



Food and Drug Administration
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993

Date: June 14, 2016

ATTN: Harald Mischak, Dr. Med. Habil, Ph.D.
Mosaiques-diagnostics GmbH
Rotenburger Str. 20
D-30659 Hannover
GERMANY

Subject: Biomarker Letter of Support

Dear Dr. Mischak,

We are issuing this Letter of Support to Mosaiques Diagnostics GmbH to encourage the further development of CKD273, a prognostic enrichment biomarker panel composed of 273 urinary peptides, to be used in combination with current measures (i.e., albuminuria, serum creatinine) in early phase clinical trials in diabetic kidney disease (DKD) to identify patients with early stage disease who may be more likely to progress. For a listing of the components of the CKD273 biomarker panel, please see Appendix 1.

Chronic Kidney Disease (CKD) is a major health problem, especially in type 2 diabetes. Many patients with DKD manifest progressive renal dysfunction, ultimately leading to end stage kidney disease. DKD is currently diagnosed by the presence of albuminuria and/or changes in serum creatinine indicating decline in estimated glomerular filtration rate (eGFR). However, risk assessment based on these and other available clinical parameters is insufficient, particularly in patients with early stages of disease. The proposed CKD273 panel is intended to be used to enrich clinical trials of early stage diabetic kidney disease with patients who are more likely to progress.

To date, published and non-published information submitted to FDA suggests that the individual peptide CKD273 biomarkers, specifically collagen fragments and alpha-1-antitrypsin fragments, may be linked to fibrosis and inflammation. These biological processes are assumed to be of relevance in the onset and progression of DKD. Based on experience with use of this biomarker panel classifier in several cross-sectional and longitudinal studies, some analyses suggest that the proteomic signature may provide added prognostic information when used with standard parameters, including albuminuria and eGFR. The prognostic value may be dependent on stage of disease since the submitted data suggests that the CKD273 signature does not appear to perform well in predicting progression to ESRD or doubling of serum creatinine in patients with more advanced disease. While the lack of correlation of the proteomic signature with clinical outcomes in late-stage DKD does not mean it cannot be predictive in early DKD, a biologic rationale for disease stage-specific prognosis, given the ongoing role of processes generating the biomarker signal in late-stage DKD, needs further consideration.

The proposed use of the CKD273 biomarker panel for prognostic enrichment is consistent with the FDA's draft guidance "Enrichment Strategies for Clinical Trials to Support Approval of Human Drugs and Biological Products". Greater experience with the use of CKD273 as a biomarker panel in DKD early phase clinical trials is needed to determine its clinical utility for prognostic enrichment, drug development decisions, and study design considerations. We further encourage the investigation of the proposed peptides in the biomarker panel, alone and in combination and potentially with the addition of novel peptides not currently represented, to determine the prognostic potential and to identify the combination that has greatest impact.

We understand the interest in evaluating the efficacy of drugs in early stages of DKD, in the belief that some drugs may be effective only in early stages of the disease. However, the more remote the clinical outcome of interest is, the more challenging and critical it becomes to predict these outcome events accurately since progressively fewer of the nominally at-risk population will go on to have these events. Further work needs to be done to identify surrogate endpoints that reliably predict treatment effects on long-term renal outcomes in early stage DKD and that can be used to establish the effectiveness of drugs intended to treat early (as opposed to later) stages of DKD disease.

Strong emphasis on applying good scientific, laboratory, and software development practices for quality control and validation of CKD273 is imperative. If, after further research, CKD273 is formally proposed as a biomarker panel for qualification, analytical validation of the tests measuring the 273 urinary peptides and validation of the algorithm that determines the panel score for CKD273 should be performed to support the clinical validation of CKD273 as a prognostic enrichment biomarker.

When including the CKD273 biomarker panel in early clinical studies, sponsors should prospectively discuss any proposed application of the clinical biomarker panel to decisions during the course of the study with the appropriate CDER review division.

Any groups (academia, industry, government) that would like to join in this effort or have information or data that may be useful can contact Harald Mischak (mischak@mosaiques.de) or view Mosaiques Diagnostics' webpage (www.mosaiques.de).

