HelmholtzZentrum münchen
German Research Center for Environmental Health

Scientific Highlight August 2016

☐ co-ordinated with the Director of the Institute / Head of Department

Department of Molecular Epigenetics

PSP-Element:
G-502890-001

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Title of the Highlight:
Specific threonine-4 phosphorylation and function of RNA polymerase II CTD during M phase progression

Keywords:
RNA Polymerase II, CTD, phosphorylation, mitosis, centrosome

Central statement of the Highlight in one sentence:
RNA polymerase II interacts specifically with centrosomes and phosphorylation of CTD threonine-4 by PLK1 is required for proper M phase progression. First evidence for an essential function of Pol II in mitotic cells.

Text of the Highlight:
Dynamic phosphorylation of Tyr1-Ser2-Pro3-Thr4-Ser5-Pro6-Ser7 heptad-repeats in the C-terminal domain (CTD) of the large subunit coordinates progression of RNA polymerase (Pol) II through the transcription cycle. Here, we describe an M phase-specific form of Pol II phosphorylated at Thr4, but not at Tyr1, Ser2, Ser5, and Ser7 residues. Thr4 phosphorylated Pol II binds to centrosomes and midbody and interacts with the Thr4-specific Polo-like kinase 1. CTD Thr4 mutants, but not Ser2 and Ser5 mutants, display severe mitosis and cytokinesis defects characterized by multipolar spindles and polyploid cells. We conclude that proper M phase progression of cells requires binding of Pol II to centrosomes to facilitate regulation of mitosis and cytokinesis in a CTD Thr4-P dependent manner.

Publications:
Hintermair, C., Voss, K., Forné, I., Heidemann, M., Flatley, A., Kremmer, E., Imhof, A., and **Eick, D**. (2016) Specific threonine-4 phosphorylation and function of RNA Polymerase II during M phase progression. *Scientific Reports* 6, 27401

Taking account of the HMGU mission:
The CTD of RNA polymerase II plays a central role in the transformation of cellular signals into epigenetic information and *vice versa*. CTD facilitates transcription of chromatin, maturation of mRNA, and reading and writing of epigenetic signals of chromatin. Understanding of the genetic and epigenetic codes is essential for the understanding and research of complex diseases.

The internal HMGU co-operation partners with whom the Highlight was compiled, if appropriate:
Institute of Molecular Immunology G-501700-003

Specific threonine-4 phosphorylation and function of RNA Polymerase II during M phase progression

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Specific threonine-4 phosphorylation and function of RNA Polymerase II during M phase progression

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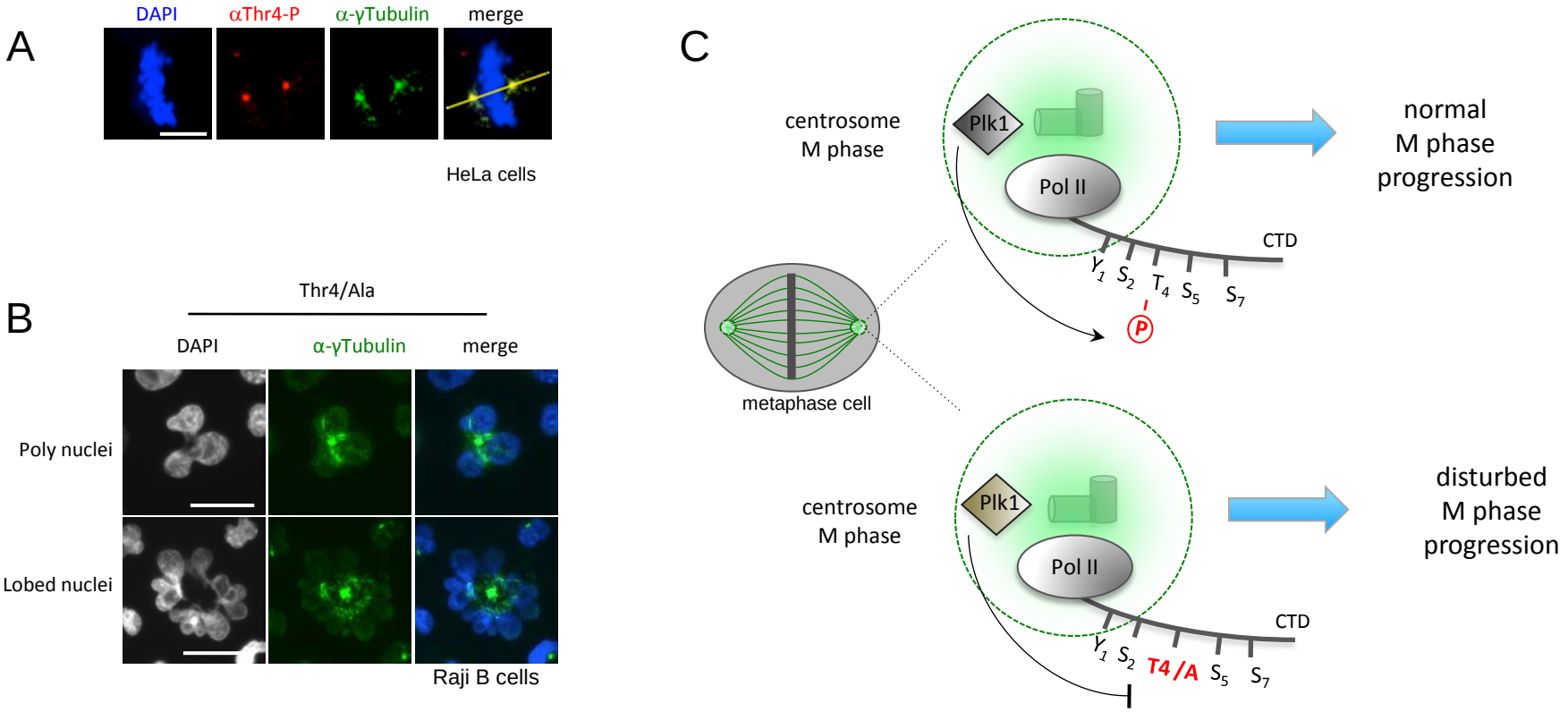

Figure 1 (A) Immunofluorescence image of mitotic HeLa cells stained with DAPI (blue), a CTD Thr4-P specific mAb, and an anti-tubulin mAb. **(B)** Overexpression of a Thr4/Ala mutant of CTD for 24 hours induces poly-nucleated cells and cells with lobed nuclei. **(C)** Model for an essential function of Pol II during mitosis.