

Disease-associated factor H variants				
Variant	CCP	Predicted effect	Pathology	fH level
I62V ¹	1	No effect on structure	AMD	High
R78G ²	1	Structural disruption	HUS	n.r.
R127L ³	2	Protein more "sticky?"	MPGN	Low
Q400K ³	7	No effect on structure	HUS	n.r.
Y402H ¹	7	No effect on structure	AMD	High
C431S ³	7	Structural disruption	MPGN	Low
C536R, C959Y ^{4,5}	9,16	Structural disruption	CIIIG	Absent
C630W ⁶	11	Structural disruption	HUS	Normal
C673Y ³	11	Structural disruption	HUS	Low/Normal
C673S ³	11	Structural disruption	MPGN	Low
V835L ⁷	14	Structural disruption	HUS	n.r.
E850K ⁶	14	No effect on structure	HUS	High
S890I ⁸	15	Protein more "sticky?"	HUS	Normal
H893R ³	15	Disrupts junction	HUS	Low
C915S ³	15	Structural disruption	HUS	Low
E936D ²	16	No effect on structure	HUS	Normal
Q950H ²	16	No effect on structure	HUS	n.r.
Y951H ²	16	Disrupts junction?	HUS	n.r.
T956M ^{9,10}	16	No effect on structure	HUS	Normal/High
C973Y ⁷	16	Structural disruption	HUS	Low/Absent
W978C ⁶	16	Structural disruption	HUS	Normal
T987A ⁷	16/17	Disrupts junction	HUS	n.r.
V1007C ⁷	17	Protein cross-linked?	HUS	Normal
Y1021F ⁶	17	Disrupts junction?	HUS	Normal
C1043R ⁶	17	Structural disruption	HUS	Normal
Q1076E ^{11,6}	18	No effect on structure	HUS	Normal
D1119G ¹¹	19	Disrupts GAG-binding site ^a	HUS	Normal
V1134G ⁶	19	Structural disruption	HUS	High
Y1142D ⁶	19	Disrupts junction	HUS	High
W1157R ⁶	19	Structural disruption	HUS	High
C1163W ²	19	Structural disruption	HUS	n.r.
R1182S ⁷	20	Disrupts GAG-binding site	HUS	n.r.
W1183R ^{6,12}	20	Disrupts GAG-binding site	HUS	Normal
W1183L ^{3,9,10}	20	Disrupts GAG-binding site	HUS	Normal/High
T1184R ¹¹	20	Disrupts GAG-binding site	HUS	Normal
L1189F ^{10,13}	20	C3b-binding?	HUS	Normal
L1189R ^{9,10}	20	C3b-binding?	HUS	Normal/High
S1191L ^{11,6}	20	Disrupts GAG-binding site	HUS	n.r.
S1191W ^{10,13}	20	Disrupts GAG-binding site	HUS	Normal
G1194D ^{2,14}	20	Structural disruption	HUS	n.r.
V1197A ^{2,9-11,15}	20	Structural disruption	HUS	Low/Normal
E1198A ²	20	Disrupts GAG-binding site	HUS	n.r.
F1199S ³	20	Structural disruption	HUS	Low
R1210C ^{2,6,10,14-16}	20	Protein cross-linked?	HUS	Normal/High
R1215G ^{17,11}	20	Disrupts GAG-binding site	HUS	Normal
R1215Q ¹⁵	20	Disrupts GAG-binding site	HUS	Normal
P1226S ⁶	20	Structural disruption	HUS	High

^aThe GAG-binding site on fH~19,20 has been delineated experimentally¹⁸.

Abbreviations used in Table : AMD = age-related macular degeneration; HUS = hemolytic uremic syndrome; MPGN = membranoproliferative glomerulonephritis; CIIIG = collagen type III glomerulopathy; GAG = glycosaminoglycan; n.r. = not reported/known. Superscript numbers after variants relate to references.

Reference: AP Herbert, DC Soares, MK Pangburn and PN Barlow.

Disease-associated sequence variations in factor H: a structural biology approach.

Adv Exp Med Biol 2006, **586**, 313-327.

