

Item S1. Resources for Autosomal Dominant Tubulointerstitial Kidney Disease

The following resources are available to patients and clinicians. For any questions about their use or the diagnosis of ADTKD, please contact kidney@wakehealth.edu

Characteristics of autosomal dominant tubulointerstitial kidney disease include:

- 1) Autosomal dominant inheritance (parent and child affected by kidney disease).
- 2) No blood and little protein in the urine.
- 3) Chronic kidney disease.

GENETIC TESTING OF ADTKD

Genetic testing for *MUC1* and *APOA4* are currently available free of charge for families with ADTKD. Please contact kidney@wakehealth.edu for further information. For information on *UMOD* or *REN* testing or other ADTKD genes, please contact kidney@wakehealth.edu

EVALUATION OF VARIANTS OF UNCERTAIN SIGNIFICANCE IN ADTKD

Variants of uncertain significance may or not cause genetic kidney disease. A list of pathogenic *UMOD* variants can be found at <https://redcap.wakehealth.edu/redcap/surveys/?s=CTYXHAK93H>

We can perform in vitro testing to determine if *REN* or *UMOD* variants are pathogenic. Please contact us at kidney@wakehealth.edu.

EVALUATION OF FAMILIES WITH INHERITED KIDNEY DISEASE OF UNKNOWN CAUSE

As part of our research, we attempt to identify new causes of inherited kidney disease. For information in this regard, please contact us at kidney@wakehealth.edu

PARTICIPATION IN PATIENT REGISTRIES

Currently, we have active patient registries for *MUC1*, *UMOD*, *REN*, and *APOA4*. We would appreciate the referral of patients for the registry. Patients will be eligible to have free laboratory testing to measure kidney function every four months. In addition, they will be provided with educational materials and webinars about ADTKD. Patients will also be made aware of upcoming clinical trials in ADTKD and invited to participate. Please contact us at kidney@wakehealth.edu

Table S1. Catalog of UMOD Pathogenic Mutations from literature, collaborator, and referral families

Amino Acid position	Nucleotide change	Sequencing Exon	Resultant Amino Acid change	Protein structure Domain	Age ESRD	ESRD ref	Reference (PMID)	Reference (PMID)	Reference (PMID)	Reference (PMID)	Reference (PMID)	Reference (PMID)	# referrals
32	c.G95A	3	p.Cys32Tyr	EGF1		16883323	21868615	16883323	collaborator data				1
32	c.C96G	3	p.Cys32Trp	EGF1	44.5	records	19465746	21654721					1
32		3	p.Cys32Thr	EGF1			referral						1
34	c.G100A	3	p.Glu34Lys	EGF1	--	21868615	21868615						1
39		3	p.Ala39Thr	EGF1	65.7	collaborator data							4
41		3	p.Cys41Tyr	EGF1			referral						1
50	c.G149C	3	p.Cys50Ser	EGF1	25.7	23723338	18950917	collaborator data					1
52	c.G155A	3	p.Cys52Tyr	EGF1	45.0	records	novel referral						1
52	c.T156G	3	p.Cys52Trp	EGF1	--	23723338	21654721	15558519					1
52		3	p.Cys52Ser	EGF1	39.8	records	referral						1
55		3	p.Gly55Ser	EGF1	53.3	collaborator data	referral						1
55	c.G163A	3	p.Gly55Ser	EGF1			29513881						
58	c.G172T	3	p.Gly58Cys	EGF1	--	23723338	20172860						
59	c.A176C	3	p.Asp59Ala	EGF1	59.0	23723338	21868615	15558519					1
59		3	p.Asp59Tyr	EGF1	45.0	collaborator data							2
63	c.C189G	3	p.Cys63Trp	EGF1	30.3	24577984	24577984						
63		3	p.Cys63Ser	EGF1	36.7	records	referral						1
63	c.T187C	3	p.Cys63Arg	EGF1			23826568						1
67		3	p.Asp67Gly										1
68	c.G202A	3	p.Glu68Lys	EGF2	43.5	records	referral						1
69	c.T205C	3	p.Cys69Arg	EGF2	--	21868615	21868615						2
69	c.G206A	3	p.Cys69Tyr	EGF2	--	23723338	20172860						
76-77		3	p.Asn76_Cys77delinsLysGly	EGF2	26.7	records	referral						1
76		3	p.Asn76Ser	EGF2	26.0	collaborator data							1
77	c.T229G	3	p.Cys77Gly	EGF2	45.0	23723338	17245395	21654721					
77	c.G230A	3	p.Cys77Tyr	EGF2	42.3	23723338	15558519	22740033					1
77		3	p.Cys77Arg	EGF2	39.0	records	referral						1
77		3	p.Cys77Trp	EGF2	--	21654721	21654721						
77		3	p.Cys77Ser	EGF2	32.0	collaborator data							1

