Supplementary Material S1. Questionnaire of the survey on Multicentric CarpoTarsal Osteolysis syndrome (MCTO)

* Mandatory answers

1) SECTION 1

-Please enter your name* (blank space)
-Please enter your email address*(blank space)
-Please enter the name of your Hospital/Istitution, City, and Country*(blank space)

2) SECTION 2- Patient information

-Gender (multiple choice) M/F/Unknown
-Ethnicity (blank space)

3) SECTION 3- Genotype

-Did the patient receive a genetic testing? (multiple choice)
- Yes, genetic analysis confirmed the diagnosis of MCTO
- No, the patient received a clinical diagnosis of MCTO
- Unknown

-Age at diagnosis (decimal years) (blank space)
-Mutation detected (blank space)
-Were parents tested for MAFB mutation? (multiple choice)
- Yes, both parents resulted negative (sporadic case)
- Yes, one parent resulted carrier (no clinical ìsymptoms of disease)
- One parent is affected
- No, parents were not tested
- Unknown

4) SECTION 4- Phenotype (onset)

-Which was the first manifestation of MCTO disease? (multiple choice)
- Bone disorder
- Kidney disorder
- Concomitant bone and kidney disorder
- Other

-If other, please specify (blank space)

5) SECTION 5-Renal disease

-Age at first kidney symptoms (decimal years) (blank space)
-Severity of proteinuria at onset(multiple choice)
- Absence of proteinuria
- Sub-nephrotic range proteinuria
- Nephrotic range proteinuria
- Unknown/Not available

-Kidney function at onset (multiple choice)
- GFR > 90 ml/min/1.73m2
- 60< GFR < 90 ml/min/1.73m2
- 30 < GFR < 60 ml/min/1.73m2
- 15< GFR < 30 ml/min/1.73m2
- GFR < 15 ml/min/1.73m2 – ESRD
- Unknown/Not available

-Hematuria (multiple choice) Yes no Unknown/Not available
-If a kidney biopsy was performed, please enter a short description of histopathological findings (blank space)
-Did the patient receive any treatment for the kidney disease? (multiple choice for each row)
Choices: Yes, with complete proteinuria remission/Yes, with proteinuria partial remission/yYes, with no response/No/Unknown
Rows: Corticosteroids/Calcineurin Inhibitors/MMF or other immunosuppressants/RAASi (ACE/ARB)

6) SECTION 6 – Bone disease

-Age at first bone symptoms(decimal years) (blank space)
-Which joint(s) were affected? (multiple choice for each row)
Choices: Yes, severe involvement/Yes, mild involvement/No/Unknown
Rows: Wrist-Carpal bones/Elbows/Ankle-tarsal bones/Hand fingers/Toes/Others
-Please enter a short description of bone disorder (blank space)
-Did the patient receive a previous misdiagnosis?(multiple choice)
- Yes, rheumatological disorder
- Yes, metabolic bone disease secondary to the kidney failure
- No
- Other

-Did the patient receive any treatment for the bone disorder? (multiple choice for each row)
Choices: Yes, with improvement/Yes, with NO improvement/No/Unknown
Rows: Nonsteroidal anti-inflammatory drugs (NSAIDs)/ Disease-modifying antirheumatic drugs (DMARDs)/ Biologic agents (TNF) /Corticosteroids /Bisphosphonates /Denosumab/Correctional surgery
-Did the patient show other symptoms? (multiple choice for each row)
Choices: Yes, severe/Yes, mild/No/Unknown
Rows: Intellectual impairment-mental disability/Eyes-sight abnormalities/hearing abnormalities/Facial dysmorphisms/others
- If other, please specify (blank space)

7) SECTION 7- Kidney outcomes

-Did the patient reach ESRD? (multiple choice)
- Yes
- No
- Unknown

-If yes, please enter the age at ESRD (decimal years) (blank space)
-Please enter RRT history (periods on HD, PD, transplant; any major complications) (blank space)
-Age at last evaluation (decimal years) (blank space)
-Severity of proteinuria at last evaluation (multiple choice)
- Absence of proteinuria
- Sub-nephrotic range proteinuria
- Nephrotic range proteinuria
- Unknown/Not available

-Kidney function at last evaluation (multiple choice)
- GFR > 90 ml/min/1.73m2
- 60< GFR < 90 ml/min/1.73m2
- 30 < GFR < 60 ml/min/1.73m2
- 15< GFR < 30 ml/min/1.73m2
- GFR < 15 ml/min/1.73m2 – ESRD
- Unknown/Not available

