound Obg as a putative active form, which has unique structural changes.

In our protein-protein docking study based on the experimental evidences, we could be able to use the final putative activated form to investigate the specific binding mode between the Obg and ribosomal protein L13. The specific binding of Obg with L13 was already reported through an affinity blot assay method [12]. The
interaction between the putative activated form of Obg and target protein (L13) was investigated through the protein-protein docking calculations. From this, two important H-bond interactions between Obg and L13 (Ser74 in Obg - Arg 144 in L13 and Arg24 in Obg - Val18 in L13) were predicted. Analyses of electrostatic potential surfaces of the Obg and L13 show that the

Figure 6. Structure comparisons for the two switch elements. The GTPase domain of apo form (blue), GTP (red), GDP (green), GDP+Pi-bound form (violet) were superimposed in order to observe structural changes in two key elements: switch1 (Lower deck) and switch2 (Upper deck). For clarity only the switch elements were represented as cartoons and the rest of the parts as lines. Each panel shows front view (A), left side view (B) and backside view (C). The arrows indicate the switch elements of the GTP-bound form.
doi:10.1371/journal.pone.0012597.g006

Figure 7. RMSF analysis of the two switch elements. RMSFs were monitored with respect to all the residues of the apo (blue), GTP (red), GDP (green), and GDP+Pi-bound form (violet), respectively.
doi:10.1371/journal.pone.0012597.g007
Obg fold has highly conserved positively charged residues in the middle of the loop and this makes the loop highly electropositive in nature and gives way for the preferential interaction with L13, which is highly electronegative. This kind of binding and electrostatic information can be further used in structure-based drug design for finding a novel antibacterial drug [30].

In conclusion, four different MD simulations were successfully performed with/without the three different nucleotides (GTP, GDP, and GDP + Pi) to investigate the effects and structural changes of GTP bound to Obg and GTPase switch elements for activation. The protein structures from the four different systems were compared using their representative structures. Although no significant structural divergences were observed in each Obg fold and GTPase domain comparison, major structural changes were found in the relative orientation of the both domains. The angle between the Obg fold domains of simulated apo and GTP bound form was observed to be almost 10 degrees less than the angles of the other bound systems (GDP and GDP+Pi) with apo form. Also, the structures of switch 1 and switch 2 elements in nucleotide binding sites were compared. The flexible nature of switch 2 element probably leads to changes in switch 1 element conformation, which in turn may influence the Obg fold and its function. The switch 2 element was distinctly changed in the GTP-bound system due to the differential binding mode of the nucleotides. When GTP was bound to Obg, its γ-phosphate oxygen was found to interact with the key residue (D212) of switch 2 element, on the contrary no such interactions were observed in other systems. The number of intermolecular hydrogen bonds and the columbic energy were monitored and compared to understand the interaction between the protein and nucleotides. It demonstrated that the GTP is more stable with the Obg compared to other nucleotides. The conclusion and results of the present study were verified by the additional simulation studies (see Figure S1 and S2, Text S1).

Thus from the present study, we were able to find the 3D structure of the putative activated form of Obg and its structural properties and one possible reasons for its conformational changes. Also we were able to predict the possible binding conformation of the activated form of Obg with L13, which is essential for the assembly with ribosome.

**Methods**

1. **Starting structure preparation for MD simulation**
   
   (1) **Protein structure**

   The 3D structure of BsObg (PDB ID: 1LNZ) was retrieved from the protein data bank (PDB). There are two monomers in apo and ppGpp-bound configurations. In previous study, no significant conformational differences between apo form and GDP or ppGpp-bound configurations were found [24]. The structure in apo configuration was taken for the present study. The hydrogen atoms and incomplete residues in the structure were added and fixed using Discovery studio (DS) (Discovery Studio 2.1, Accelrys Inc., San Diego, CA, USA).