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83	c.C249G	3	p.Cys83Trp	EGF2			29424336						
83		3	p.Cys83Ser	EGF2	20.5	collaborator data							1
83		3	p.Cys83Trp	EGF2	29.0	collaborator data	29424336						1
85		3	p.Asn85Lys	EGF2	55.0	referral							1
85		3	p.Asn85Ser	EGF2	41.0	referral							1
88	c.G263T	3	p.Gly88Val	EGF2	51.5	collaborator data							1
88		3	p.Gly88Asp	EGF2	65.6	collaborator data							8
91	c.272_274del	3	p.Ser91del	EGF2			novel						5
92		3	p.Cys92Gly	EGF2	31.5	collaborator data							1
92		3	p.Cys92Arg	EGF2		collaborator data							1
92	c.G275A	3	p.Cys92Tyr	EGF2			referral						2
93-97	c.278_289del insCCGCCTCC T	3	p.Val93- Gly97delinsAA SC	EGF2	50.5	22034507	15558519	21654721	22034507	14531790	20172860	15673476	14
94	c.C282G	3	p.Cys94Trp	EGF2	42.5	records	referral	collaborator data					2
94		3	p.Cys94Tyr										1
103	c.G307T	3	p.Gly103Cys	EGF3	32.0	records	12471200	21654721	15558519				1
105		3	p.Gly105Cys	EGF3	47.0	collaborator data							1
106	c.T316G	3	p.Cys106Gly	EGF3	53.7	records	referral						2
106	c.G317A	3	p.Cys106Tyr	EGF3	--	23723338	20172860						2
106	c.G317T	3	p.Cys106Phe	EGF3		records	referral						5
109		3	p.Val109Glu	EGF3	--	23988501	23988501						
112	c.T334C	3	p.Cys112Arg	EGF3	64.0	23723338	21868615	15558519					1
112	c.G335A	3	p.Cys112Tyr	EGF3			novel						1
120	c.G359A	3	p.Cys120Tyr	EGF3	--		28605509	homozygous					
120		3	p.Cys120Arg	EGF3	36.0		referral						1
126	c.T376C	3	p.Cys126Arg	EGF3	52.0	23723338	21868615	15558519	22740033				1
128	c.A383G	3	p.Asn128Ser	EGF3	50.6	records	21654721	15558519	17065110	collaborator data	records		4
135	c.T403G	3	p.Cys135Gly	EGF3	40's	25786455	25786455						
135	c.T403A	3	p.Cys135Ser	EGF3	--	23723338	15558519	21654721	21868615				1
135	c.G404A	3	p.Cys135Tyr	EGF3	44.7	records	referral						2
135	c.G404T	3	p.Cys135Phe	EGF3	45.0	records	referral						2

