Biochemical and Biophysical Research Communications 463 (2015) 88–94

Contents lists available at ScienceDirect

Biochemical and Biophysical Research Communications

journal homepage: www.elsevier.com/locate/ybbrc

DDA3 targets Cep290 into the centrosome to regulate spindle positioning

Haiyu Song [1], Ji Eun Park [1], Chang-Young Jang*

Research Center for Cell Fate Control, College of Pharmacy, Sookmyung Women's University, Seoul 140-742, Republic of Korea

ARTICLE INFO

Article history:
Received 17 April 2015
Available online 18 May 2015

Keywords:
Cep290
DDA3
Centrosome
Astral spindle
Spindle positioning

ABSTRACT

The centrosome is an important cellular organelle which nucleates microtubules (MTs) to form the cytoskeleton during interphase and the mitotic spindle during mitosis. The Cep290 is one of the centrosomal proteins and functions in cilia formation. Even-though it is in the centrosome, the function of Cep290 in mitosis had not yet been evaluated. In this study, we report a novel function of Cep290 that is involved in spindle positioning. Cep290 was identified as an interacting partner of DDA3, and we confirmed that Cep290 specifically localizes in the mitotic centrosome. Depletion of Cep290 caused a reduction of the astral spindle, leading to misorientation of the mitotic spindle. MT polymerization also decreased in Cep290-depleted cells, suggesting that Cep290 is involved in spindle nucleation. Furthermore, DDA3 stabilizes and transports Cep290 to the centrosome. Therefore, we concluded that DDA3 controls astral spindle formation and spindle positioning by targeting Cep290 to the centrosome.

1. Introduction

Cell division is essential for the proliferation of eukaryotic cells and produces two daughter cells from a single cell. The processes of cell division are sequential events, and is known as the cell cycle. The final goal of the cell cycle is to separate sister chromatids and cellular components into two daughter cells [1]. For this purpose, all chromosomes are aligned at the metaphase plate in metaphase and two centrosomes start to pull the chromosomes and generate tension between sister-kinetochores. Perfect chromosome alignment leads to spindle assembly checkpoint (SAC) silence and activates APC/C which degrades the seperase inhibitor, securin. As anaphase onset, activated separase dissolves the cohesion between sister-chromatids which can move toward the spindle pole by the pulling force of the spindle [2].

The mitotic spindle controls accurate spindle positioning, chromosome alignment, faithful chromosome segregation, and cleavage furrow formation correctly by spindle MT dynamics [3]. Spindle positioning is governed by the interaction between astral MTs and the cell cortex. Astral MTs anchor the spindle pole to the cortex. Abnormal spindle rotation induces chromosome mis-segregation and mitotic delay. Previously, it has been reported that spindle formation is specifically important for bipolarity and requires MT-associated proteins (MAPs) and centrosomal proteins at M-phase entry [4]. Centrosomal proteins control MT organization such as γ-tubulin ring complexes (γ-TuRCs). γ-TuRCs localize to the MT organizing center in the centrosome and nucleate MTs. Loss of γ-TuRC proteins leads to the generation of monopolar spindles and abnormal centrosome maturation [5].

In animal cells, centrosomes functions in MT organization, cell polarity, and cilium formation [6]. Centrosomes contain two centrioles that are duplicated once per cell cycle. Centriolar satellites are centrosome-associated structures, defined by the protein PCM-1. A key function of satellites lies in targeting centriolar and PCM-1 from the cytoplasm to the centrosome through MTs [2]. Loss of PCM-1 leads to the reduction of centrin and pericentrin in centrosomes in cycling cells and primary cilia assembly [7]. CEP family proteins are components of centrosome and essential for cell division. These proteins primarily control centriole duplication, MT-kinetochore (KT) assembly, bipolarity, and mitotic progression [8]. Thirty-one CEP proteins have been identified and many of them are being evaluation. Among them, Cep27, a component of Augmin complex, plays a critical role of centrosome-independent MT generation. Another CEP protein, Cep55, is expressed in cancer cells and important for faithful cytokinesis [9,10].

Mutations of several CEP proteins tend to cause disorder. For example, mutations of Cep290, known as BBS14 or KIAA0373, are observed in ciliopathies which are a group of diseases associated with ciliary dysfunction such as retinal degeneration, Joubert

* Corresponding author. Fax: +82 2 710 9871.
E-mail address: cyjang@sookmyung.ac.kr (C.-Y. Jang).
[1] Both authors contributed equally to this work.

