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CLINICAL REPORT

A novel *CEP57* variant associated with mosaic variegated aneuploidy syndrome in a Chinese female presenting with short stature, microcephaly, brachydactyly, and small teeth

Biyun Feng[1,2] | **Guoying Chang**[1,2] | **Qianwen Zhang**[1,2] | **Xin Li**[1,2] | **Yijun Tang**[1,2] | **Shili Gu**[1,2] | **Yirou Wang**[1,2] | **Jian Wang**[3] | **Xiumin Wang**[1,2]

[1]Department of Endocrinology and Metabolism, Shanghai Children's Medical Center, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

[2]Center for Brain Science, Shanghai Children's Medical Center, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

[3]Department of Medical Genetics and Molecular Diagnostic Laboratory, Shanghai Children's Medical Center, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

Correspondence
Xiumin Wang, Department of Endocrinology and Metabolism, Shanghai Children's Medical Center, School of Medicine, Shanghai Jiao Tong University, Shanghai, China.
Email: wangxiumin1019@126.com

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Abstract

Background: Mosaic variegated aneuploidy (MVA) syndrome is a rare, autosomal recessive genetic disease. Here, we report an ultra-rare case of MVA syndrome associated with a *CEP57* variant.

Methods: We retrospectively analyzed the clinical data of a 9-year-old female patient and surveyed her family members. Whole-exome sequencing and karyotype analysis were performed; suspected mutations were verified using Sanger sequencing.

Results: The patient presented with intrauterine growth restriction, short stature, microcephaly, facial dysmorphism, brachydactyly, and small teeth, and she showed unsatisfactory response to GH replacement therapy. Laboratory tests revealed high insulin-like growth factor-1 levels. Karyotype analysis of the peripheral blood showed mosaic variegated aneuploidies. Whole-exome and Sanger sequencing revealed a novel homozygous nonsense variant, NM_014679.4: c.312T>G, in *CEP57* that leads to translation termination (p.Tyr104*). The parents were heterozygous carriers of the identified variant.

Conclusion: This study presents an ultra-rare case of *CEP57*-driven MVA syndrome, identifying a novel homozygous nonsense variant of *CEP57* (p.Tyr104*). Our findings enrich the *CEP57* mutational spectrum and emphasize the importance of genetic testing in patients with microcephaly and short stature. Furthermore, we conclude that growth hormone treatment is ineffective in such patients.

KEYWORDS

CEP57, microcephaly, mosaic variegated aneuploidy (MVA), short stature, whole-exome sequencing

Biyun Feng and Guoying Chang contributed equally to this work.

1 | INTRODUCTION

Mosaic variegated aneuploidy (MVA) syndrome is a rare autosomal recessive disorder characterized by chimeric aneuploidy with trisomy and monosomy in different chromosomes and tissues (Hanks et al., 2004). The clinical manifestations of MVA include intrauterine growth restriction, developmental delay, microcephaly, facial anomalies, and intellectual disability. Additionally, this disease could be associated with susceptibility to different tumors, particularly leukemia, Wilms tumor, and rhabdomyosarcoma (Brightman et al., 2018; Pinson et al., 2014).

Mutations in *BUB1B* (MIM#257300), *CEP57* (MIM#614114), and *TRIP13* (MIM#617598) cause MVA1, MVA2, and MVA3, respectively. *BUB1B* is involved in the formation of spindle assembly checkpoints (SAC), whereas the *TRIP13* gene plays a role in maintaining SAC activity. The *CEP57* gene is located on chromosome 11q21, contains 11 exons and encodes a 500-amino acid protein. The CEP57 protein plays an important role in centrosomal localization and microtubular stabilization during mitosis. It has been reported that the *CEP57* gene is closely associated with skeletal development and tumor suppression (Aziz et al., 2018). Mutations in the *CEP57* gene can cause MVA2 with specific manifestations, including hypothyroidism, short limb ends, and congenital heart disease, which are not observed in MVA1 and MVA3 (Snape et al., 2011). To the best of our knowledge, only 12 cases of MVA2 have been reported to date. Here, we present the first report of such a case in China.

