A peptide adhesive molded by magnesium glues Rubisco’s subunits together

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Rubisco enzymes play central roles in carbon fixation, with potential importance in biotechnology, but have eluded a full description of their multistep assembly and function. A new article describes the fascinating discovery that some archaeal Rubiscos contain a built-in assembly domain inserted into an otherwise canonical Rubisco fold, providing a tremendous expansion of our understanding of the diversity of naturally occurring Rubiscos.

Rubisco forms I and II are found in photosynthetic organisms and are responsible for almost all carbon fixation on earth, converting CO₂ and the sugar ribulose 1,5-bisphosphate (RuBP) into 3-phosphoglycerate as part of the Calvin-Benson-Bassham (CBB) cycle (1). Form I Rubiscos (L8S8) partner the catalytic large subunits (LSU) with small subunits (SSU) to ensure optimal activity and are known to undergo a complex folding and assembly process. Formation of the holoenzyme requires highly specific chaperones such as RbcX, Raf1, and Raf2 to coordinate proper oligomerization to the hexadecameric state (2, 3). However, the mechanistic details of assembly and catalysis remain only partially understood, limiting biotechnological applications of these intriguing enzymes. Form II and Form III Rubiscos lack SSU. Form III Rubiscos, while using conserved active site features to catalyze the same carboxylation reaction as Form I (L8S8) Rubiscos. The RAD consists of only 29 residues, compared with the 110–160 residues of the SSU that adopt the structure of a four-stranded anti-parallel β-sheet (4). In the Form I hexadecameric assembly, each SSU contacts a substantial surface area of two adjacent LSU. In contrast, the RAD may be more appropriately classified as a subdomain, as it is unlikely to form an independently folding unit. Interestingly, M. burtonii Rubisco achieves full functionality only upon substrate-assisted assembly to ring-like complexes (5). It is tempting to speculate that, prior to assembly, part of the RAD helix may be disordered, presumably because it would lack magnesium ion coordination. Upon binding of an appropriate carbohydrate such as RuBP to the active sites, conformational adjustments may be transmitted over a distance of 44 Å to the dimer-dimer contact surfaces, thereby triggering assembly from the L2 to the L10 form. In this scenario, part of the RAD domain would undergo a disorder-order transition that is induced by RuBP binding, thereby facilitating magnesium ion coordination (Fig. 1).

With this structural information in hand, Gunn et al. (6) return to the classification of the M. burtonii Rubisco: their assessment of its sequence homology suggests it is intermediate between Forms II and III. However, based on both structure and function, Gunn et al. (6) choose to group this protein with Form III Rubiscos, defining a new subclass named IIIB.
The built-in assembly domain of the archaeal \textit{M. burtonii} Rubisco provides a possible route to bypass the need for assembly factors, thereby providing opportunities for Rubisco engineering without the necessity to co-engineer a large array of auxiliary proteins. The co-evolution of assembly factors such as RbcX, Raf1, and Raf2 provides for interaction specificity with cognate large or small subunits of Rubisco. For this reason, the functional expression of Rubisco holoprotein in heterologous organisms remains quite challenging (8). Will we be able to learn from the structural and dynamical features of the RAD domain to design novel Rubisco proteins that undergo facile assembly in transgenic organisms? If so, the effects of improved Rubisco kinetics on photosynthetic performance and biomass accumulation could be evaluated more rapidly.

References