http://dx.doi.org/10.1016/j.bbrc.2015.05.028
0006-291X/

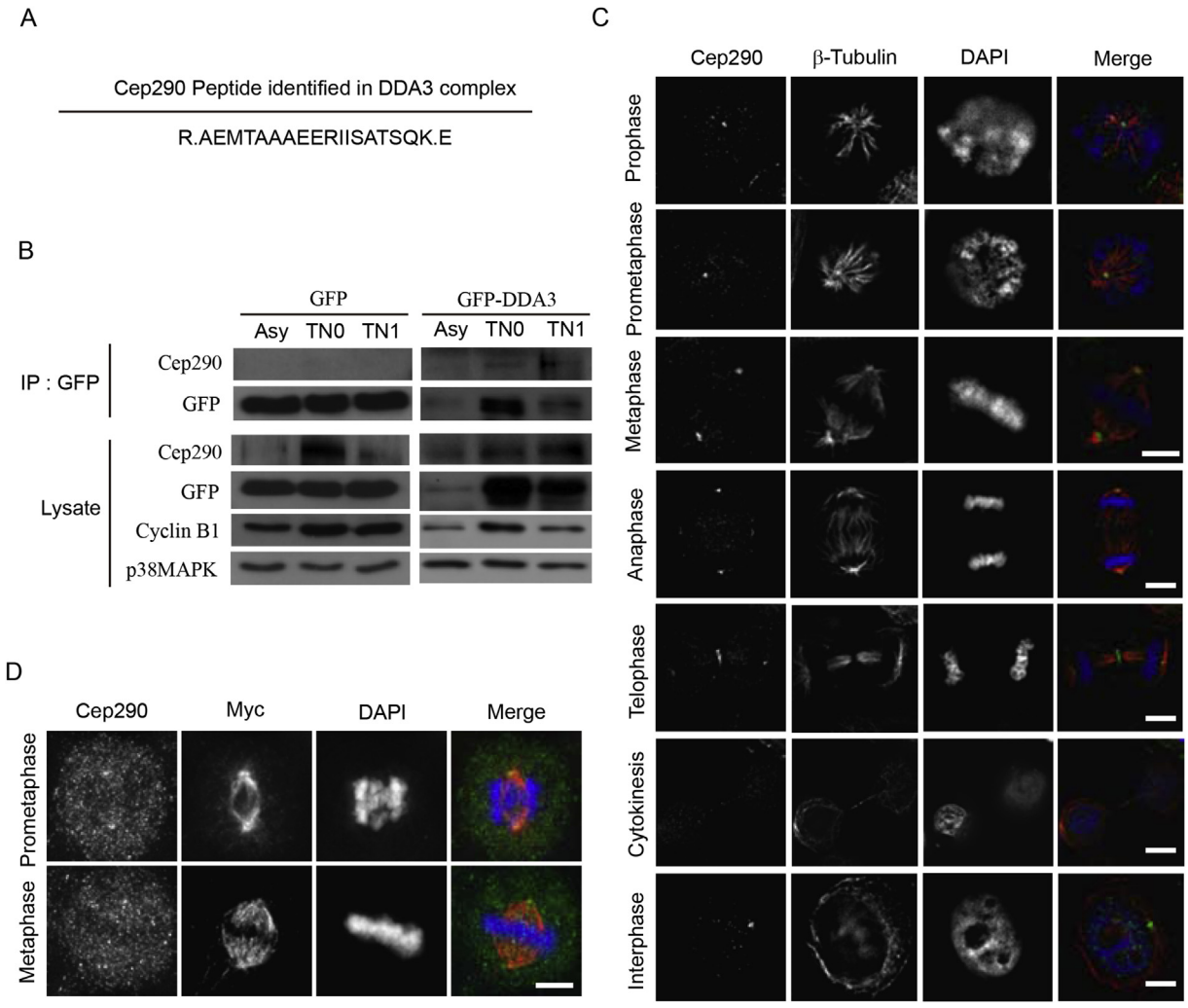


Fig. 1. Cep290 interacts with DDA3 and localizes in the centrosome. (A) A peptide of Cep290 identified in the DDA3 complex purified from mitotic cells. (B) HeLa cells were synchronized by a thymidine-nocodazole block, released into fresh media, and harvested at the indicated times. Cell lysates were analyzed via immunoprecipitation and Western blotting with indicated antibodies. (C) HeLa cells were fixed with MeOH and stained with antibodies as indicated. Images are maximum projections from z stacks of representative cells stained for Cep290 (green), β–tubulin or Plk1 (red), and DNA (blue). (D) 28 h after transfection, HeLa cells were fixed with MeOH and stained with antibodies as indicated. Images are maximum projections from z stacks of representative cells stained for Cep290 (green), Myc (red), and DNA (blue). Scale bars, 5 μm. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