   (2) **Nucleotide structures**

   The crystal structure of the Obg protein was complexed with ppGpp. We used the coordinates of ppGpp-bound form, and then, conserved binding mode of nucleotides. The four model systems were developed for MD simulations: apo form, GTP, GDP, GDP+Pi. Two magnesium ions (Mg^{2+}) in the crystal structure were also considered for the simulation.
2. Computational details

The MD simulations were run on the Linux multi-node parallel cluster computer. All the MD simulations were carried out using the GROMACS program (version 3.3.1) [31,32] with GROMOS87 force field. The Gromacs topology files for the nucleotides were generated using the PRODRG (http://davapc1.bioch.undee.ac.uk/programs/prodrg/) [33]. The initial structure was immersed in an orthorhombic water box (0.8 nm thickness) and the net charge was neutralized by the addition of Cl\(^-\) and Mg\(^{2+}\) counterions. Long range electrostatics were handled using the particle mesh Ewald method [34]. In a system, protein alone consists of 3,336 atoms and the entire system is made up of approximately 57,500 atoms, which includes 18,300 water molecules (Table 1). The steepest descent energy minimization was used to remove possible bad contacts from the initial structures until energy convergence reached 2,000 kJ/(mol·nm). The systems were subject to equilibration at 300 K and normal pressure constant (1 bar) for 100 ps under the conditions of position restraints for heavy atoms and LINCS constraints [35] for all bonds. For all the systems considered for study, we performed 10 ns production run under periodic boundary conditions with NPT ensemble. Cutoff distances for the calculation of the electrostatic and Lennard-Jones interaction were 0.9 and 1.4 nm, respectively. The time step of the simulation was set to 2 fs, and the coordinates were saved for analysis every 1 ps.

3. Analysis

All visualizations were done using PyMOL and the DS. Trajectory analyses were carried out using tools built inside the GROMACS package. \(C_b\) RMSDs and RMSFs were calculated by least squares fit. The protein structures from the four different systems were compared using their representative structure. The representative structures were selected from each simulation (last 2 ns) and those were the most closed conformation to the average.
The acceptor distance cut-off value assigned was 0.35 nm. Measured for computing the number of H-bonds, donor-acceptor distance cut-off value assigned was 0.35 nm.

Figure 10. Interaction energy between the Obg protein and the nucleotides. The number of H-bonds (A), short range electrostatic energy (B) and short range Leonard-Jones potentials (C) of the GTPase domain with GTP (red), GDP (green) and GDP-Pi (violet) were monitored during the 10 ns MD simulation time. doi:10.1371/journal.pone.0012597.g010

Supporting Information

Text S1 Supplementary results and discussion. Found at: doi:10.1371/journal.pone.0012597.s001 (0.03 MB DOC)

Figure S1 RMSD plot for eight additional model structures and binding mode of GTP structures with the model structures. (A) Root-mean-square deviations (RMSDs) of the Cα atoms with respect to the starting coordinates over the eight additional MD simulations were measured. The RMSDs for 01_2702ps, 02_8806ps, 02_3330ps, 02_4365ps, 03_2099ps, 03_9581ps, 04_8265ps, and 04_9275ps systems are represented in light blue, dark blue, red, red light, light green, light green, light violet, and dark violet lines, respectively. (B) Binding conformations of each GTP system (GTP-bound system in red, 02_3330ps in dark red, and 02_4365ps in light red) in GTPase domains were compared along with residues having H-bond and hydrophobic interaction. The GTP and interacting residues are shown in stick model.

Found at: doi:10.1371/journal.pone.0012597.s002 (1.62 MB TIF)

Figure S2 Interaction energy of the nucleotides with the Obg protein in the six additional simulations. The number of H-bonds (A), short range electrostatic energy (B) of nucleotides with the GTPase domain in additional systems were monitored during the 2 ns MD simulation time.

Found at: doi:10.1371/journal.pone.0012597.s003 (0.76 MB TIF)

Acknowledgments

Special thanks to Nagakumar Bharatham (Nanyang Technological University), Kavitha Bharatham (Bioinformatics Institute), Sundarapandian Thangapandian, Chanin Park, Ayoung Baek, Swan Hwang, Minky Son, and Youngsik Son for helpful discussions.