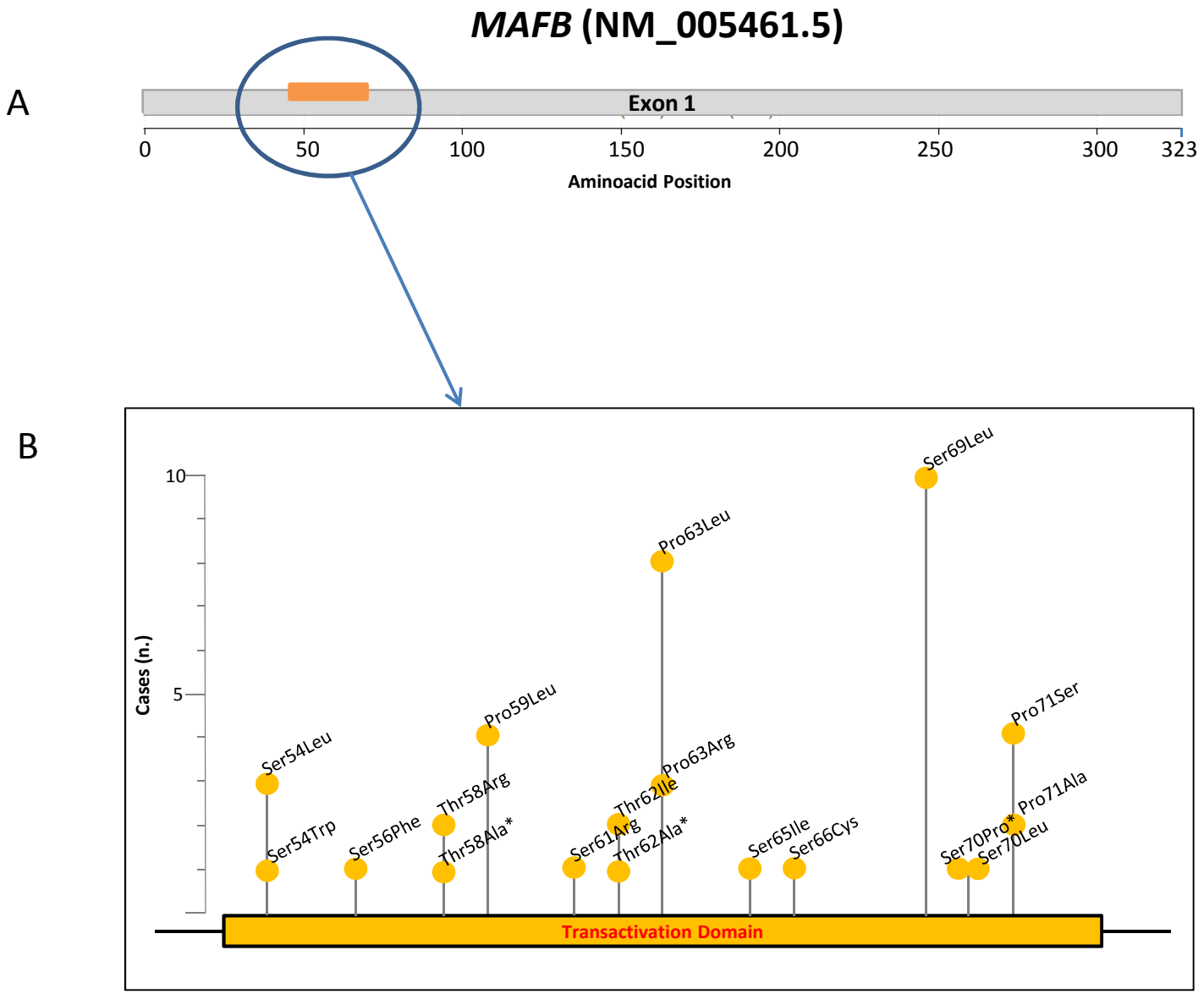
-Is the patient still alive? (multiple choice)
- Yes
- No
- Unknown

Supp. Table S1: List of variants reported by literature and variants collected by ERKNET survey.

	Nucleodite change (NM_005461.5)	Aminoacid change	ClinVar (accession n.)	Published cases (n.)	Survey cases (n.)	Cases with kidney involvement n. (%)	ACMG classification*	Ref
1	c.161C>T	p.Ser54Leu	VCV000030773	3		1(33%)	P/LP	(9, 17)
2	c.161C>G	p.Ser54Trp		1	1	1 (50%)	LP	(4)
3	c.167C>T	p.Ser56Phe		1			P	(7)
4	c.172A>G	p.Thr58Ala			1	1 (100%)	LP	present paper
5	c.173C>G	p.Thr58Arg	VCV000684763	1	1	2 (100%)	P	(15)
6	c.176C>T	p.Pro59Leu		5		4 (80%)	P	(1 ,4, 5, 8)
7	c.183C>A	p.Ser61Arg		1		1 (100%)	LP	(12)
8	c.184A>G	p.Thr62Ala	VCV000807627		1	1 (100%)	P	present paper
9	c.185C>T	p.Thr62Ile	VCV000803608	1	1	2 (100%)	P	(5)
10	c.188C>T	p.Pro63Leu		4	4	6 (75%)	P	(4, 9)
11	c.188C>G	p.Pro63Arg		3		3 (100%)	P	(2, 4)
12	c.194G>T	p.Ser65Ile		1		1 (100%)	LP	(4)
13	c.197C>G	p.Ser66Cys		1		1 (100%)	P	(4)
14	c.206C>T	p.Ser69Leu	VCV000030769	9	1	5 (50%)	LP	(3, 16, 5)
15	c.208T>C	p.Ser70Pro			1		P	present paper
16	c.209C>T	p.Ser70Leu	VCV000030770	1		1 (100%)	P	(5)
17	c.211C>G	p.Pro71Ala		2		2 (100%)	P	(12)
18	c.211C>T	p.Pro71Ser	VCV000030771	3	1	2 (50%)	P	(1, 5)
	Variant not reported			5		4 (80%)		(11, 13, 14)

(*) ACGM Classification: classification of the variant according to the American College of Medica Genetics and Genomics guideline. (Genetics in Medicine, 2015; 17 pp.405-424). LP: Likely Pathogenic; P: Pathogenic.

Supp.Mat. Figure S1



Legend: (A) schematic representation of the *MAFB* gene; in orange the transactivation domain contains cluster of missense variants. (B) Distribution of identified variant and number of observed cases. (*) New variants described in the present manuscript