UMOD Mutations that Cause Uromodulin Kidney Disease

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Uromodulin Kidney Disease Research and Support

Mutations in the *UMOD* gene are responsible for Uromodulin Kidney Disease (UKD). Currently, there are over 100 known mutations that cause UKD (Figure 1, Table 1). Approximately 48% of mutations result in the substitution of the amino acid cysteine, which is important for maintaining protein structure.

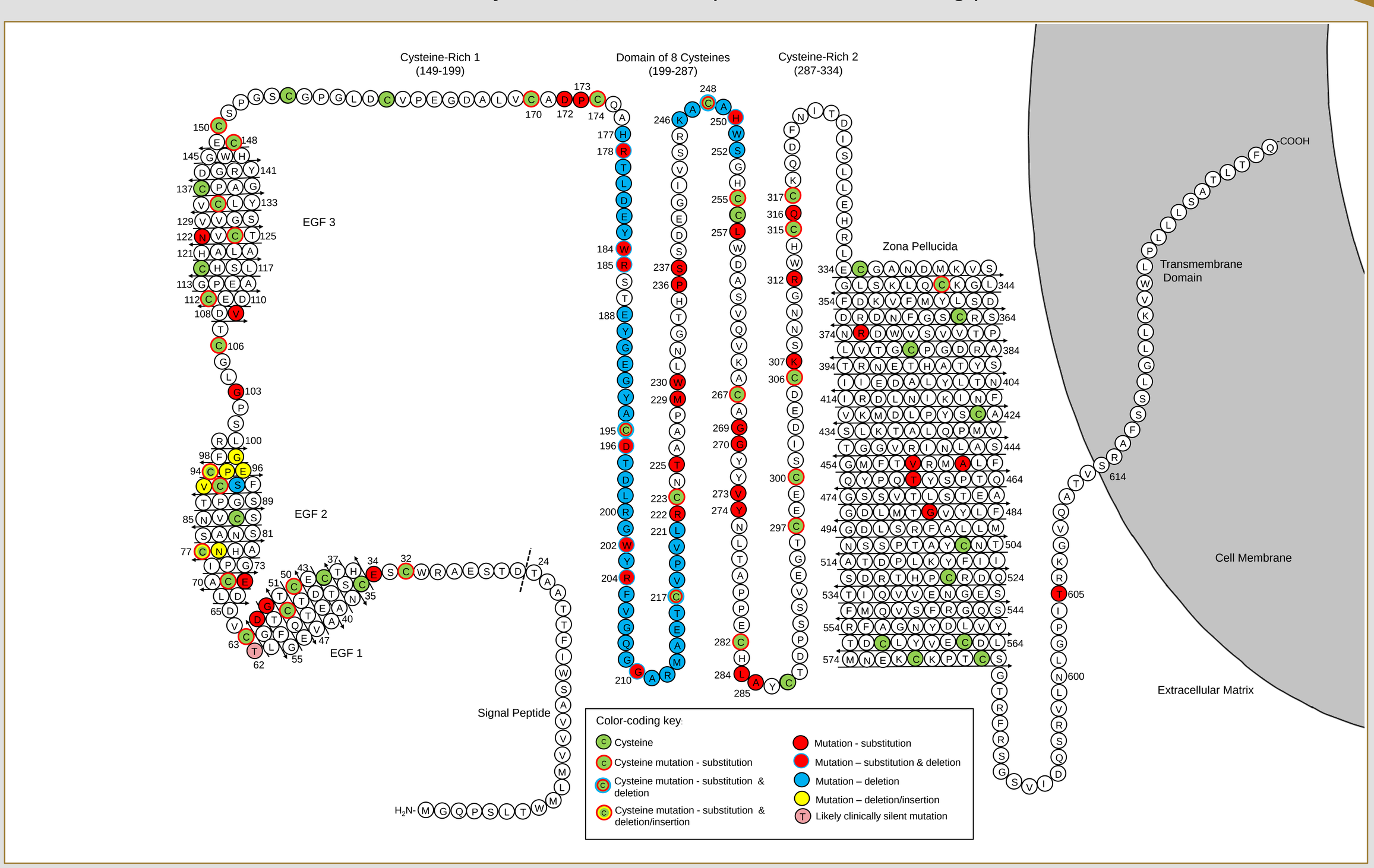

Figure 1. Amino acid structure of Uromodulin shown with UKD causing mutations. Amino acids are numbered, cysteines and known mutations are highlighted and described in the color-coding key.