We describe a case of MVA2 caused by a homozygous variant of the *CEP57* gene, which was diagnosed via karyotype analysis and whole-exome sequencing. We further analyzed the phenotypes of all reported patients with *CEP57* variants and the therapeutic effect after growth hormone (GH) replacement therapy. Based on these findings, we propose the significance of genetic testing in patients with microcephaly and short stature.

2 | MATERIALS AND METHODS

2.1 | Patients

A 9-year-old girl presented with short stature, microcephaly, facial dysmorphism, congenital heart disease, and brachydactyly was referred to the Department of Endocrinology and Metabolism at Shanghai Children's Medical Center. Physical examination, survey of the family members, laboratory investigations, and x-ray and magnetic resonance imaging (MRI) were conducted.

2.2 | Chromosome analysis

Lymphocytes were isolated from the patient's peripheral blood for cell culture, hypotonic treatment, and fixation. Appropriate specimens were selected for slide preparation, Giemsa staining, and chromosome banding.

2.3 | Whole-exome sequencing

WES was performed to make a clear clinical diagnose. Two milliliters of peripheral blood was collected from the patient and her parents. Blood was stored in ethylenediaminetetraacetic acid anticoagulant tubes for examination. Exons were captured using the Agilent Sureselect method. High-throughput sequencing was performed using the Illumina sequencing platform, sequencing data were matched and analyzed using the NextGENe software, and variation filtering and interpretation were performed using the Ingenuity online software system.

3 | RESULTS

The proband, a 9-year-old Chinese female, was the second child of non-consanguineous parents. She was born via a cesarean section at 37 weeks, with a birth length of 45 cm (−2.82 SD) and birth weight of 2500 g (−2.14 SD). After birth, she experienced recurrent respiratory infections, which improved after 3 years of age. Her psychomotor development was normal. All of her family members were healthy. The heights of her father, mother, and 15-year-old sister were 172 cm (−0.11 SD), 155 cm (−1.04 SD), and 164 cm (+0.76 SD), respectively.

Growth retardation was observed after 2 years of age. She was treated with GH in a local hospital from 2 to 9 years of age for short stature. The drug dose was 0.15–0.17 $U \cdot kg^{-1} \cdot d^{-1}$. Her height increase velocity was 6–10 cm per year. GH therapy was withdrawn intermittently for a total of 1 year because of high levels of insulin-like growth factor 1 (IGF-1) when she was 6–7 years old. During this period, her height velocity was 4–6 cm per year. Blood glucose, HbA1c, and cancer biomarker levels were within the normal ranges. Her IGF-1 level was 599 ng/ml (+3 SD) at the last follow-up. Brain MRI revealed a small pituitary without other abnormal signs. Her bone age was approximately 10 years, whereas her current age was 9 years (Figure 1).

At the age of 5, echocardiography revealed a patent ductus arteriosus, and thus the patient underwent careful observation by a cardiovascular pediatrician.