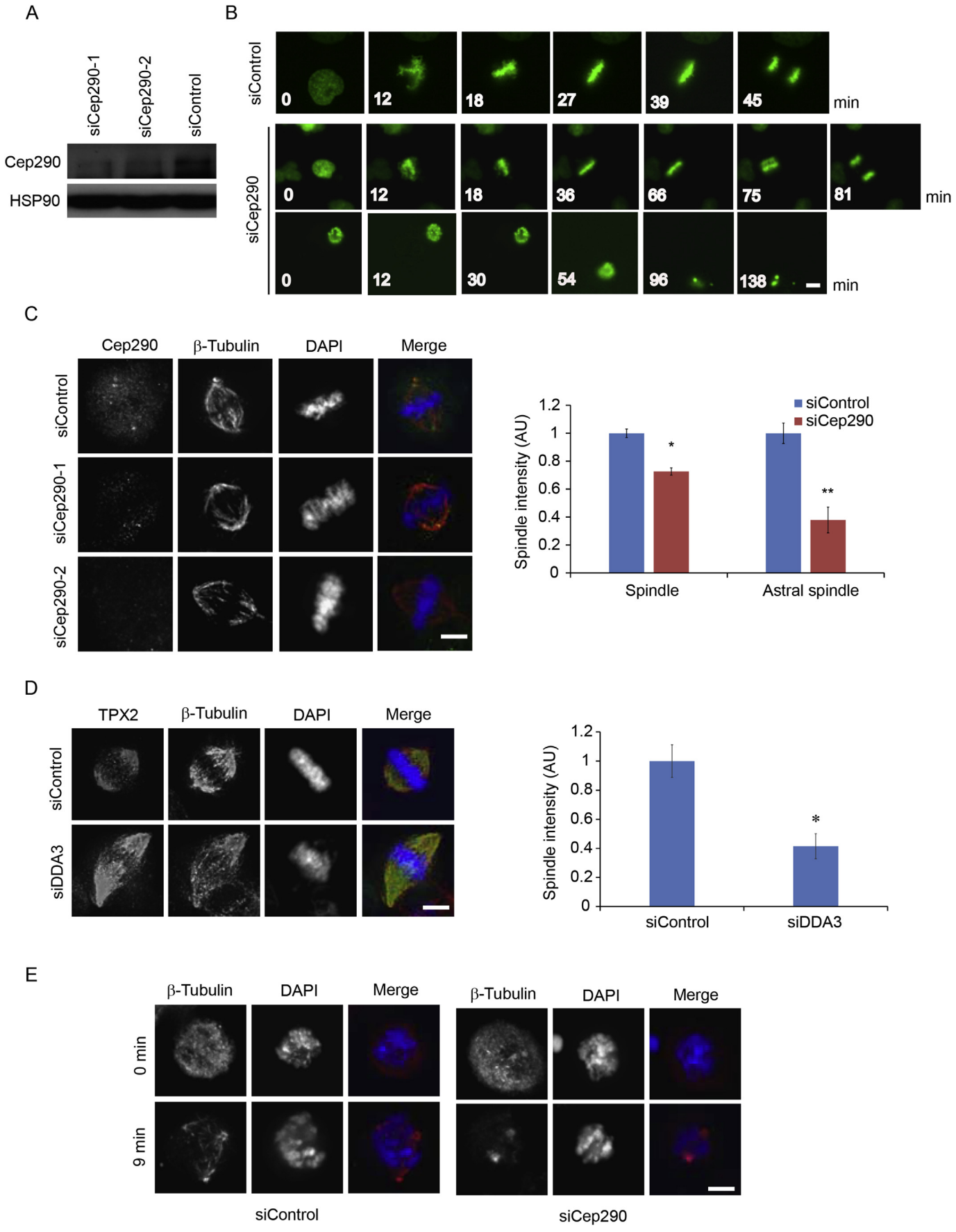
syndrome type 5, and Bardet-Biedl syndrome type 14 (BBS14) [11]. Cep290 is a satellite protein that localizes at the transition zone between basal body and cilia [8]. Recently, it has been reported that Cep290 plays a role in the ciliary transport process and is associated with several satellite proteins. For example, loss of centriolar satellites in PCM-1 depleted cells led to relocalization of Cep290 from satellites to the centrosome [12]. Another satellite proteins such as SSX2IP and NPHP5 promote the ciliary entry of the BBSome and the BBSome integrity together with Cep290 [13,14]. Moreover, depletion of Cep290 results in the redistribution of centriolar satellites around the centrosome. It also has been suggested that CEP290 may form complexes with several MT-based transport proteins.

Despite the fact that Cep290 is a protein that localizes at the centrosome, its function through mitosis is unclear. Interestingly, we identified Cep290 as an interacting partner with DDA3 through proteomic analysis by mass spectrometry. DDA3 is known as a novel MAP that is highly phosphorylated in mitotic cells and acts as MT-destabilizing factor and controls spindle dynamics [15]. Further, DDA3 controls chromosome congression via interaction with MCAK [16]. Based on this information, we hypothesized that Cep290 may have functions in mitosis via interaction with DDA3 and spindle MTs. Here, we confirmed the functions of Cep290 in the mitotic process. We demonstrated that Cep290 localizes at the centrosome, and the depletion of Cep290 protein causes several defects such as asymmetric spindle and decrease of astral spindle during mitosis. Moreover, DDA3 regulates the stability and the localization of Cep290 by their interaction. We concluded that DDA3 transports Cep290 into the centrosome to regulate astral spindle formation and spindle orientation.

2. Materials and methods

2.1. Chemicals and antibodies

Antibodies against Plk1, Cyclin B1, Hsp 90, p38MAPK, and Myc were purchased from Santa Cruz Biotechnology (USA). Antibodies against Centrin, TPX2, and γ-tubulin were purchased from Abcam (USA), GeneTex (USA), and Sigma (USA), respectively. Rabbit antibodies against DDA3 and GFP were described previously [15,17].