Sincerely,



Janet Woodcock, M.D.
Director, CDER
U.S. Food and Drug Administration

I. Appendix

List of the 273 urinary peptides that compose CKD273 biomarker panel

#	Sequence	Peptide name	Swiss-Prot name
1	KGDTGPPGP	Collagen alpha-1 (III) chain [629-637]	CO3A1_HUMAN
2	SpGEAGRpG	Collagen alpha-1 (I) chain [522-530]	CO1A1_HUMAN
3	GpPpGpPpG	Collagen alpha-1 (I) chain [145-154]	CO1A1_HUMAN
4	DGKTGPPGPA	Collagen alpha-1 (I) chain [550-559]	CO1A1_HUMAN
5	GRpGpPpG	Collagen alpha-1 (I) chain [563-572]	CO1A1_HUMAN
6	VLNLGPITR	Uromodulin [598-606]	UROM_HUMAN
7	YQTNKAKH	Cystatin-B [85-92]	CYTB_HUMAN
8	ApGDKGESGPS	Collagen alpha-1 (I) chain [777-787]	CO1A1_HUMAN
9	PpGSAGAPGKDG	Collagen alpha-1 (I) chain [1143-1154]	CO1A1_HUMAN
10	SpGPDGKTGPP	Collagen alpha-1 (I) chain [546-556]	CO1A1_HUMAN
11	MGPRGpPpG	Collagen alpha-1 (I) chain [217-227]	CO1A1_HUMAN
12	GpGSDGKPGpG	Collagen alpha-1 (III) chain [544-555]	CO3A1_HUMAN
13	GPDKGTGPPGPA	Collagen alpha-1 (I) chain [548-559]	CO1A1_HUMAN
14	GDRGEpGpPpG	Collagen alpha-1 (I) chain [800-810]	CO1A1_HUMAN
15	GEYKFQNAL	Serum albumin [423-431]	ALBU_HUMAN
16	GpGSDGKpGpPpG	Collagen alpha-1 (III) chain [544-555]	CO3A1_HUMAN
17	ApGDRGEpGpP	Collagen alpha-1 (I) chain [798-808]	CO1A1_HUMAN
18	MGKVVNPTQK	Alpha-1-antitrypsin [409-418]	A1AT_HUMAN
19	GpAGPPGpPpG	Collagen alpha-1 (III) chain [174-186]	CO3A1_HUMAN
20	GGpGSDGKpGpPpG	Collagen alpha-1 (III) chain [543-555]	CO3A1_HUMAN
21	GpPpGpPGPPGPS	Collagen alpha-1 (I) chain [1181-1193]	CO1A1_HUMAN
22	PpGEAGKpGEQG	Collagen alpha-1 (I) chain [651-662]	CO1A1_HUMAN
23	GPPGpPpGpPGPPS	Collagen alpha-1 (I) chain [1181-1193]	CO1A1_HUMAN
24	SGSVIDQSRVL	Uromodulin [589-599]	UROM_HUMAN
25	DDGEAGKpGRpG	Collagen alpha-1 (I) chain [231-242]	CO1A1_HUMAN
26	SpGPDGKTGPPGP	Collagen alpha-1 (I) chain [546-558]	CO1A1_HUMAN
27	DGPAGApGTpGPQG	Collagen alpha-1 (I) chain [940-953]	CO1A1_HUMAN
28	GpPpGPDGNKGEpG	Collagen alpha-2 (I) chain [613-625]	CO1A2_HUMAN
29	GpPpGEAGKpGEQG	Collagen alpha-1 (I) chain [650-662]	CO1A1_HUMAN
30	GQDGRpGpPpG	Collagen alpha-1 (I) chain [560-572]	CO1A1_HUMAN
31	DKGETGEQGDRG	Collagen alpha-1 (I) chain [1095-1106]	CO1A1_HUMAN
32	SPGPDGKTGPPGpA	Collagen alpha-1 (I) chain [546-559]	CO1A1_HUMAN
33	SpGERGETGPPGP	Collagen alpha-1 (III) chain [796-808]	CO3A1_HUMAN
34	TIDEKGTEAAGAM	Alpha-1-antitrypsin [363-375]	A1AT_HUMAN
35	SpGSpGPDGKTGPP	Collagen alpha-1 (I) chain [543-556]	CO1A1_HUMAN
36	SpGGPGSDGKpGpPpG	Collagen alpha-1 (III) chain [541-555]	CO3A1_HUMAN
37	SpGAKGDRGETGPA	Collagen alpha-1 (I) chain [1029-1042]	CO1A1_HUMAN
38	TGPGGDKGDTGPPGP	Collagen alpha-1 (III) chain [623-637]	CO3A1_HUMAN
39	SpGGpGSDGKpGpPpG	Collagen alpha-1 (III) chain [541-555]	CO3A1_HUMAN
40	SpGERGETGPPGPA	Collagen alpha-1 (III) chain [796-809]	CO3A1_HUMAN
41	DSGSSEEQGGSSRA	Polymeric-immunoglobulin receptor [626-	PIGR_HUMAN