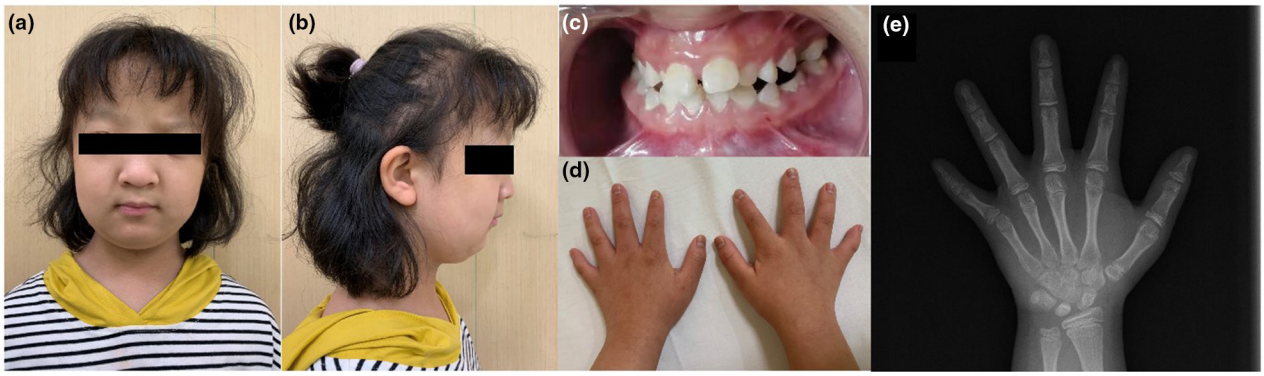
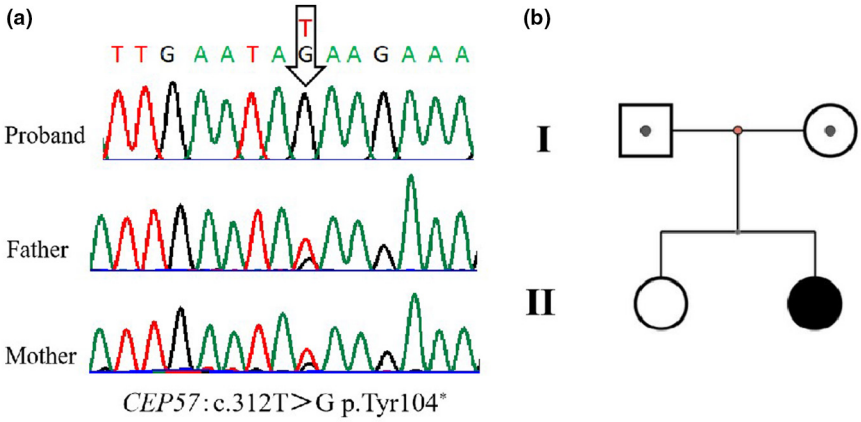


FIGURE 1 Image of the patient. (a, b) Facial abnormalities included long face, large forehead, facial asymmetry, low-set ears, wide nasal bridge and nasal tip, small mandible and retrognathia. (c) Small and sparse teeth (d) Short fingers. (e) X-ray of the left hand

FIGURE 2 (a) Sanger sequencing indicated a novel homozygous nonsense mutation (c.312T>G, p.Tyr104* in exon 3) in the patient. Both the parents carried heterozygous variants at this locus. Black arrow shows mutant base. (b) The family tree



The most recent examination revealed severe growth retardation with microcephaly. Her height was 121 cm (−2.35 SD) and her weight was 27.35 kg (−0.26 SD), with a head circumference of 46 cm (< −3 SD). She presented with dysmorphic features, including a long face, large forehead, facial asymmetry, low-set ears, wide nasal bridge and nasal tip, small mandible, and retrognathia. Her teeth were small after replacement of massive saprodontia and her fingers were short (Figure 1).

WES revealed a c.312T > G mutation in the *CEP57* gene (NM_014679.4), a novel homozygous variant that leads to the termination of protein translation (p.Tyr104*). This mutation could not be found in gnomAD and ClinVar database but is classified as likely pathogenic according to the guidelines recommended by the American College of Medical Genetics and Genomics (ACMG). This variant of *CEP57* is believed to cause MVA2 and no other causative genes were found through WES. Sanger sequencing indicated that both of the patient's parents were heterozygous carriers of the identified variant (Figure 2).

Chromosomal analysis revealed a normal female karyotype. Based on the WES results, we performed a re-review of the karyotypes. The results suggested that 79 of 100 cells were 46,XX, whereas 21 cells showed aneuploidies. As the proportion of aneuploidy in all of the cases reported to date was more than 20%, our findings confirmed the diagnosis of MVA (Figure 3).

4 | DISCUSSION

Based on our review of 14 articles retrieved from PubMed, 12 cases of MVA2 caused by *CEP57* variants are summarized in Supplementary Table S1. These cases were identified in Mexico, the Caucasus, Morocco, and Pakistan (Santos-Simarro et al., 2021). To date, four *CEP57* variants have been reported to cause MVA2. The most common variant was c.915_925dup11, which was observed in 10 of the 12 cases, six from Morocco, three from Mexico, and one from the Caucasus. All reported variants were distributed in exons 3, 5, 7, and 9. Mutations in *CEP57* have not been reported in Chinese patients, here represents a Chinese female carrying a novel *CEP57* variant c.312T > G (p.Tyr104*, in exon 3), which was classified as a likely pathogenic variant (PVS1 + PM2) according to ACMG guidelines.