A
siCep290-1
siCep290-2
siControl
Cep290
HSP90
B
siControl
0
12
18
27
39
45
min
siCep290
0
12
18
36
66
75
81
min
0
12
30
54
96
138
min
C
Cep290
β-Tubulin
DAPI
Merge
siControl
siCep290-1
siCep290-2
Spindle intensity (AU)
1.2
1
0.8
0.6
0.4
0.2
0
siControl
siCep290
*
**
Spindle
Astral spindle
D
TPX2
β-Tubulin
DAPI
Merge
siControl
siDDA3
Spindle intensity (AU)
1.2
1
0.8
0.6
0.4
0.2
0
*
siControl
siDDA3
E
β-Tubulin
DAPI
Merge
0 min
9 min
siControl
siCep290

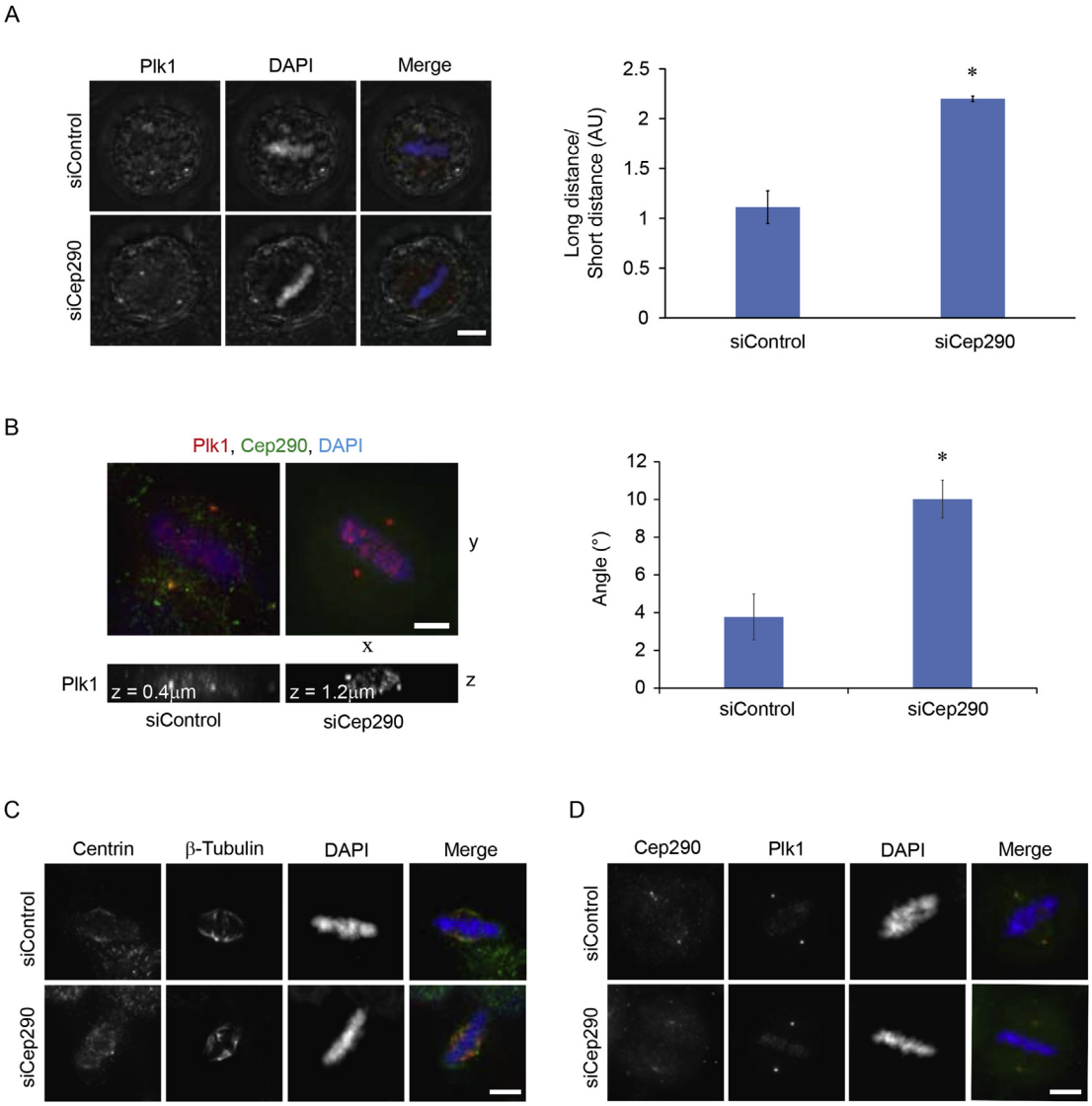


Fig. 3. Cep290 controls spindle positioning. (A) HeLa cells were transfected with a siControl or siCep290. Images are maximum projections from z stacks of representative cells stained for Plk1 (red) and DNA (blue). The distance between pole and cortex was measured. Then, the ratio between two pole-to-cortex distances was calculated and plotted. Error bars show SEM. *, $p < 1.33762 \times 10^{-5}$. (B) Images are maximum projections from z stacks of representative cells stained for Cep290 (green), Plk1 (red), and DNA (blue). The angles between the axis crossing the two poles of metaphase spindles and the cover slip were measured. Error bars show SEM. *, $p < 0.000386$. (C and D) Images are maximum projections from z stacks of representative cells stained for Centrin or Cep290 (green), β-tubulin or Plk1 (red), and DNA (blue). AU, arbitrary units. Scale bars, 5 μm. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Anti-β-tubulin E7 monoclonal antibody was obtained from the Developmental Studies Hybridoma Bank (USA).

