CellPress

Review

Aurora Kinases Throughout Plant Development

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Aurora kinases are evolutionarily conserved key mitotic determinants in all eukaryotes. Yeasts contain a single Aurora kinase, whereas multicellular eukaryotes have at least two functionally diverged members. The involvement of Aurora kinases in human cancers has provided an in-depth mechanistic understanding of their roles throughout cell division in animal and yeast models. By contrast, understanding Aurora kinase function in plants is only starting to emerge. Nevertheless, genetic, cell biological, and biochemical approaches have revealed functional diversification between the plant Aurora kinases and suggest a role in formative (asymmetric) divisions, chromatin modification, and genome stability. This review provides an overview of the accumulated knowledge on the function of plant Aurora kinases as well as some major challenges for the future.

Trends

Aurora kinases are key mitotic regulators in plants.

α-Aurora and β-Aurora kinases from plants are functionally divergent.

Plant Aurora kinases differ from their animal counterparts.

Aurora kinases have diverse roles throughout plant development.

Formative divisions require higher mitotic kinase levels than do proliferative divisions.

Aurora Kinases

Serine/threonine Aurora kinases are indispensable for eukaryotic cell division and have been intensively studied in mammals and yeast [1,2]. Aurora was first discovered in *Drosophila* where mutant analysis revealed monopolar spindle formation, which is why the protein was called Aurora, reminiscent of the Northern light (*aurora borealis*) [3]. Deregulation of Aurora kinase activity has been shown to be involved in mitotic failures leading to cancer [4]. Thus, Aurora kinases are valuable targets for anticancer therapeutics, and an enormous body of research has brought about detailed understanding of the molecular pathways in which Aurora kinases are involved (Figure 1A).

While the yeasts ***Saccharomyces cerevisiae*** and ***Schizosaccharomyces pombe*** (see Glossary) each contain only one Aurora homolog, Ipl1p (increase in ploidy 1) and Ark1 (Aurora-related kinase 1), respectively [5,6], ***Caenorhabditis elegans***, *Drosophila melanogaster*, and *Xenopus laevis* contain two Aurora kinases: Aurora A and Aurora B [4]. Mammals have three Aurora kinases, A, B, and C (Figure 1). In animals and yeast, multiple substrates of Aurora kinases were characterized [4], most of which function in mitosis with roles ranging from chromosome alignment, centrosome separation and maturation, chromatin modifications and condensation to (bipolar) spindle assembly, spindle checkpoint control, and cytokinesis [4,7,8]. The first Aurora phosphorylation consensus site was identified for Ipl1p [9] and was later also adapted for human Aurora A to {[Arg/Lys/Asp] – Arg – $X_{(1,2)}$ – [Ser/Thr] – hydrophobic residue ≠Pro} [10–12].

In contrast to yeast and animals, the role of plant Aurora kinases is only starting to emerge. Based on phylogenetic analysis, localization, and functional divergence, plant Aurora kinases can be clustered into two subclades, α-Aurora and β-Aurora (Figure 1A,B). While higher plants have members in both groups, lower plants such as *Marsilea* (*M. vestita*) and *Physcomitrella* (*P. patens*) only contain α-Aurora kinases [13]. The *Arabidopsis* (*A. thaliana*) genome encodes

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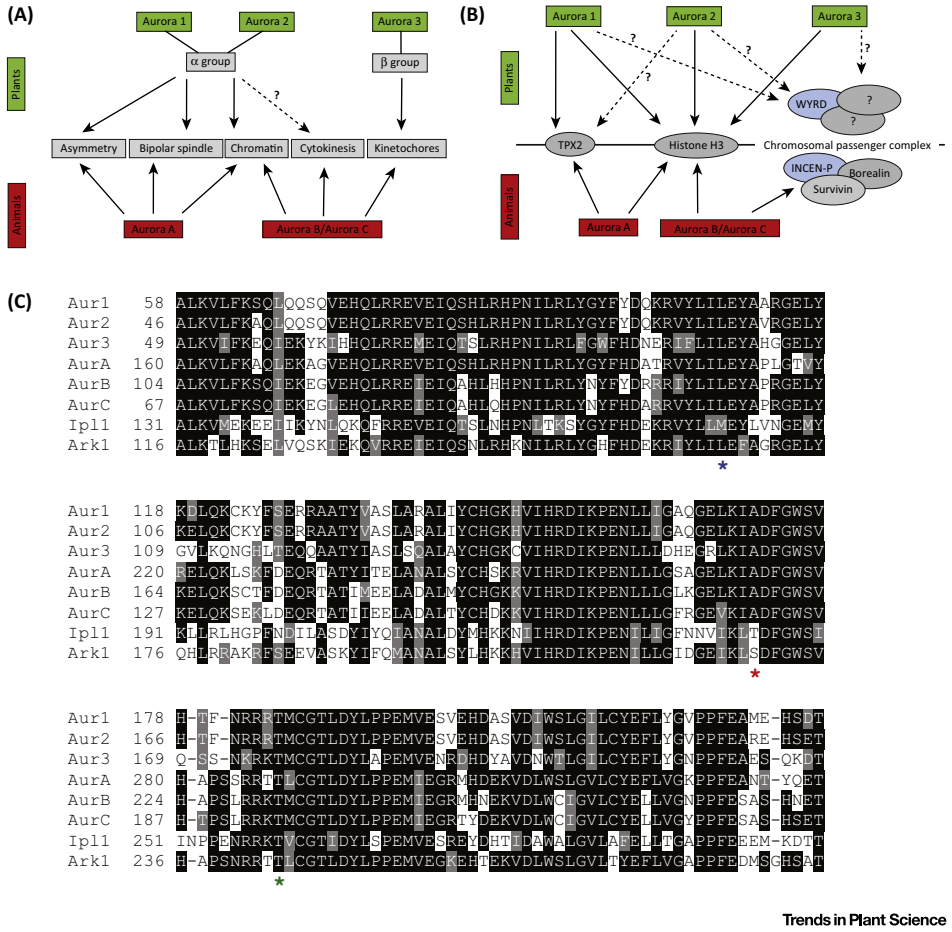