CEP57 encodes a 500-amino acid protein, whose secondary structure comprises two α-helical coiled-coil

domains connected by a flexible linker region. The N-terminal region plays a role in the localization of *CEP57* to the centrosome and in the multimerization of the protein. The C-terminus of *CEP57* participates in nucleating, bundling, and anchoring microtubules to the centrosomes within basket-like structures (Snape et al., 2011). The variant c.312T>G (p.Tyr104*) in exon 3 is located on the N-terminal coiled-coil domain, which functions as a centrosome localization domain (Figure 4). The CEP family protein is the active component of the centrosome, constituting pericentriolar material and stabilizing the spindle poles and microtubule (Wu et al., 2012). *CEP57* has also been reported to play an important role in mitosis by interacting with MAD1-MAD2 (components of SAC) and activating SAC, thus ensuring correct chromosome segregation (Zhou et al., 2016) and explaining the aneuploidies found in MVA syndrome.

The clinical manifestations and genetic features of previously reported patients and the present case are summarized in Table 1. More detailed information is showed in Supplementary Table S1. The proband exhibited typical features of MVA syndrome, including facial anomalies, short stature, intrauterine growth restriction, microcephaly, brachydactyly, small teeth, congenital heart disease, and recurrent infections. Intellectual disability was not observed in the present case. Among the six reported patients with intellectual disability, five had a homozygous variant (c.915_925dup11) of the *CEP57* gene, and we speculated that this phenotype might be related to a specific variant site (Dery et al., 2020). Congenital heart diseases (7/11) and vascular malformations (5/12) were existed in approximately half of the patients, while the proband only presented with PDA. Facial features like long face, large forehead, facial asymmetry, low-set ears, wide nasal bridge and nasal tip, small mandible and retrognathia were observed as described in the literature. Microcephaly accounts for 5/12 while 3/12 showed macrocephaly or relative macrocephaly. The variant of fibroblast growth factor 2 (FGF2) is observed in 32% of patients with craniosynostosis, and CEP57 acts as an FGF2 partner. In addition, CEP57 constitutes part of the CEP57-CEP63-CEP152 centrosomal complex, while CEP152 is associated with MCPH9. Based on these facts, *CEP57* may be implicated in the pathogenesis of microcephaly (Lukinavičius et al., 2013). Small teeth seemed to be an uncommon feature, which was only seen in a pair of Moroccon brothers (Dery et al., 2020).

An increased risk of childhood malignancies was observed in MVA1 and MVA3 patients. Mutations in the *BUB1B* and *TRIP13* genes influence the function of the SAC, causing MVA1 and MVA3, which are both strongly associated with cancers such as gastrointestinal neoplasm, rhabdomyosarcoma, and Wilms tumor (Hanks et al., 2004; Rio Frio et al., 2010; Yost et al., 2017). It has been reported that haploinsufficiency caused by the *CEP57* variant impairs tumor suppression (Aziz et al., 2018). However, none of the reported patients with the *CEP57* variant developed malignancy, similarly to our patient (Table 2). Further studies are needed to determine the correlation between *CEP57* variants and tumorigenesis.

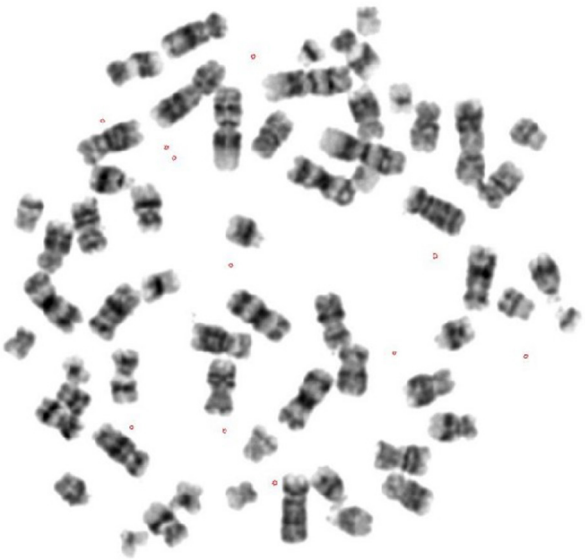


FIGURE 3 One of the 21 abnormal karyotype, showing 59,XX,-2,+3,-4,+5,-6,+8,-9,-11,-13,-15,-16,-17,-19,- 20,-21