		639]	
42	ApGEDGRpGPPGPO	Collagen alpha-1 (II) chain [511-524]	CO2A1_HUMAN
43	GSpGGpGSDGKpGPPG	Collagen alpha-1 (III) chain [540-555]	CO3A1_HUMAN
44	SpGERGETGPPGPAG	Collagen alpha-1 (III) chain [796-810]	CO3A1_HUMAN
45	DGPpGRDGOqGHKG	Collagen alpha-2 (I) chain [933-946]	CO1A2_HUMAN
46	GPPGPpGppGPPGPPS	Collagen alpha-1 (I) chain [1178-1193]	CO1A1_HUMAN
47	VIDQSRVNLNGPI	Uromodulin [592-604]	UROM_HUMAN
48	GLPGPpGpGSFLSN	Collagen alpha-1 (XVII) chain [1255-1270]	COHA1_HUMAN
49	PpGKNGDDGEAGKpG	Collagen alpha-1 (I) chain [225-239]	CO1A1_HUMAN
50	GLpGTGGPpGENGKpG	Collagen alpha-1 (III) chain [642-657]	CO3A1_HUMAN
51	TIDEKGTEAAGAMF	Alpha-1-antitrypsin [363-376]	A1AT_HUMAN
52	DEAGSEADHEGTHS	Fibrinogen alpha chain [605-618]	FIBA_HUMAN
53	SpGRDGSpGAKGDRG	Collagen alpha-1 (I) chain [1023-1037]	CO1A1_HUMAN
54	ApGKNGERGGpGGpGP	Collagen alpha-1 (III) chain [589-604]	CO3A1_HUMAN
55	SpGENGApGQmGPRG	Collagen alpha-1 (I) chain [291-305]	CO1A1_HUMAN
56	YTKKVQVSTPTL	Serum albumin [435-447]	ALBU_HUMAN
57	GPPGKNGDDGEAGKPG	Collagen alpha-1 (I) chain [224-239]	CO1A1_HUMAN
58	DQSRVNLNGPITR	Uromodulin [594-606]	UROM_HUMAN
59	DGQPGAKGEpGDAGAK	Collagen alpha-1 (I) chain [820-835]	CO1A1_HUMAN
60	GpPGKNGDDGEAGKpG	Collagen alpha-1 (I) chain [224-239]	CO1A1_HUMAN
61	DGQpGAKGEpGDAGAK	Collagen alpha-1 (I) chain [820-835]	CO1A1_HUMAN
62	GLSMDGGGSPKGDVDP	Sodium/potassium-transporting ATPase gamma chain [3-18]	ATNG_HUMAN
63	VGPPGPpGpPGPPGPPS	Collagen alpha-1 (I) chain [1174-1190]	CO1A1_HUMAN
64	GSpGSpGPDGKTGPPGp	Collagen alpha-1 (I) chain [542-558]	CO1A1_HUMAN
65	FSDSPITVTVPEV	Clusterin [410-423]	CLUS_HUMAN
66	GSDDDDEPPPLPRL	Membrane associated progesterone receptor component 1 [54-67]	PGRC1_HUMAN
67	GpIGppGpPGLPGPPGP	Collagen alpha-1(V) chain [1525-1541]	CO5A1_HUMAN
68	VIDQSRVNLNGPIT	Uromodulin [592-605]	UROM_HUMAN
69	GLpGpPGSNGNPGpGp	Collagen alpha-1 (III) chain [879-895]	CO3A1_HUMAN
70	SLGSPSGEVSHPRKT	Alpha-2-HS-glycoprotein [325-339]	FETUA_HUMAN
71	PpGEAGKpGEQGVpGD	Collagen alpha-1 (I) chain [651-666]	CO1A1_HUMAN
72	DGQpGAKGEpGDAGAKG	Collagen alpha-1 (I) chain [820-836]	CO1A1_HUMAN
73	SpGSPGPDGKTGPPGPAG	Collagen alpha-1 (I) chain [543-560]	CO1A1_HUMAN
74	GSEADHEGTHSTKRG	Fibrinogen alpha chain [608-622]	FIBA_HUMAN
75	YKRKANDESNEHS	Osteopontin [246-258]	OSTP_HUMAN
76	SpGSpGPDGKTGPPGpAG	Collagen alpha-1 (I) chain [543-560]	CO1A1_HUMAN
77	IDQSRVNLNGPITR	Uromodulin [593-606]	UROM_HUMAN
78	NDGApGKNGERGGpGGp	Collagen alpha-1 (III) chain [586-602]	CO3A1_HUMAN
79	TGLSMDGGGSPKGDVDP	Sodium/potassium-transporting ATPase gamma chain [2-18]	ATNG_HUMAN
80	ApGGKGDAGApGERGPpG	Collagen alpha-1 (III) chain [670-687]	CO3A1_HUMAN