Nucleotide change	Exon	Resultant Amino Acid change	Protein structure Domain	Mean ESRD
c.G95A	4	p.Cys32Tyr	EGF1	
c.C96G	4	p.Cys32Trp	EGF1	44.5[1]
c.G100A	4	p.Glu34Lys	EGF1	
c.G149C	4	p.Cys50Ser	EGF1	29[2]
c.G155A	4	p.Cys52Tyr	EGF1	45[1]
c.T156G	4	p.Cys52Trp	EGF1	
	4	p.Cys52Ser	EGF1	39.8[1]
c.G172T	4	p.Gly58Cys	EGF1	
c.A176C	4	p.Asp59Ala	EGF1	59[2]
c.A184C	4	p.Thr62Pro	EGF1	likely clinically silent mutation
	4	p.Cys63Ser	EGF1	36.7[1]
c.G202A	4	p.Glu68Ala	EGF2	43.5[1]
c.T205C	4	p.Cys69Arg	EGF2	
c.G206A	4	p.Cys69Tyr	EGF2	
		p.AsnLys76-77CysGly	EGF2	26.7[1]
c.T229G	4	p.Cys77Gly	EGF2	45[2]
c.G230A	4	p.Cys77Tyr	EGF2	36.6[2]
	4	p.Cys77Arg	EGF2	39[1]
	4	p.Cys77Trp	EGF2	
c.272_274del	4	p.Ser91del	EGF2	
c.G275A	4	p.Cys92Tyr	EGF2	
c.278_289delinsCCGCCTCCT	4	p.Val93-Gly97delinsAlaAlaSerCys	EGF2	50.5[3]
c.C282G	4	p.Cys94Trp	EGF2	42.6[1]
c.G307T	4	p.Gly103Cys	EGF3	32[1]
c.T316G	4	p.Cys106Gly	EGF3	53.7[1]
c.G317A	4	p.Cys106Tyr	EGF3	
c.G317T	4	p.Cys106Phe	EGF3	
		p.Val109Glu	EGF3	
c.T334C	4	p.Cys112Arg	EGF3	64[2]
c.G335A	4	p.Cys112Tyr	EGF3	
c.T376C	4	p.Cys126Arg	EGF3	52[2]
c.A383G	4	p.Asn128Ser	EGF3	45[1]
c.T403A	4	p.Cys135Ser	EGF3	
c.G404A	4	p.Cys135Tyr	EGF3	44.7[1]
c.G404T	4	p.Cys135Phe	EGF3	45[1]
c.T442C	4	p.Cys148Arg	EGF3	42.7[1]
c.G443A	4	p.Cys148Tyr	EGF3	44.4[1]

Nucleotide change	Exon	Resultant Amino Acid change	Protein structure Domain	Mean ESRD
c.G443C	4	p.Cys148Ser	EGF3	44[1]
c.T444G	4	p.Cys148Trp	EGF3	39[2]
c.T448A	4	p.Cys150Ser	Cys-Rich 1	
c.G449C	4	p.Cys150Ser	Cys-Rich 1	
c.G509A	4	p.Cys170Tyr	Cys-Rich 1	
c.C514G	4	p.Asp172His	Cys-Rich 1	60[1]
c.C518T	4	p.Pro173Leu	Cys-Rich 1	
c.T520C	4	p.Cys174Arg	Cys-Rich 1	60[2]
c.529_555del	4	p.His177-Arg185del	Cys-Rich 1	46[1]
c.G533C	4	p.Arg178Pro	Cys-Rich 1	49.7[1]
c.G552C	4	p.Trp184Cys	Cys-Rich 1	
c.C553T	4	p.Arg185Cys	Cys-Rich 1	
c.C553G	4	p.Arg185Gly	Cys-Rich 1	39[1]
c.C553A	4	p.Arg185Ser	Cys-Rich 1	48.3[2]
c.G554A	4	p.Arg185His	Cys-Rich 1	61[1]
c.563_661del	4	p.Glu188-Leu221del	Cys-Rich 1	38[2]
c.G584T	4	p.Cys195Phe	Cys-Rich 1	
c.G584A	4	p.Cys195Tyr	Cys-Rich 1	
c.CG585_586TA	4	p.Asp196Asn	Cys-Rich 1	
c.G586A	4	p.Asp196ASn	Cys-Rich 1	
c.G586T	4	p.Asp196Tyr	Cys-Rich 1	36[2]
c.G605C	4	p.Trp202Ser	Dom 8 Cys	33.4[1]
c.C610G	4	p.Arg204Gly	Dom 8 Cys	
c.G628A	4	p.Gly210Ser	Dom 8 Cys	
c.G629A	4	p.Gly210Asp	Dom 8 Cys	
c.T649C	4	p.Cys217Arg	Dom 8 Cys	51.7[1]
c.T649G	4	p.Cys217Gly	Dom 8 Cys	36[2]
c.C651G	4	p.Cys217Trp	Dom 8 Cys	47[2]
c.G665C	4	p.Arg222Pro	Dom 8 Cys	47[2]
c.T667C	4	p.Cys223Arg	Dom 8 Cys	53[2]
c.C668A	4	p.Cys223Tyr	Dom 8 Cys	49[2]
c.C674T	4	p.Thr225Met	Dom 8 Cys	40[2]
c.C674A	4	p.Thr225Lys	Dom 8 Cys	31.5[2]
		p.Met229Arg	Dom 8 Cys	52.5[2]
c.T668C	4	p.Trp230Arg	Dom 8 Cys	
c.C706T	4	p.Pro236Ser	Dom 8 Cys	84[1]
c.C707T	4	p.Pro236Leu	Dom 8 Cys	63[4]
		p.Pro236Arg	Dom 8 Cys	