2.2. Cell culture and transfection

HeLa cells were cultured in Dulbecco's Modified Eagle's medium (DMEM, WelGENE Inc.) supplemented with 10% fetal bovine serum (FBS, Invitrogen), penicillin (100 units/mL), and 100 μg/mL streptomycin (Invitrogen). The cells were maintained at 37 °C in a humidified atmosphere containing 5% CO_2. siRNAs were synthesized by Bioneer, Inc. (South Korea). The sequence targeting Wip1 (siCep290-1 and siCep290-2) was 5′-CUAAGUACAGGGACAUCUU-3′ and 5′-CACUUACGGACUUCGUUAAUU-3′. The control siRNA (siGL2) was 5′-CGTACGCGGAATACTTCGATT-3′. siRNAs were transfected

Fig. 2. Cep290 is involved in astral spindle formation. (A) HeLa cells were transfected with control (siControl) or Cep290-specific siRNAs (siCep290-1 and siCep290-2). Cells were harvested at 72 h post-transfection and lysates were analyzed by Western blotting against the indicated antibodies. (B) HeLa/GFP-Histone H2B cells were transfected with siRNAs and imaged for GFP-Histone H2B by time lapse starting from 60 h after transfection. Images were captured every 3 min to monitor mitotic progression. (C) HeLa cells were transfected with a siControl or siCep290. Images for β-tubulin were acquired under a constant exposure time. β-tubulin immunofluorescence intensity on spindles was quantified and normalized to control sample ($n = 10$ cells for each quantification). *, $p < 0.025736$; **, $p < 0.00049$ (two-tailed t test relative to control cells). Error bars, SEM. (D) 72 h after siRNA transfection, HeLa cells were fixed with MeOH and stained with antibodies as indicated. Images, which were acquired under a constant exposure time, are maximum projections from z stacks of representative cells stained for TPX2 (green), β-tubulin (red), and DNA (blue). β-tubulin immunofluorescence intensity on astral spindles was quantified and normalized to control sample ($n = 10$ cells for each quantification). *, $p < 0.000256$ (two-tailed t test relative to control cells). Error bars, SEM. (E) HeLa cells were transfected with a siControl or siCep290. Control or Cep290-depleted cells were treated with 1 μg/ml nocodazole for 3 min, released to fresh media for 9 min, fixed with MeOH, and analyzed by immunofluorescence staining of β-tubulin. AU, arbitrary units. Scale bars, 5 μm. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

into HeLa cells using DharmaFect 1 (Dharmacon, Inc.). DNA transfection was performed using Lipofectamine 2000 (Invitrogen, USA) as instructed by the manufacturer.

2.3. Immunofluoresence

HeLa cells on coverglasses were fixed with methanol at −20 °C for 30 min. Alternatively, cells were extracted with the BRB80-T buffer (80 mM PIPES, pH 6.8, 1 mM $MgCl_2$, 5 mM EGTA, and 0.5% Triton X-100) and fixed with 4% paraformaldehyde for 15 min at room temperature (Fig. 1B). The fixed cells were then permeabilized and blocked with PBS-BT (1 × PBS, 3% BSA, and 0.1% Triton X-100) for 30 min at room temperature. Coverslips were then incubated in primary and secondary antibodies diluted in PBS-BT. Images were acquired using an LSM image examiner (Carl Zeiss, Germany) under a Zeiss LSM510 confocal microscope and 63× oil immersion lens. Alternatively, images were acquired with AxioVision 4.8.2 (Carl Zeiss) under a Zeiss Axiovert 200 M microscope using a 1.4 NA plan-Apo 100× oil immersion lens and a HRm CCD camera. Deconvolved images were obtained using AutoDeblur v9.1 and AutoVisualizer v9.1 (AutoQuant Imaging).

2.4. Live cell image

For time-lapse microscopy, HeLa cells stably expressing GFP-H2B were cultured in Leibovitz's L-15 medium (Invitrogen) supplemented with 10% fetal bovine serum (Invitrogen) and 2 mM L-glutamine (Invitrogen). Cells were placed into a sealed growth chamber heated to 37 °C and observed on a Zeiss Axiovert 200 M microscope with a 20× lens. Images were acquired every 3 min for 5 h with AxioVision 4.8.2 (Carl Zeiss).

3. Results and disscussion

3.1. Cep290 interacts with DDA3 and localizes in centrosome during mitosis

When the DDA3 complex was purified from mitotic cells synchronized by thymidine-nocodazole treatment [15], Cep290 was identified as a DDA3 interacting partner during mitosis through mass spectrometry analysis (Fig. 1A). To confirm this interaction, HeLa cells stably expressing GFP or GFP-DDA3 were arrested at prometaphase by treating with thymidine-nocodazole, released into drug-free media and mitotic cells were harvested at the indicated time. We confirmed that the expression level of Cep290 was increased and strongly interacted with DDA3 in early mitosis (Fig. 1B). To investigate mitotic function of Cep290 as an interacting partner with DDA3, we determined the localization of Cep290 in mitotic cells. Throughout the cell cycle, including mitosis, Cep290 localizes in the centrosome (Fig. 1C). Interestingly, Cep290 also localized at the midbody in telophase, suggesting that Cep290 also appears to be involved in cytokinesis. To further analyze the relationship between Cep290 and DDA3 in early mitosis, HeLa cells were transfected with myc-DDA3 and observed by microscope. Cep290 and DDA3 co-localized around the centrosome in prometaphase and metaphase (Fig. 1D), suggesting that DDA3 and Cep290 cooperate with each other around the centrosome in early mitosis.