81	GPpGEAGKpGEQGVpGD	Collagen alpha-1 (I) chain [650-666]	CO1A1_HUMAN
82	SGDSDDEPPPLPRL	Membrane associated progesterone receptor component 1 [53-67]	PGRC1_HUMAN
83	SVIDQSRVNLGPIT	Uromodulin [591-605]	UROM_HUMAN
84	ApGSKGDTGAKGEPpVVG	Collagen alpha-1 (I) chain [438-455]	CO1A1_HUMAN
85	DGApGKNGERGGpGGPpGp	Collagen alpha-1 (III) chain [587-604]	CO3A1_HUMAN
86	MpGSpGpGSDGKpGpPG	Collagen alpha-1 (III) chain [538-555]	CO3A1_HUMAN
87	PMSIPPEVKFNKPF	Alpha-1-antitrypsin [32-45]	A1AT_HUMAN
88	EGSpGRDGSpGAKGDRG	Collagen alpha-1 (I) chain [1021-1037]	CO1A1_HUMAN
89	VGPpGppGPPGPPPSAG	Collagen alpha-1 (I) chain [1177-1195]	CO1A1_HUMAN
90	GSpGSpGPDGKTGPPGpAG	Collagen alpha-1 (I) chain [542-560]	CO1A1_HUMAN
91	LSALEEYTKKLNTQ	Apolipoprotein A-I [254-267]	APOA1_HUMAN
92	SGSVIDQSRVNLGPI	Uromodulin [589-604]	UROM_HUMAN
93	SpGEAGRpGEAGLpGAKG	Collagen alpha-1 (I) chain [522-539]	CO1A1_HUMAN
94	GLpGTGGPpGENGKPGEP	Collagen alpha-1 (III) chain [642-659]	CO3A1_HUMAN
95	KpGEQGVpGDLGApGPSG	Collagen alpha-1 (I) chain [657-674]	CO1A1_HUMAN
96	DEAGSEADHEGTHSTK	Fibrinogen alpha chain [605-620]	FIBA_HUMAN
97	GpPGPpGTSGHpGSpGSpG	Collagen alpha-1 (III) chain [180-198]	CO3A1_HUMAN
98	PpGEAGKpGEQGVpGDLG	Collagen alpha-1 (I) chain [651-668]	CO1A1_HUMAN
99	SpGSNGApGQRGEPpQG	Collagen alpha-1 (III) chain [358-375]	CO3A1_HUMAN
100	NGApGNDGAKGDAGApGApG	Collagen alpha-1 (I) chain [700-719]	CO1A1_HUMAN
101	VRYTKKVPQVSTPTL	Serum albumin [433-447]	ALBU_HUMAN
102	VVSLGSPSGEVSHPRKT	Alpha-2-HS-glycoprotein [323-339]	FETUA_HUMAN