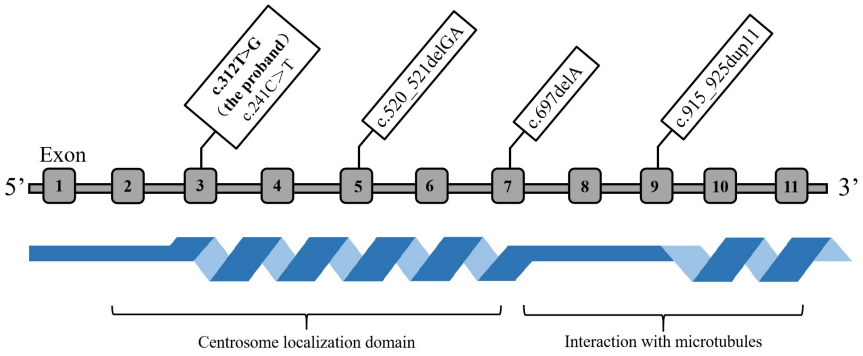


FIGURE 4 The schematic diagram of the distribution of reported mutations and c.312T>G (the proband) in CEP57 gene as well as protein pattern diagram encoded by CEP57 gene

TABLE 1 Clinical and genetic features of the patient and reported MVA2 patients with mutations in CEP57

	Previous reports	The proband	Total
Age	3wk ~ 29y	9 y	3 wk ~ 29 y
Sex	Male(*9), Female(*3)	Female	Male(*9), Female(*4)
Ethnicity	Mexico(*3), Caucasian(*2), Morocco(*6), Pakistan(*1)	China(*1)	/
Intellectual disability	6/10	−	6/11
IUGR	10/12	+	11/13
Growth retardation	12/12	+	13/13
Microcephaly	5/11	+	6/12
Cardiac anomalies	7/11	+	8/12
Facial dysmorphism			
Skull anomalies	11/11	+	12/12
Deep set eyes	7/9	−	7/10
Ears anomalies	8/9	−	8/10
Micrognatia	9/9	+	10/10
Rhizomelic shortening/Short fingers	10/12	+	11/13
Single palmar crease/clinodactyly	7/7	−	7/8
Cancer	0/12	−	0/13
Mosaic Aneuploidy	12/12	+	13/13
Double gene mutation	1/12	−	1/13

Abbreviations: IUGR, intrauterine growth restriction; *7 7 cases; wk, week; y, year.

TABLE 2 Characteristics of MVA caused by different genes

	BUB1B	CEP57	TRIP13
Syndrome	MVA1	MVA2	MVA3
Function	Composing SAC	Locating to the centrosome; bundling and anchoring microtubules; activating SAC	Maintaining the activity of SAC
Age	Birth~68 y	3 wk ~ 29 y	2.5 y ~ 43 y
Tumor type	Liver cancer Prostate cancer Rhabdomyosarcoma Leukemia	None reported	Wilms tumor

Abbreviations: SAC, spindle assembly checkpoint; MVA, mosaic variegated aneuploid.

All patients harboring *CEP57* variants presented with growth retardation, including our case. The proband had been treated with GH since 2 years of age. Brain MRI showed a small pituitary. Her height velocity increased initially, but a secondary decrease was subsequently observed, and her height was still <P3 at age 9, despite high levels of IGF-1. She also had short fingers. *CEP57* is essential for the nuclear translocation of FGF2, a key modulator of ossification, which may explain the skeletal manifestations mentioned above (Meunier et al., 2009). Similarly, four patients treated with GH while none of them responded to GH replacement therapy persistently. One Moroccan patient only showed short-term response to GH. This is probably because variants of *CEP57* are closely associated with skeletal development, even long-term GH treatment did not improve adult height (Aziz et al., 2018).