3.2. Cep290 regulates astral spindle formation

To investigate the function of Cep290 in mitosis, we depleted Cep290 protein with siRNA in HeLa cells (Fig. 2A). We took advantage of HeLa cells stably expressing GFP-H2B to analyze mitotic defects in the absence of Cep290 protein via live cell image. Depletion of Cep290 caused mitotic catastrophe in prometaphase (about 40% within mitotic cells), suggesting that Cep290 might be involved in centrosome maturation and bipolar spindle formation as a centrosomal protein. In contrast, some cells showed normal mitotic progression without any alteration (Fig. 2B), suggesting that residual levels of Cep290 are enough for mitotic progression. Interestingly, Cep290-depletion decreased the amount of spindle and astral spindle in metaphase cells (Fig. 2C). Previously, it has been reported that depletion of DDA3 caused chromosome misalignment and spindle hyper-stabilization [15]. Therefore, we asked whether DDA3-depletion also affects astral spindle formation. Even though the mitotic spindles are stabilized and increased, the amount of astral spindle was decreased in DDA3-depleted cells (Fig. 2D). Next, we determined whether Cep290 is involved in spindle polymerization. As expected, Cep290-depleted cells showed slower MT regrowth than control cells (Fig. 2E), indicating that Cep290 participates in spindle nucleation and polymerization. These data suggest that Cep290 and DDA3 control astral spindle formation and MT nucleation from the centrosome.

3.3. Cep290 controls spindle positioning

Because the function of astral spindle is to fix the centrosome to the cortex, we confirmed the spindle orientation in Cep290-depleted cells. Cep290-depletion caused asymmetric cortical distribution because two distances between spindle pole and adjacent cortex in each Cep290-depleted cell were different (Fig. 3A). Moreover, the angle between the axis of the metaphase spindle and that of the plate surface was increased by two-fold in Cep290-depleted cells. To determine whether Cep290-depletion caused mislocalization of centrosomal proteins, we checked their localization. Depletion of Cep290 with siRNA did not significantly alter the amount of centrosomal proteins such as Centrin and Plk1 in centrosomes (Fig. 3C and D), but the metaphase spindles were misoriented in Cep290-depleted cells compared to control cells. Taken together, we concluded that Cep290 might be involved in spindle positioning upon its function in astral spindle formation.

3.4. DDA3 stabilizes and targets Cep290 to the centrosome

Next, we investigated the functional relation between Cep290 and DDA3. At first, we confirmed the localization of DDA3 in Cep290-depleted cells. The level of DDA3 on the mitotic spindle did not change in Cep290-depleted cells (Fig. 4A). Also, we confirmed the localization of Cep290 after transfection of DDA3 siRNA in the centrosome. Consistent with previous data [15], the level of γ-tubulin was not changed by DDA3-depletion. Interestingly, the level of Cep290 protein was substantially decreased in DDA3-depleted cells (Fig. 4B), indicating that DDA3 stabilizes Cep290 protein. Furthermore, Cep290 was also dramatically decreased in the centrosome in DDA3-depleted cells (Fig. 4C). Therefore, we tested whether DDA3 regulates the targeting of Cep290 into the centrosome as well as the stability of Cep290. Even though the Cep290 was not increased by ectopic expression of Myc-DDA3 (Fig. 4D), its protein levels were increased in the centrosome (Fig. 4E). These data indicate that DDA3 is involved in the movement of Cep290 into the centrosome. We concluded that DDA3 controls the stability and the transport of Cep290 into the centrosome to regulate astral spindle formation and spindle positioning in mitosis.

Cep290 localizes at the basal body, centrosome, and satellites, and participates in cilia formation. In accordance with previous reports, PCM-1 and MTs are tightly associated with the localization of Cep290 [13]. When MTs were disrupted by nocodazole treatment in hTERT-RPE cells, the localization of Cep290 at satellites substantially decreased [18]. Moreover, Cep290 relocalized from