103	TGSpGSpGPDGKTGpGpAG	Collagen alpha-1 (III) chain [586-604]	CO1A1_HUMAN
104	NDGApGKNGERGGpGGpGP	Collagen alpha-1 (I) chain [541-560]	CO3A1_HUMAN
105	GPpGEAGKpGEQGVpGDLG	Collagen alpha-1 (I) chain [650-668]	CO1A1_HUMAN
106	GPpGPpGKNGDDGEAGKpG	Collagen alpha-1 (I) chain [221-239]	CO1A1_HUMAN
107	GEKPSGEAGTAGPpGTpGP	Collagen alpha-2 (I) chain [844-863]	CO1A2_HUMAN
108	GPpGEAGKpGEQGVpGDLG	Collagen alpha-1 (I) chain [650-668]	CO1A1_HUMAN
109	GNDGApGKNGERGGpGGpGP	Collagen alpha-1 (III) chain [585-604]	CO3A1_HUMAN
110	EAIMSPPEVKFNKP	Alpha-1-antitrypsin [378-393]	A1AT_HUMAN
111	QGEAGQKGDAGAPpQpSG	Collagen alpha-2 (I) chain [851-870]	CO1A2_HUMAN
112	NDGAKGDAGApGApGSQGApG	Collagen alpha-1 (I) chain [705-725]	CO1A1_HUMAN
113	VIDQSRVNLGPITRK	Uromodulin [592-607]	UROM_HUMAN
114	GLpGTGGpPGENGKPGEPp	Collagen alpha-1 (III) chain [642-661]	CO3A1_HUMAN
115	GPpGEGRAGEpGTAGPTGpp	Collagen alpha-2 (VIII) chain [490-509]	CO8A2_HUMAN
116	GVIDQSRVNLGPITR	Uromodulin [590-606]	UROM_HUMAN
117	DEAGSEADHEGTHSTKR	Fibrinogen alpha chain [605-621]	FIBA_HUMAN
118	IGPpGPAGApGDKGESGSPGP	Collagen alpha-1 (I) chain [769-789]	CO1A1_HUMAN
119	ApGApGGKGDAGApGERGpG	Collagen alpha-1 (III) chain [667-687]	CO3A1_HUMAN
120	NSGEPGApGSKGDTGAKGEP	Collagen alpha-1 (I) chain [432-451]	CO1A1_HUMAN
121	AADHDVGSSELPEGVLGAL	ProSAAS [221-239]	PCSK1_HUMAN
122	NGApGEAGRDGNpGNDGPpG	Collagen alpha-2 (I) chain [918-937]	CO1A2_HUMAN
123	NSGEPGApGSKGDTGAKGEP	Collagen alpha-1 (I) chain [432-451]	CO1A1_HUMAN