Trends in Plant Science

Figure 1. Functional Divergence Between Plant and Animal Aurora Kinases. (A) Animal and plant Aurora kinases are involved in various mitotic processes. Animals have three Aurora kinases (A–C) [4]. *Arabidopsis* also has three Aurora kinases that are subdivided into the α-Aurora (Aurora 1 and 2) and β-Aurora (Aurora 3) groups [13]. Similarly to animal Aurora A, the α-Aurora group of *Arabidopsis* is involved in establishing bipolar spindles, chromatin (histone) modifications, and asymmetry during formative divisions [19,60,64]. Further functions of animal Aurora A kinases involve centrosome maturation, centrosome separation, and possibly DNA repair [65]. In addition, a putative function in cytokinesis, a feature of animal Aurora B/C, was also attributed to α-Aurora kinases [4,13,15,18]. The β-Aurora kinase Aurora 3 is involved in kinetochore–microtubule attachment comparable to animal Aurora B/C [4,44]. Furthermore, Aurora B contributes to chromatin condensation, sister chromatid cohesion, mitotic spindle assembly, and chromosome bi-orientation, but this has not yet been demonstrated for plant Aurora kinases [7,8,66]. Dotted lines represent hypothetical connections. (B) The specificity of Aurora kinases depends on their interaction partners. Animal Aurora A mainly interacts with TPX2 (targeting protein for *Xenopus* kinesin-like protein 2) [23], whereas Aurora B/C mainly function as members of the chromosomal passenger complex (CPC). Interaction partners and substrates for plant Aurora kinases remain scarce. All three *Arabidopsis* Aurora kinases 1, 2, and 3 can phosphorylate histone H3, as can animal Aurora A/B/C [4,36]. In addition, AtAurora 1 can interact with and phosphorylate the plant homolog of TPX2 [31]. Whether this is a unique feature of Aurora 1, or if TPX2 is a substrate for both members of the α-Aurora group, still needs to be investigated. No CPC has been identified in plants to date. Recently, however, it has been suggested that the protein WYRD might be part of a plant CPC [34]. It remains to be established which plant Aurora kinase might partner with this complex, and the exact composition of the plant complex needs to be determined. Dotted lines represent hypothetical connections. (C) (Partial) sequence alignment of *Arabidopsis* AtAurora kinase 1 (AT4G32830; UniProtKB: Q9M077), AtAurora kinase 2 (AT2G25880; UniProtKB:Q683C9) and AtAurora kinase 3 (AT2G45490; UniProtKB: Q64629), human Aurora kinase A (UniProtKB: O14965), Aurora kinase B (UniProtKB: Q96GD4), and Aurora kinase C (UniProtKB: Q9UQB9), as well as the homologs Ipl1p (UniProtKB: J8PVQ6) and Ark1 (UniProtKB: O59790) of *S. cerevisiae* and *S. pombe*, respectively. The blue asterisk indicates the gatekeeper residue in the hinge region of the kinase domain which has been modified (L166A) to obtain an analog-sensitive kinase of Ark1 [55]. The red asterisk marks residue T244 of Ipl1p in the ATP-binding pocket. Modification of this residue to T244A results in a kinase that is sensitive to the bulky ATP analog 1-NA-PP1 [56]. Human and *Arabidopsis* Aurora kinases already possess an alanine residue at this position. The green asterisk points to T288 of human Aurora kinase A, the activation loop of the kinase, which is conserved in all homologs displayed here [67]. For a complete sequence alignment of Aurora kinases from different species please refer to [13].

Glossary

Asymmetric cell division (ACD): cell division program in which one or both of the daughter cells acquire a different cellular fate than the mother cell.

Bright yellow 2 (BY-2): *Nicotiana tabacum* cv. tobacco cell suspension culture line; model plant system comparable to HeLa cells for human research.

***Caenorhabditis elegans* (*C. elegans*):** nematode model organism; first multicellular organism whose genome was completely sequenced.

Centromeric histone 3 (CenH3): important for kinetochore–DNA attachment during mitosis.

***Chlamydomonas reinhardtii*:** single-cell green algae; algal model organism.

Chromosomal passenger complex (CPC): composed of Aurora B, inner centromere protein, borealin, and survivin in animals; regulates key mitotic events.

Cyclin-dependent kinase A1 (CDKA1): core cell cycle kinase in plants; single gene in *Arabidopsis*; homolog of human CDK1 and the yeast cdc2/CDC28.

Endoreplication: a cell-cycle variant in which cells exit their cell cycle before mitosis and repeat S-phases without dividing, normally entering the elongating stage.

Inner centromere protein (INCEN-P): part of the CPC.

Microtubule-associated protein of approximately 65 kDa (MAP65): bundles antiparallel microtubules.

Microtubule-organizing center (MTOC): involved in the organization of mitotic spindles and microtubule nucleation.

Partitioning-defective (PAR) complex: important during neuron development for the asymmetric distribution of polarity determinants during cell division. Subunits are not conserved in plants.

Pre-prophase band (PPB): microtubule- and actin-rich ring which transiently labels the future division plane before mitosis in plant cells.

Protein phosphatase 1 (PP1): serine/threonine phosphatase.

Retinoblastoma protein (pRb): tumor-suppressor protein; inhibits cell-cycle progression.

RETINOBLASTOMA-RELATED 1 (RBR1): *Arabidopsis* homolog of Rb.