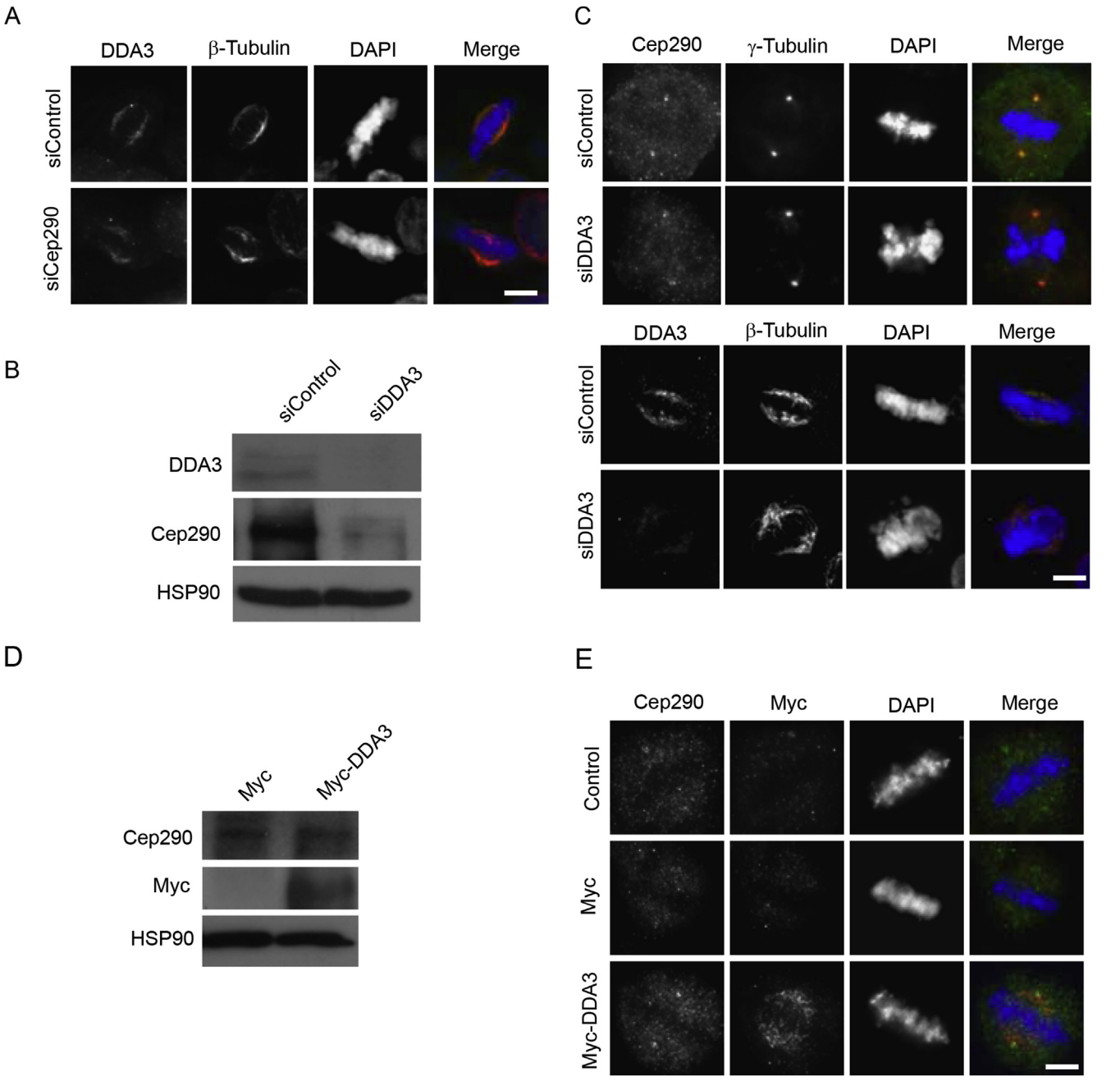


Fig. 4. DDA3 controls the stability and the localization of Cep290. (A) HeLa cells were transfected with a siControl or siCep290. Images are maximum projections from z stacks of representative cells stained for DDA3 (green), β-tubulin (red), and DNA (blue). (B and C) HeLa cells were transfected with a siControl or siDDA3. Cells were harvested at 72 h post-transfection and lysates were analyzed by Western blotting against the indicated antibodies. The cells were fixed with MeOH and stained with antibodies as indicated. Images are maximum projections from z stacks of representative cells that were stained for Cep290 or DDA3 (green), γ-tubulin or β-tubulin (red), and DNA (blue). (D and E) HeLa cells were transfected with a Myc or Myc-DDA3 plasmid. Cells were harvested at 28 h post-transfection and lysates were analyzed by Western blotting against the indicated antibodies. The cells were fixed with MeOH and stained with antibodies as indicated. Images are maximum projections from z stacks of representative cells that were stained for Cep290 (green), Myc (red), and DNA (blue). Scale bars, 5 μm. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

satellites to the centrosome in PCM-1 depleted cells [12]. In this study, we elucidated the function of Cep290 in mitosis as a centrosomal protein and the relationship between DDA3 and Cep290. DDA3 interacts with Cep290 in early mitosis to stabilize and target Cep290 into centrosome for proper astral spindle formation and spindle positioning. Thus, the interaction between Cep290 and DDA3 play an important role in spindle positioning during mitosis.

During mitosis, depletion of γ-TuRCs causes the defects in spindle positioning because it regulates the stability of astral MTs and the interaction between the cortex and astral MTs [5]. However, centrosomal proteins including γ-tubulin were not altered in Cep290-or DDA3-depleted cells (Fig. 3C, D, and 4C), suggesting that Cep290 and DDA3 are not involved in γ-TuRC formation. However, Cep290-knockdown induced several defects such as a reduction of the astral spindle and spindle density, and misorientation of the spindle (Figs. 2 and 3). It has been reported that Cep290 is a component of the MT-membrane linkages in the transition zone [19]. Therefore, it is a possibility that misorientation in Cep290-knockdown condition might be caused by a weakened interaction between MT and membrane.

In summary, we demonstrated that DDA3 interacts with Cep290 during early mitosis and targets it into centrosome. Furthermore, Cep290 functions as a centrosomal protein to control astral spindle formation by regulating MT polymerization. Our novel data clearly shows that the interaction between DDA3 and Cep290 is essential for spindle orientation and spindle positioning during mitosis. However, the molecular mechanism explaining how Cep290 control MT polymerization and spindle orientation in the centrosome remains to be elucidated.

Conflict of interest

None.

Acknowledgments

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIP) (2011-0030074) and the Sookmyung Women's University Research Grants (1-1303-0219).

Transparency document

Transparency document related to this article can be found online at http://dx.doi.org/10.1016/j.bbrc.2015.05.028.