Author Contributions

Conceived and designed the experiments: YL WYB KWL. Performed the experiments: YL SK. Analyzed the data: YL SK. Contributed reagents/materials/analysis tools: YL. Wrote the paper: YL WYB PL CNW JDB KWL.

References

1. Bourne HR, Sanders DA, McCormick F (1991) The GTPase superfamily: conserved structure and molecular mechanism. Nature 349: 117–127.
2. Bourne HR, Sanders DA, McCormick F (1991) The GTPase superfamily: a conserved switch of diverse cell functions. Nature 348: 125–132.
3. Lipe DD, Wolf YI, Kossin EV, Aravind L (2002) Classification and evolution of P-loop GTPases and related ATPases. J Mol Biol 317: 41–72.
4. Caldon CE, March PE (2005) Function of the universally conserved bacterial GTPases. Curr Opin Microbiol 6: 135–139.
5. Trach K, Hoch JA (1989) The Bacillus subtilis spo0B stage 0 sporulation operon encodes an essential GTP-binding protein. J Bacteriol 171: 1362–1371.
6. Kok J, Trach KA, Hoch JA (1994) Effects on Bacillus subtilis of a conditional lethal mutation in the essential GTP-binding protein Obg. J Bacteriol 176: 7155–7160.
7. Vidwans SJ, Irrton K, Grossman AD (1993) Possible role for the essential GTP-binding protein Obg in regulating the initiation of sporulation in Bacillus subtilis. J Bacteriol 175: 3300–3311.
8. Kuo S, Demeler B, Haldenwang WG (2008) The growth-promoting and stress response activities of the Bacillus subtilis GTP-binding protein Obg are separable by mutation. J Bacteriol 190: 6625–35.
9. Makkodo J, Bhart A, Koch M, Skidmore J (1997) Identification of an essential Caulobacter crescentus gene encoding a member of the Obg family of GTP-binding proteins. J Bacteriol 179: 6426–6431.
10. Okamoto S, Ochi K (1998) An essential GTP-binding protein functions as a regulator for differentiation in Streptomyces coelicolor. Mol Microbiol 30: 107–119.
11. Slominska M, Konopa G, Wegryn G, Czyz A (2002) Impaired chromosome partitioning and synchronization of DNA replication initiation in an insertion mutation in the Vibrio harveyi cgtA gene coding for a common GTP-binding protein. Biochim J 362: 579–84.
12. Scott JM, Ju J, Mitchell T, Haldenwang WG (2000) The Bacillus subtilis GTP binding protein Obg and regulators of the σ70 stress response transcription factor cofractionate with ribosomes. J Bacteriol 182: 2771–2777.
13. Scott JM, Haldenwang WG (1999) Obg, an essential GTP binding protein of Bacillus subtilis, is necessary for stress activation of transcription factor σE. J Bacteriol 181: 4653–4660.
14. Kobayashi G, Moriya S, Wada C (2001) Deficiency of essential GTP-binding protein ObgE in Escherichia coli inhibits chromosome partition. Mol Microbiol 41: 1037–1051.
15. Dutkiewicz R, Slominska M, Wegryn G, Czyz A (2002) Overexpression of the cgtA (shbZ, obgE) gene, coding for an essential GTP-binding protein, impairs the regulation of chromosomal functions in Escherichia coli. Curr Microbiol 45: 440–445.
16. Liu B, Thauer DA, Maddock JR (2004) The Caulobacter crescentus CtgA protein coordinates with the free 50S ribosomal subunit. J Bacteriol 186: 481–489.
17. Datta K, Skidmore JM, Pu K, Maddock JR (2004) The Caulobacter crescentus GTPase CtgA is required for progression through the cell cycle and for maintaining 50S ribosomal subunit levels. Mol Microbiol 54: 1379–1392.