Diagnosis of MVA syndrome depends on the typical presentation and genetic testing. WES revealed a novel homozygous variant of the *CEP57* gene, which was reported to cause aneuploidy, in contrast to our initial karyotype outcome. Similar to a patient described in the literature who had a normal karyotype but five of 22 cells suggested aneuploidy after reanalysis (Brightman et al., 2018), 21 of 100 cells of our patient displayed aneuploidy upon secondary analysis. This may be attributed to selection bias

during chromosomal analysis. In addition, some studies have proposed that patients with a mild phenotype may have a low proportion of aneuploidy, these patient may therefore be underdiagnosed (Callier et al., 2005). For this reason, genetic testing like WES is a key to the diagnosis of patients with severe short stature, microcephaly, and classical features of MVA. Chromosome analysis can be used to confirm the diagnosis.

In conclusion, we report a novel homozygous nonsense variant of *CEP57* related to MVA 2 syndrome. Compared to previously reported 12 cases, our case showed facial anomalies, pre and postnatal growth retardation, microcephaly, brachydactyly, and PDA without severe phenotype like intellectual disability, vascular malformations, and other endocrine abnormalities. Mild phenotype relates to a low proportion of aneuploidy, thus a re-review of the karyotype is necessary. Genetic testing such as WES is recommended to reach a final diagnosis. GH therapy should be considered cautiously due to the poor response of long-term treatment and risk of cancer. The malignancy of MVA caused by the *CEP57* variant is hitherto unknown, and the links between *CEP57*, aneuploidy, and cancer need to be clarified in more cases and further studies.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICAL COMPLIANCE

The study was approved by the ethics committee of Shanghai Children's Medical Center, Shanghai Jiaotong University School of Medicine (Shanghai, China) (SCMCIRB-Y2019049) prior to molecular analysis. Careful counseling was provided to the patient and her parents to obtain informed consent.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Biyun Feng https://orcid.org/0000-0003-0828-3036
Qianwen Zhang https://orcid.org/0000-0001-8115-982X
Jian Wang https://orcid.org/0000-0003-3391-5250

REFERENCES

Aziz, K., Sieben, C. J., Jeganathan, K. B., Hamada, M., Davies, B. A., Velasco, R. O. F., Rahman, N., Katzmann, D. J., & van Deursen, J. M. (2018). Mosaic-variegated aneuploidy syndrome mutation or haploinsufficiency in Cep57 impairs tumor suppression. *Journal of Clinical Investigation*, *128*(8), 3517–3534. https://doi.org/10.1172/JCI120316

Brightman, D. S., Ejaz, S., & Dauber, A. (2018). Mosaic variegated aneuploidy syndrome caused by a CEP57 mutation diagnosed by whole exome sequencing. *Clinical Case Reports*, *6*(8), 1531–1534. https://doi.org/10.1002/ccr3.1655

Callier, P., Faivre, L., Cusin, V., Marle, N., Thauvin-Robinet, C., Sandre, D., Rousseau, T., Sagot, P., Lacombe, E., Faber, V., & Mugneret, F. (2005). Microcephaly is not mandatory for the diagnosis of mosaic variegated aneuploidy syndrome. *American Journal of Medical Genetics. Part A*, *137*(2), 204–207. https://doi.org/10.1002/ajmg.a.30783

Dery, T., Chatron, N., Alqahtani, A., Pugeat, M., Till, M., Edery, P., Sanlaville, D., Schluth-Bolard, C., Nicolino, M., Lesca, G., & Putoux, A. (2020). Follow-up of two adult brothers with homozygous CEP57 pathogenic variants expands the phenotype of mosaic variegated aneuploidy syndrome. *European Journal of Medical Genetics*, *63*(11), 104044. https://doi.org/10.1016/j.ejmg.2020.104044

Hanks, S., Coleman, K., Reid, S., Plaja, A., Firth, H., Fitzpatrick, D., Kidd, A., Méhes, K., Nash, R., Robin, N., Shannon, N., Tolmie, J., Swansbury, J., Irrthum, A., Douglas, J., & Rahman, N. (2004). Constitutional aneuploidy and cancer predisposition caused by biallelic mutations in BUB1B. *Nature Genetics*, *36*(11), 1159–1161. https://doi.org/10.1038/ng1449