- (1) Hageman, G. S.; Anderson, D. H.; Johnson, L. V.; Hancox, L. S.; Taiber, A. J.; Hardisty, L. I.; Hageman, J. L.; Stockman, H. A.; Borchardt, J. D.; Gehrs, K. M.; Smith, R. J.; Silvestri, G.; Russell, S. R.; Klaver, C. C.; Barbazetto, I.; Chang, S.; Yannuzzi, L. A.; Barile, G. R.; Merriam, J. C.; Smith, R. T.; Olsh, A. K.; Bergeron, J.; Zernant, J.; Merriam, J. E.; Gold, B.; Dean, M.; Allikmets, R. *Proc Natl Acad Sci U S A* 2005, **102**, 7227-7232. Epub 2005 May 7223.
- (2) Caprioli, J.; Castelletti, F.; Bucchioni, S.; Bettinaglio, P.; Bresin, E.; Pianetti, G.; Gamba, S.; Brioschi, S.; Daina, E.; Remuzzi, G.; Noris, M. *Hum Mol Genet* 2003, **12**, 3385-3395. Epub 2003 Oct 3328.
- (3) Dragon-Durey, M. A.; Fremeaux-Bacchi, V.; Loirat, C.; Blouin, J.; Niaudet, P.; Deschenes, G.; Coppo, P.; Herman Fridman, W.; Weiss, L. *J Am Soc Nephrol* 2004, **15**, 787-795.
- (4) Ault, B. H. *Pediatr Nephrol* 2000, **14**, 1045-1053.
- (5) Ault, B. H.; Schmidt, B. Z.; Fowler, N. L.; Kashtan, C. E.; Ahmed, A. E.; Vogt, B. A.; Colten, H. R. *J Biol Chem* 1997, **272**, 25168-25175.
- (6) Neumann, H. P.; Salzmann, M.; Bohnert-Iwan, B.; Mannuelian, T.; Skerka, C.; Lenk, D.; Bender, B. U.; Cybulla, M.; Riegler, P.; Konigsrainer, A.; Neyer, U.; Bock, A.; Widmer, U.; Male, D. A.; Franke, G.; Zipfel, P. F. *J Med Genet* 2003, **40**, 676-681.
- (7) Saunders, R. E.; Goodship, T. H.; Zipfel, P. F.; Perkins, S. J. *Hum Mutat* 2006, **27**, 21-30.
- (8) Noris, M.; Bucchioni, S.; Galbusera, M.; Donadelli, R.; Bresin, E.; Castelletti, F.; Caprioli, J.; Brioschi, S.; Scheiflinger, F.; Remuzzi, G. *J Am Soc Nephrol* 2005, **16**, 1177-1183. Epub 2005 Mar 1130.
- (9) Perez-Caballero, D.; Gonzalez-Rubio, C.; Gallardo, M. E.; Vera, M.; Lopez-Trascasa, M.; Rodriguez de Cordoba, S.; Sanchez-Corral, P. *Am J Hum Genet* 2001, **68**, 478-484.
- (10) Esparza-Gordillo, J.; Goicoechea de Jorge, E.; Buil, A.; Carreras Berges, L.; Lopez-Trascasa, M.; Sanchez-Corral, P.; Rodriguez de Cordoba, S. *Hum Mol Genet* 2005, **14**, 703-712. Epub 2005 Jan 2020.
- (11) Richards, A.; Buddles, M. R.; Donne, R. L.; Kaplan, B. S.; Kirk, E.; Venning, M. C.; Tielemans, C. L.; Goodship, J. A.; Goodship, T. H. *Am J Hum Genet* 2001, **68**, 485-490.
- (12) Remuzzi, G.; Ruggenenti, P.; Codazzi, D.; Noris, M.; Caprioli, J.; Locatelli, G.; Gridelli, B. *Lancet* 2002, **359**, 1671-1672.
- (13) Rodriguez de Cordoba, S.; Esparza-Gordillo, J.; Goicoechea de Jorge, E.; Lopez-Trascasa, M.; Sanchez-Corral, P. *Mol Immunol* 2004, **41**, 355-367.
- (14) Perkins, S. J.; Goodship, T. H. *J Mol Biol* 2002, **316**, 217-224.
- (15) Caprioli, J.; Bettinaglio, P.; Zipfel, P. F.; Amadei, B.; Daina, E.; Gamba, S.; Skerka, C.; Marziliano, N.; Remuzzi, G.; Noris, M. *J Am Soc Nephrol* 2001, **12**, 297-307.
- (16) Sanchez-Corral, P.; Perez-Caballero, D.; Huarte, O.; Simckes, A. M.; Goicoechea, E.; Lopez-Trascasa, M.; de Cordoba, S. R. *Am J Hum Genet* 2002, **71**, 1285-1295. Epub 2002 Nov 1286.
- (17) Warwicker, P.; Goodship, T. H.; Donne, R. L.; Pirson, Y.; Nicholls, A.; Ward, R. M.; Turnpenny, P.; Goodship, J. A. *Kidney Int* 1998, **53**, 836-844.
- (18) Herbert, A. P.; Uhrin, D.; Lyon, M.; Pangburn, M. K.; Barlow, P. N. *J Biol Chem* 2006.