References

[1] S.L. Kline-Smith, C.E. Walczak, Mitotic spindle assembly and chromosome segregation: refocusing on microtubule dynamics, Mol. Cell. 15 (2004) 317–327.
[2] F. Barenz, D. Mayilo, O.J. Gruss, Centriolar satellites: busy orbits around the centrosome, Eur. J. Cell Biol. 90 (2011) 983–989.
[3] A. Desai, T.J. Mitchison, Microtubule polymerization dynamics, Annu Rev. Cell. Dev. Biol. 13 (1997) 83–117.
[4] F. Barenz, D. Inoue, H. Yokoyama, J. Tegha-Dunghu, S. Freiss, S. Draeger, D. Mayilo, I. Cado, S. Merker, M. Klinger, B. Hoeckendorf, S. Pilz, K. Hupfeld, H. Steinbeisser, H. Lorenz, T. Ruppert, J. Wittbrodt, O.J. Gruss, The centriolar satellite protein SSX2IP promotes centrosome maturation, J. Cell Biol. 202 (2013) 81–95.
[5] A. Bouissou, C. Verollet, H. de Forges, L. Haren, Y. Bellaiche, F. Perez, A. Merdes, B. Raynaud-Messina, gamma-tubulin ring complexes and EB1 play antagonistic roles in microtubule dynamics and spindle positioning, EMBO J. 33 (2014) 114–128.
[6] C.J. Staples, K.N. Myers, R.D.D. Beveridge, A.A. Patil, A.J.X. Lee, C. Swanton, M. Howell, S.J. Boulton, S.J. Collis, The centriolar satellite protein Cep131 is important for genome stability, J. Cell Sci. 125 (2012) 4770–4779.
[7] H. Jin, S.R. White, T. Shida, S. Schulz, M. Aguiar, S.P. Gygi, J.F. Bazan, M.V. Nachury, The conserved bardet-biedl syndrome proteins assemble a coat that traffics membrane proteins to cilia, Cell 141 (2010), 1208–U1198.
[8] A. Kumar, V. Rajendran, R. Sethumadhavan, R. Purohit, CEP proteins: the knights of centrosome dynasty, Protoplasma 250 (2013) 965–983.
[9] W.M. Zhao, A. Seki, G.W. Fang, Cep55, a microtubule-bundling protein, associates with centralspindlin to control the midbody integrity and cell abscission during cytokinesis, Mol. Biol. Cell 17 (2006) 3881–3896.
[10] J.Q. Tao, X.F. Zhi, Y. Tian, Z. Li, Y. Zhu, W.Z. Wang, K.L. Xie, J. Tang, X.Y. Zhang, L.J. Wang, Z.K. Xu, CEP55 contributes to human gastric carcinoma by regulating cell proliferation, Tumor Biol. 35 (2014) 4389–4399.
[11] L. Wang, Y. Yang, J. Song, L. Mao, X. Wei, Y. Sun, S. Yang, F. Mu, H. Wang, Y. Niu, Two novel mutations in the C-terminal region of centrosomal protein 290 (CEP290) result in classic joubert syndrome, J. Child. Neurol. 30 (2015) 772–776.
[12] T.R. Stowe, C.J. Wilkinson, A. Iqbal, T. Stearns, The centriolar satellite proteins Cep72 and Cep290 interact and are required for recruitment of BBS proteins to the cilium, Mol. Biol. Cell 23 (2012) 3322–3335.
[13] J. Kim, S.R. Krishnaswami, J.G. Gleeson, CEP290 interacts with the centriolar satellite component PCM-1 and is required for Rab8 localization to the primary cilium, Hum. Mol. Genet. 17 (2008) 3796–3805.
[14] M. Barbelanne, D. Hossain, D.P. Chan, J. Peranen, W.Y. Tsang, Nephrocystin proteins NPHP5 and Cep290 regulate BBSome integrity, ciliary trafficking and cargo delivery, Hum. Mol. Genet. 24 (2015) 2185–2200.
[15] C.Y. Jang, J. Wong, J.A. Coppinger, A. Seki, J.R. Yates, G.W. Fang, DDA3 recruits microtubule depolymerase Kif2a to spindle poles and controls spindle dynamics and mitotic chromosome movement, J. Cell Biol. 181 (2008) 255–267.
[16] C.Y. Jang, G.W. Fang, DDA3 associates with MCAK and controls chromosome congression, Biochem. Biophys. Res. Commun. 407 (2011) 610–614.
[17] J. Wong, G.W. Fang, HURP controls spindle dynamics to promote proper interkinetochore tension and efficient kinetochore capture, J. Cell Biol. 173 (2006) 879–891.
[18] M. Klinger, W.B. Wang, S. Kuhns, F. Barenz, S. Drager-Meurer, G. Pereira, O.J. Gruss, The novel centriolar satellite protein SSX2IP targets Cep290 to the ciliary transition zone, Mol. Biol. Cell 25 (2014) 495–507.
[19] B. Craige, C.C. Tsao, D.R. Diener, Y.Q. Hou, K.F. Lechtreck, J.L. Rosenbaum, G.B. Witman, CEP290 tethers flagellar transition zone microtubules to the membrane and regulates flagellar protein content, J. Cell Biol. 190 (2010) 927–940.