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is clear that such studies are going to be critical for understanding the process of protein synthesis. In addition, Jennifer Doudna (Howard Hughes Medical Intstitute and Yale University) presented the cryo-EM reconstruction of the HCV-IRES bound to the 40S ribosomal subunit, which was done in collaboration with Joachim Franck. The IRES forms an extended structure that has a broad interface with the 40S subunit, and several localized changes in the conformation of the 40S subunit upon IRES binding provide clues as to how the IRES primes the ribosome for translation.

Particularly impressive advances in the field of RNA–protein interactions have been made in the area of structural biology. Notwithstanding the stellar structures of the ribosome that emerged in the past year, our structural understanding of RNA–protein complexes is rapidly increasing, and in addition to those contributions previously mentioned, there were two structures that had a high impact at the meeting. Catherine Mazza (Steven Cusack's laboratory, EMBL Grenoble, in collaboration with Iain Mattaj, EMBL Heidelberg) presented the crystal structure of the nuclear Cap Binding Complex (CBC), and Oliver Weichenrieder (The Netherlands Cancer Institute, formerly of Steven Cusack's laboratory), presented the structure of the ALU domain of the signal recognition particle.

The setting of the meeting was at the Lakeway Inn on the shores of Lake Travis outside Austin, Texas. This proved to be an excellent venue for the meeting, although the hotel proved to be somewhat audio-challenged. The food was well-prepared for the most part, with a generous offering of various styles of barbecue. These people understand barbecue. The meeting also featured a trip into downtown Austin to sample the famous Austin music scene and restaurant fare. A tour of the Institute for Cellular and Molecular Biology at the University of Texas, Austin revealed expansive Texas-sized lab modules that left the UCSF contingent slack-jawed. Also, there was a sunset boat cruise on Lake Travis that ended without incident due to diligent crowd-control measures by the crew, who were clearly experienced with scientists confined in a close space with a bar over water. Finally, we were treated to a sampling of the local vintages, and I am sad to report that Texas Red is a much better fluorophore than it is a wine.

This meeting was a reprise of a synonymously titled meeting held on the Jersey Shore in May of 1998. I attended both meetings, and what is remarkable is how far our understanding of RNA–protein interactions has come in the past three years. There were only a handful of structures of RNA–protein complexes presented at that first meeting, and the biochemistry of RNA–protein complexes was by comparison rudimentary. During the subsequent three-year period, the functional view available has advanced considerably, and we now know that transcription, processing, and translation are not compartmentalized processes, but are rather a carefully orchestrated continuous process.

In summary, the organizers are to be congratulated for putting together such an outstanding program. The breadth of topics and the depth of the speakers made for a remarkable snapshot of the state of our understanding of RNA–protein interactions in biology. If the slope of the trajectory indicated by the first and second "Proteins that Bind RNA" meetings continues, the third meeting, which we will hopefully cajole the organizers into hosting, should be even more spectacular.

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picture story

Reining in CDK

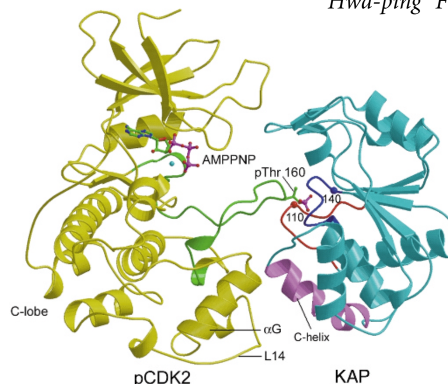
Cell growth and division are essential to life. In eukaryotes, the sequence of events leading to these processes is coordinated by a family of proteins called cyclin-dependent kinases (CDKs). The activity of CDKs is tightly controlled, and defects in its regulation often result in abnormal tissue growth and cancer. Thus, understanding the molecular mechanism of how CDK activity is controlled is important for understanding cancer biology.

The kinase activity of a CDK is activated by binding to its effector partner protein in the cyclin family, and by phosphorylation of a conserved Thr in CDK. Deactivation requires both degradation of the cyclin molecule and dephosphorylation by a CDK-associated phosphatase. To define the structural basis of CDK dephosphorylation that leads to inactivation, Song *et al*. (*Mol. Cell*, 7, 615–626; 2001) have determined the crystal structure of phosphorylated CDK2 (pCDK2) in complex with a kinase-associated phosphatase (KAP).

The structure reveals that the active site of KAP (the catalytic residues at positions 110 and 140 are marked by spheres; KAP is cyan) interacts almost exclusively with the phosphate moiety of the phosphorylated Thr (pThr 160) in CDK2 (yellow). Specific recognition between the two proteins is mostly mediated by residues in the C-terminal lobe of CDK2 (αG helix and L14 loop) and those in the C-terminal helix (magenta) of KAP; these residues are removed from the active site of KAP. Thus, specific recognition of pCDK2 by KAP requires the native fold of the CDK2 molecule; notably, the sequence of the kinase activation segment (green) bearing the phosphorylated Thr residue does not play a significant role.

The kinase activation segment (green) is drawn away from the surface of pCDK2 in the complex. This conformation is different from that in all other determined structures of pCDK2, indicating that local unfolding may be necessary to expose the phosphate moiety for interaction with KAP. The kinase is in the active conformation, similar to that observed in the pCDK2–cyclin complex. This suggests that KAP may preferentially recognize pCDK2 in the context of the activated complex. The structure of the pCDK2–KAP complex therefore provides insights into the dephosphorylation — and inactivation — mechanism of CDKs.

Hwa-ping Feng



Adapted from Song *et al.*

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