Lukinavičius, G., Lavogina, D., Orpinell, M., Umezawa, K., Reymond, L., Garin, N., Gönczy, P., & Johnsson, K. (2013). Selective chemical crosslinking reveals a Cep57-Cep63-Cep152 centrosomal complex. *Current Biology*, *23*(3), 265–270. https://doi.org/10.1016/j.cub.2012.12.030

Meunier, S., Navarro, M. G., Bossard, C., Laurell, H., Touriol, C., Lacazette, E., & Prats, H. (2009). Pivotal role of translokin/CEP57 in the unconventional secretion versus nuclear translocation of FGF2. *Traffic*, *10*(12), 1765–1772. https://doi.org/10.1111/j.1600-0854.2009.00985.x

Pinson, L., Mannini, L., Willems, M., Cucco, F., Sirvent, N., Frebourg, T., Quarantotti, V., Collet, C., Schneider, A., Sarda, P., Geneviève, D., Puechberty, J., Lefort, G., & Musio, A. (2014). CEP57 mutation in a girl with mosaic variegated aneuploidy syndrome. *American Journal of Medical Genetics Part A*, *164*(1), 177–181. https://doi.org/10.1002/ajmg.a.36166

Rio Frio, T., Lavoie, J., Hamel, N., Geyer, F. C., Kushner, Y. B., Novak, D. J., Wark, L., Capelli, C., Reis-Filho, J. S., Mai, S., Pastinen, T., Tischkowitz, M. D., Marcus, V. A., & Foulkes, W. D. (2010). Homozygous BUB1B mutation and susceptibility to gastrointestinal neoplasia. *New England Journal of Medicine*, *363*(27), 2628–2637. https://doi.org/10.1056/NEJMoa1006565

Santos-Simarro, F., Pacio, M., Cueto-Gonzalez, A. M., Mansilla, E., Valenzuela-Palafoll, M. I., Lopez-Grondona, F., Lledín, M. D., Schuffelmann, C., Del Pozo, A., Solis, A., Vallcorba, P., Lapunzina, P., Suso, J. J. M., Siccha, S. M., Montejo, J. M., Mena, R., Jiménez-Rodríguez, C., García-Miñaúr, S., & Palomares-Bralo, M. (2021).

Mosaic variegated aneuploidy syndrome 2 caused by biallelic variants in CEP57, two new cases and review of the phenotype. *European Journal of Medical Genetics*, *64*(11), 104338. https://doi.org/10.1016/j.ejmg.2021.104338

Snape, K., Hanks, S., Ruark, E., Barros-Núñez, P., Elliott, A., Murray, A., Lane, A. H., Shannon, N., Callier, P., Chitayat, D., Clayton-Smith, J., FitzPatrick, D. R., Gisselsson, D., Jacquemont, S., Asakura-Hay, K., Micale, M. A., Tolmie, J., Turnpenny, P. D., Wright, M., ... Rahman, N. (2011). Mutations in CEP57 cause mosaic variegated aneuploidy syndrome. *Nature Genetics*, *43*(6), 527–529. https://doi.org/10.1038/ng.822

Wu, Q., He, R., Zhou, H., Yu, A. C., Zhang, B., Teng, J., & Chen, J. (2012). Cep57, a NEDD1-binding pericentriolar material component, is essential for spindle pole integrity. *Cell Research*, *22*(9), 1390–1401. https://doi.org/10.1038/cr.2012.61

Yost, S., de Wolf, B., Hanks, S., Zachariou, A., Marcozzi, C., Clarke, M., de Voer, R., Etemad, B., Uijttewaal, E., Ramsay, E., Wylie, H., Elliott, A., Picton, S., Smith, A., Smithson, S., Seal, S., Ruark, E., Houge, G., Pines, J., ... Rahman, N. (2017). Biallelic TRIP13 mutations predispose to Wilms tumor and chromosome missegregation. *Nature Genetics*, *49*(7), 1148–1151. https://doi.org/10.1038/ng.3883

Zhou, H., Wang, T., Zheng, T., Teng, J., & Chen, J. (2016). Cep57 is a Mis12-interacting kinetochore protein involved in kinetochore targeting of Mad1-Mad2. *Nature Communications*, *7*, 10151. https://doi.org/10.1038/ncomms10151

SUPPORTING INFORMATION

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