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135		3	p.Cys135Trp	EGF3			referral						1
137		3	p.Cys137Arg	EGF3	48.0	collaborator data							1
148	c.G443A	3	p.Cys148Tyr	EGF3	44.4	records	12471200	21654721	15585519				3
148	c.G443C	3	p.Cys148Ser	EGF3	44.0	records	referral						2
148	c.T444G	3	p.Cys148Trp	EGF3	39.0	23723338	14570709	21654721	15558519				
150	c.T448A	3	p.Cys150Ser	Cys-Rich 1	50.0	20172860	20172860	collaborator data					2
150	c.G449C	3	p.Cys150Ser	Cys-Rich 1	--	23723338	21868615	14570709	15558519				
150		3	p.Cys150Tyr	Cys-Rich 1									1
153		3	p.Gly153Cys	Cys-Rich-1	57.0	collaborator data	27729211						2
155	c.T__C	3	p.Cys155Arg	Cys-Rich-1	--		25436415						
170	c.G509A	3	p.Cys170Tyr	Cys-Rich 1	58.5	23723338	21868615	15558519	collaborator data				2
172	c.C514G	3	p.Asp172His	Cys-Rich 1	60.0	records	21868615						2
173	c.C518G	3	p.Pro173Arg	Cys-Rich 1	--		28509303						
173	c.C518T	3	p.Pro173Leu	Cys-Rich 1			referral						1
173		3	p.Pro173Thr	Cys-Rich 1	51.0	collaborator data							1
174	c.T520C	3	p.Cys174Arg	Cys-Rich 1	60.0	23723338	referral						1
177-185	c.529_555del	3	p.His177-Arg185del	Cys-Rich1	46.0	records	15558519	12471200					22
178	c.G533C	3	p.Arg178Pro	Cys-Rich 1	49.7	records	referral						13
180		3	p.Leu180Pro	Cys-Rich 1			referral						1
180		3	p.Leu180Val	Cys-Rich 1									1
184	c.G552C	3	p.Trp184Cys	Cys-Rich 1	--	21868615	21868615	collaborator data					1
185	c.C553T	3	p.Arg185Cys	Cys-Rich 1	38.0	21868615	21868615	collaborator data					4
185	c.C553G	3	p.Arg185Gly	Cys-Rich 1	39.0	records	21654721	19465746					1
185	c.C553A	3	p.Arg185Ser	Cys-Rich 1	37.1	23723338	21868615	15558519	collaborator data				2
185	c.G554A	3	p.Arg185His	Cys-Rich 1	59.3	records	21868615						3
188-221	c.563_661del	3	p.Glu188-Leu221del	Cys-Rich1	38.5	23723338	15558519	21868615	21654721	collaborator data			1
195	c.G584T	3	p.Cys195Phe	Cys-Rich 1	--	23723338	21654721	15558519					
195	c.G584A	3	p.Cys195Tyr	Cys-Rich 1			referral						1
196	.CG585_586T	3	p.Asp196Asn	Cys-Rich 1	56.5	21868615	21868615						1
196	c.G586A	3	p.Asp196Asn	Cys-Rich 1	--	23723338	20172860	19465746					
196		3	p.Asp196Ala	Cyst-Rich-1	40.0	collaborator data							1

