



ABSTRACT

“Toward Deciphering the Network Architecture of Cyclin-Dependent Kinase Action”

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Cyclin-dependent kinases are the central regulators of the cell cycle and as such key to growth, development and reproduction. The function of CDKs is conserved from yeast to plants and for example, expression of CDKA;1, the plant Cdk1 homolog, can complement yeast *cdc2* or *Cdc28* mutants. In addition, recent studies have shown that the molecular mechanistic of Cdk1-like kinases are conserved across kingdoms, e.g. the requirement for its activation through phosphorylation of a conserved Thr residue in their T-loop. In contrast to the conserved enzymatic function, the regulatory network of their action appears to have undergone dramatic changes during two billion years of eukaryotic evolution. This is illustrated by the recent finding that a Cdc25-Wee1 regulatory module is absent in the flowering plant *Arabidopsis*. Through extensive studies in yeast and humans, a comprehensive picture of CDK function has been revealed. We are interested in the properties of the network architecture of CDK action to understand general principles of cellular organization and coordination by cell-cycle control. As a starting point, we are following three complementing approaches to identify CDKA;1 substrates in *Arabidopsis* as a eukaryote very distantly related to metazoans and yeast. First, we exploit a modified bimolecular complementation assays to identify kinase substrates. Second, we have generated a gatekeeper mutant of CDKA;1 that can rescue *cdka;1* mutants. In the gatekeeper variant the ATP binding pocket is mutated in such a way that bulky derivatives of ATP can be accepted by the kinase allowing the identification of proteins that were phosphorylated by this kinase variant. Third, we are analyzing the phospho-proteome of weak-loss-of-function mutants of CDKA;1. These approaches are providing a growing list of putative CDKA;1 substrates in *Arabidopsis*. Here, I will give a progress report of our current attempts and compare the so far identified substrates with data from yeast and humans.