18. Wout P, Pu K, Sullivan SM, Reese V, Zhou S, et al. (2004) The Escherichia coli GTPase CtgA cofractionates with the 50S ribosomal subunit and interacts with SpoT, a ppGpp synthetase/hydrolase. J Bacteriol 186: 5249–5257.
19. Sikora AE, Zielke R, Datta K, Maddock JR (2006) The Vibrio harveyi GTPase CgtAv is essential and is associated with the 50S ribosomal subunit. J Bacteriol 188: 1205–1210.
20. Sato A, Kobayashi G, Hayashi H, Yoshida H, Wada A, et al. (2005) The GTP binding protein Obg homolog ObgE is involved in ribosome maturation. Genes Cells 10: 393–408.
21. Tan J, Jakob U, Bardwell JCA (2002) Overexpression of two different GTPases rescues a null mutation in a heat-induced rRNA methyltransferase. J Bacteriol 184: 2892–2898.
22. Jiang M, Datta K, Walker A, Strahler J, Bagamasbad P, et al. (2006) The Escherichia coli GTPase CgtAc is involved in late steps of large ribosome assembly. J Bacteriol 188: 6757–6770.
23. Comartin DJ, Brown ED (2006) Non-ribosomal factors in ribosome subunit assembly are emerging targets for new antibacterial drugs. Curr Opin Pharmacol 6: 453–458.
24. Buglio J, Shen V, Hakimian P, Lima CD (2002) Structural and biochemical analysis of the Obg GTP binding protein. Structure 10: 1581–1592.
25. Kukimoto-Niino M, Murayama K, Inoue M, Terada T, Tame JR, et al. (2004) Crystal structure of the GTP-binding protein Obg from Thermus thermophilus HB8. J Mol Biol 337: 761–770.
26. Milburn MV, Tong L, deVos AM, Brunger A, Yamazumi Z, et al. (1990) Molecular switch for signal transduction: structural differences between active and inactive forms of protooncogenic ras proteins. Science 247: 939–945.
27. Pai EF, Krenkel U, Petsko GA, Goody RS, Kabsch W, et al. (1990) Structure of the guanine-nucleotide-binding domain of the Ha-ras oncogene product p21 in the triphosphate conformation. EMBO J 9: 2351–2359.
28. Lin B, Skidmore JM, Bhatt A, Pfeffer SM, Pavloski L, et al. (2001) Alanine scan mutagenesis of the switch I domain of the Caulobacter crescentus CgtA protein reveals critical amino acids required for in vivo function. Mol Microbiol 39: 924–934.
29. Wittinghofer A (2002) Obg, a G domain with a beautiful extension. Structure 10: 1471–1472.
30. Lee Y, Bang WY, Kim S, Lazar P, Balk BD, et al. (2009) Binding Mode Analysis of Bacillus subtilis Obg with Ribosomal Protein L13 through Computational Docking Study. Interdisciplinary Bio-Central 1: 1–6.
31. Berendsen HJC, van der Spoel D, van Drunen R (1995) GROMACS - a message-passing parallel molecular-dynamics implementation. Comput Phys Commun 91: 43–56.
32. van der Spoel D, Lindahl E, Hess B, van Buuren AR, Apol E, et al. (2005) Gromacs User Manual version 3.3, http://www.gromacs.org.
33. Schuttelkopf AW, van Aalten DMF (2004) Prodig: a tool for high-throughput crystallography of protein-ligand complexes. Acta Crystallogr D 60: 1355–1363.
34. Darden T, York D, Pedersen L (1993) Particle mesh Ewald: an N·log(N) method for Ewald sums in large systems. J Chem Phys 98: 10089–10092.
35. Hess B, Bekker H, Berendsen HJC, Fraaije JGEM (1997) LINCS: a linear constraint solver for molecular simulations. J Comput Chem 18: 1463–1472.
36. Brigo A, Lee KW, Iurcu Mustata G, Briggs JM (2005) Comparison of multiple molecular dynamics trajectories calculated for the drug-resistant HIV-1 integrase T66I/M154I catalytic domain. Biophys J 88: 3072–82.