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196	c.G586T	3	p.Asp196Tyr	Cys-Rich 1	37.8	23723338	21868615	19203555	22740033	collaborator data			2
197	c.G589T	3	p.Glu197X	Cys-Rich 1	33.0	27489562	27489562						
201		3	p.Gly201Asp	Dom 8 Cys		collaborator data							1
202		3	p.Trp202Arg	Dom 8 Cys	38.0	collaborator data							1
202		3	p.Trp202Cys	Dom 8 Cys	55.0	records							1
202	c.G605C	3	p.Trp202Ser	Dom 8 Cys	38.5	records	21654721	15558519					2
203		3	p.Tyr203Asp	Dom 8 Cys	64.0	records	referral						1
204		3	p.Arg204Pro	Dom 8 Cys		collaborator data							1
204	c.C610G	3	p.Arg204Gly	Dom 8 Cys	45.5	23723338	21868615	15558519	collaborator data	records			3
209		3	p.Gly209Asp	Dom 8 Cys	46.0	collaborator data							1
210	c.G628A	3	p.Gly210Ser	Dom 8 Cys	--	21868615	21868615						
210	c.G629A	3	p.Gly210Asp	Dom 8 Cys			novel						1
210		3	p.Gly210Arg	Dom 8 Cys		collaborator data							1
210		3	p.Gly210Ser	Dom 8 Cys		collaborator data							2
212		3	p.Arg212Cys	Dom 8 Cys	57.7	collaborator data							3
217	c.T649C	3	p.Cys217Arg	Dom 8 Cys	51.4	records	12471200	21654721	15558519	collaborator data			2
217	c.T649G	3	p.Cys217Gly	Dom 8 Cys	36.5	23723338	21868615	15558519	collaborator data				1
217	c.C651G	3	p.Cys217Trp	Dom 8 Cys	47.0	23723338	19465746	22740033	21654721				
217		3	p.Cys217Phe	Dom 8 Cys	32.0	collaborator data							1
219		3	p.Pro219Leu	Dom 8 Cys		collaborator data							1
222	c.G665C	3	p.Arg222Pro	Dom 8 Cys	49.2	23723338	21868615	15558519	collaborator data				1
223	c.T667G	3	p.Cys223Gly	Dom 8 Cys	41.9		29569962						
223	c.T667C	3	p.Cys223Arg	Dom 8 Cys	53.0	23723338	19465746	2274003	21654721				1
223	c.C668A	3	p.Cys223Tyr	Dom 8 Cys	49.0	23723338	15558519	21654721	15327389	12900848			3
223		3	p. Cys223Gly	Dom 8 Cys	56.0	collaborator data							1
225	c.C674T	3	p.Thr225Met	Dom 8 Cys	39.0	23723338	21868615	15558519	collaborator data				4
225	c.C674A	3	p.Thr225Lys	Dom 8 Cys	31.5	23723338	21654721	14531790	15558519				
229	c.T686G	3	p.Met229Arg	Dom 8 Cys	52.5	23723338	21654721	16883323					2
230	c.T688C	3	p.Trp230Arg	Dom 8 Cys	--	23723338	23197950	20172860					3
235		3	p.His235Gln	Dom 8 Cys	51.5	collaborator data							2
235		3	p.His235Tyr	Dom 8 Cys	--		referral						1
236	c.C707G	3	p.Pro236Arg	Dom 8 Cys			30976393						

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236	c.C706T	3	p.Pro236Ser	Dom 8 Cys	84.0	records	referral						2
236	c.C707T	3	p.Pro236Leu	Dom 8 Cys	50.0	16883323	21868615	15558519	collaborator data	records			6
236	c.C707G	3	p.Pro236Arg	Dom 8 Cys	45.0	23723338	21654721	collaborator data	records				5
236		3	p.Pro236Gln	Dom 8 Cys	--	23988501	23988501						
237	c.C710G	3	p.Ser237Cys	Dom 8 Cys	--	21868615	21868615	collaborator data					1
245		3	p.Arg245Pro	Dom 8 Cys	--								1
246-252	c.737_754del	3	p.Lys246-Ser252del	Dom 8 Cys	46.0	records	referral	7296976					1
247	c.G739C	3	p.Ala247Pro	Dom 8 Cys	60.0	26798464	26798464						
248	c.G743C	3	p.Cys248Ser	Dom 8 Cys	--	23723338	20172860						
248	c.C744G	3	p.Cys248Trp	Dom 8 Cys	34.3	23723338	21654721	15558519	17245395	14531790			3
250		3	p.His250Gln	Dom 8 Cys		collaborator data							1
250	c.A749T	3	p.His250Leu	Dom 8 Cys	--	21868615	21868615	collaborator data					1
255	c.G764A	3	p.Cys255Tyr	Dom 8 Cys	55.7	15253706	21654721	15558519	17065110	15253706			1
256		3	p.Cys256Tyr	Dom 8 Cys	48.3	collaborator data							1
257	c.T770C	3	p.Leu257Pro	Dom 8 Cys	44.6	records	referral						2
258		3	p.Trp258Cys	Dom 8 Cys			referral						1
267	c.G800T	3	p.Cys267Phe	Dom 8 Cys			referral						1
269	c.G805T	3	p.Gly269Cys	Dom 8 Cys			referral						1
270		3	p.Gly270Cys	Dom 8 Cys			referral						1
272		3	p.Tyr272del	Dom 8 Cys	62.0	collaborator data							1
273	c.G817A	3	p.Val273Leu	Dom 8 Cys	--	21868615	21868615	collaborator data					1
273		3	p.Val273Phe	Dom 8 Cys	62.5	23723338	21654721						1
274	c.A821G	3	p.Tyr274Cys	Dom 8 Cys	--	20172860	20172860						1
274	c.T820C	3	p.Tyr274His	Dom 8 Cys	46.0	records	referral						1
282	c.T844C	3	p.Cys282Arg	Dom 8 Cys	--	21868615	21868615	15558519					1
282	c.T844A	3	p.Cys282Ser	Dom 8 Cys			referral						1
284	c.T851C	3	p.Leu284Pro	Dom 8 Cys			referral						1
285	c.C855A	3	p.Ala285Glu	Dom 8 Cys	--	21868615	21868615						1
286		3	p.Tyr286Cys	Dom 8 Cys	42.5	records	referral						1
287		3	p.Cys287Tyr	Dom 8 Cys			referral						1
287		3	p.Cys287Arg	Dom 8 Cys									1