Nucleotide change	Exon	Resultant Amino Acid change	Protein structure Domain	Mean ESRD
c.C710G	4	p.Ser237Cys	Dom 8 Cys	
c.737_754del	4	p.Lys246-Ser252del	Dom 8 Cys	46[1]
c.G743C	4	p.Cys248Ser	Dom 8 Cys	
c.C744G	4	p.Cys248Trp	Dom 8 Cys	34.3[2]
c.A749T	4	p.His250Leu	Dom 8 Cys	
c.G764A	4	p.Cys255Tyr	Dom 8 Cys	48.7[5]
c.T770C		p.Leu257Pro	Dom 8 Cys	44.6[1]
c.G800T	4	p.Cys267Phe	Dom 8 Cys	
c.G805T	4	p.Gly269Cys	Dom 8 Cys	
		p.Gly270Cys	Dom 8 Cys	
c.G817A	4	p.Val273Leu	Dom 8 Cys	
		p.Val273Phe	Dom 8 Cys	62.5[2]
c.A821G	4	p.Tyr274Cys	Dom 8 Cys	
c.T820C		p.Tyr274His	Dom 8 Cys	46[1]
c.T844C	4	p.Cys282Arg	Dom 8 Cys	
c.T844A		p.Cys282Ser	Dom 8 Cys	
c.T851C	4	p.Leu284Pro	Dom 8 Cys	
c.C855A	4	p.Ala285Glu	Dom 8 Cys	
c.T891G	5	p.Cys297Trp	Cys-Rich 2	39[1]
c.G893A	5	p.Cys297Tyr	Cys-Rich 2	
c.T898G	5	p.Cys300Gly	Cys-Rich 2	58.5[2]
c.G899A	5	p.Cys300Arg	Cys-Rich 2	
		p.Cys300Tyr	Cys-Rich 2	
c.G917A	5	p.Cys306Tyr	Cys-Rich 2	
c.A920C	5	p.Lys307Thr	Cys-Rich 2	49[2]
c.T943C	5	p.Arg312Cys	Cys-Rich 2	
c.T943C	5	p.Cys315Arg	Cys-Rich 2	31[6]
c.G944A	5	p.Cys315Tyr	Cys-Rich 2	
c.A947C	5	p.Gln316Pro	Cys-Rich 2	65.5[2]
c.C950A	5	p.Cys317Tyr	Cys-Rich 2	56[2]
c.T1039G	6	p.Cys347Gly	ZP	
c.G1124A	6	p.Arg375Gln	ZP	
		p.Val458Leu	ZP	
c.C1382A	8	p.Ala461Glu	ZP	
c.C1406T	8	p.Thr469Met	ZP	
c.G1462A	8	p.Gly488Arg	ZP	
c.G1462C	8	p.Gly488Arg	ZP	
c.A1815G	9	p.Thr605Gly	chain	49[7]

Table 1. *UMOD* mutations and resulting Uromodulin changes. Nucleotide change is the mutation that occurs to the DNA sequence. The position of the nucleotide, the original nucleotide, the mutation, and exon location are given. The resultant amino acid changes is how the protein is changed as a result of the DNA mutation. The position of the amino acid, the original amino acid, the resultant amino acid from the mutation, and the protein domain where it occurs are given. The mean ESRD for the mutation is given, if known, with reference(1-7).

Acknowledgements

The original model was drawn by Dr. J.J. Turner[1], and was based on a previously reported model (van Rooijen et al, *Glycobiology* 1999), and models of the EGF-like domains in thrombomodulin (Fuentes-Prior et al, *Nature* 2000) and fibrillin (Yuan et al, *J Mol Biol* 2002).

The following have contributed significantly to the development of the current figure: Sian E. Piret[2], Rajesh V. Thakker[2], Stanislav Kmoch[3], Kateřina Hodaňová[3], Kendrah Kidd[4], Vicki Robins[4], Anthony Bleyer[4].

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