Bleyer et al, AJKD, "Autosomal Dominant Tubulointerstitial Kidney Disease"

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297	c.T891G	4	p.Cys297Trp	Cys-Rich 2	39.0	records	20151160	21868615					2
297	c.G893A	4	p.Cys297Tyr	Cys-Rich2	--	21868615	21868615						
300	c.T898G	4	p.Cys300Gly	Cys-Rich2	58.5	23723338	15983957	21654721	15558519	20172860	17065110		2
300	c.G899A	4	p.Cys300Arg	Cys-Rich2	--	23723338	referral						1
300		4	p.Cys300Tyr	Cys-Rich2	--	21654721	21654721						
300		4	p.Cys300Ser	Cys-Rich2									1
306	c.T917A	4	p.Cys306Ser	Cys-Rich2	37.0	27764983	27764983						
306	c.G917A	4	p.Cys306Tyr	Cys-Rich2			novel						2
307	c.A920C	4	p.Lys307Thr	Cys-Rich2	49.0	23723338	15673476	21654721					
315	c.T943C	4	p.Cys315Arg	Cys-Rich2	31.0	15983957	21654721	14570709	15558519				2
315	c.G944A	4	p.Cys315Tyr	Cys-Rich2	45.0	21868615	21868615	collaborator data					2
316	c.A947C	4	p.Gln316Pro	Cys-Rich2	65.5	23723338	15983957	21654721					
317	c.T949G	4	p.Cys317Gly	Cys-Rich2	40.0	27795632	27795632						
317	c.C950A	4	p.Cys317Tyr	Cys-Rich2	56.0	23723338	21654721	14570709	15558519				2
333		4	p. Leu333Pro	Cys-Rich2		collaborator data							1
375	c.G1124A	5	p.Arg375Gln	ZP	--	18846391	18846391						
458	c.G1372T	7	p.Val458Leu	ZP			referral	18846391					2
461	c.C1382A	7	p.Ala461Glu	ZP	--	23723338	21868615	21060763					1
469	c.C1406T	7	p.Thr469Met	ZP	--	21868615	21868615						
488		7	p.Gly488Asp	ZP	33.5	collaborator data							2
488	c.G1462A	7	p.Gly488Arg	ZP	--	21868615	21868615	collaborator data					1
488	c.G1462C	7	p.Gly488Arg	ZP	--	19465746	19465746						
550	c.1648G	8	p.Val550Ile	ZP			31068150						
605	c.A1815G	8	p.Thr605Gly	chain	49.0	22776760	22776760						

Please reach out to Anthony J. Bleyer ableyer@wakehealth.edu or Kendrah Kidd kkidd@wakehealth.edu for updates or questions.

Full list available: <https://redcap.link/UMOD.mutations> and will be updated in 2025.