124	EGSpGRDGSpGAKGDRGET	Collagen alpha-1 (I) chain [1021-1039]	CO1A1_HUMAN
125	DAGPAGPKGEpGSpGENGApG	Collagen alpha-1 (I) chain [279-299]	CO1A1_HUMAN
126	PMSIPPEVKFNKPFVF	Alpha-1-antitrypsin [381-396]	A1AT_HUMAN
127	DDGEAGKpGRpGERGpPGp	Collagen alpha-1 (I) chain [231-249]	CO1A1_HUMAN
128	NTKSPLFMGKVVNPTQK	Alpha-1-antitrypsin [402-418]	A1AT_HUMAN
129	GApGApGGKGDAGApGERGpPpG	Collagen alpha-1 (III) chain [666-687]	CO3A1_HUMAN
130	MGVVSLGSPSGEVSHPRKT	Alpha-2-HS-glycoprotein [321-339]	FETUA_HUMAN
131	DkGETGEQGDRIkGHRG	Collagen alpha-1 (I) chain [1095-1112]	CO1A1_HUMAN
132	APEAQVSVQPNFQQDKF	Prostaglandin-H2 D-isomerase [23-39]	PTGDS_HUMAN
133	GDDGEAGKpGRpGERGpPpGP	Collagen alpha-1 (I) chain [230-249]	CO1A1_HUMAN
134	GEKGPSGEAGTAGpGTpGPQG	Collagen alpha-2 (I) chain [844-865]	CO1A2_HUMAN
135	kGNDGApGKNGERGGpGpGP	Collagen alpha-1 (III) chain [584-604]	CO3A1_HUMAN
136	EAIPMSIPPEVKFNKPF	Alpha-1-antitrypsin [378-394]	A1AT_HUMAN
137	GDDGEAGKpGRpGERGPPpGp	Collagen alpha-1 (I) chain [230-249]	CO1A1_HUMAN
138	GEKpSGEAGTAGpGTpGPQG	Collagen alpha-2 (I) chain [844-865]	CO1A2_HUMAN
139	LRTLNPDSQLQLTTGNG	Alpha-1-antitrypsin [124-141]	A1AT_HUMAN
140	LLSPYSYSTTAVVTNPKE	Transthyretin (Prealbumin) [130-147]	TTHY_HUMAN
141	DGESGRpGRpGERGLpGPpG	Collagen alpha-1 (III) chain [230-249]	CO3A1_HUMAN
142	AGpPGPPpGpGTSGHpGSpGSpG	Collagen alpha-1 (III) chain [176-198]	CO3A1_HUMAN
143	EGSpGRDGSpGAKGDRGETGP	Collagen alpha-1 (I) chain [1021-1041]	CO1A1_HUMAN
144	GLpGTGGPpGENGKpGEPpKG	Collagen alpha-1 (III) chain [642-663]	CO3A1_HUMAN
145	GEpGGKGERGApGEKGEpGPpG	Collagen alpha-1 (III) chain [819-840]	CO3A1_HUMAN
146	SESpGHpGQpGpPGPPApGp	Collagen alpha-1 (III) chain [1174-1195]	CO3A1_HUMAN
147	SGNAGpPpGPpGAGKEGGKpPRG	Collagen alpha-1 (I) chain [889-911]	CO1A1_HUMAN
148	pPGEAGkPGEQGVPGDLGApGP	Collagen alpha-1 (I) chain [648-669]	CO1A1_HUMAN
149	SGSVIDQSRVNLNGPITRK	Uromodulin [589-607]	UROM_HUMAN
150	ALLSPYSYSTTAVVTNPKE	Transthyretin (Prealbumin) [129-147]	TTHY_HUMAN
151	PpGEAGKpGEQGVpGDLGApGP	Collagen alpha-1 (I) chain [648-669]	CO1A1_HUMAN
152	VVVKLFSDPITVTPVEV	Clusterin [405-423]	CLUS_HUMAN
153	DAGApGAPGGKGDAGApGERGpPpG	Collagen alpha-1 (III) chain [664-687]	CO3A1_HUMAN
154	NGDDGEAGKpGRpGERGpPpGP	Collagen alpha-1 (I) chain [229-249]	CO1A1_HUMAN
155	GNSGEpGApGSKGDTGAKGEpGP	Collagen alpha-1 (I) chain [431-453]	CO1A1_HUMAN
156	DAHKSEVAHRFKDLGEEN	Serum albumin [25-42]	ALBU_HUMAN
157	EGSpGRDGSpGAKGDRGETGPA	Collagen alpha-1 (I) chain [1020-1041]	CO1A1_HUMAN
158	GPpGEAGkPGEQGVPGDLGApGP	Collagen alpha-1 (I) chain [647-669]	CO1A1_HUMAN
159	GApGNDGAKGDAGApGApGSQGApG	Collagen alpha-1 (I) chain [701-725]	CO1A1_HUMAN
160	SNGNpGppGPSGSPGKDGPPpGpAG	Collagen alpha-1 (III) chain [886-909]	CO3A1_HUMAN
161	DGQPGAKGEpGDAGAKGDAGPpGP	Collagen alpha-1 (I) chain [820-843]	CO1A1_HUMAN
162	DGKTGpPGPAGQDRPGpPpGpp	Collagen alpha-1 (I) chain [550-572]	CO1A1_HUMAN

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163	DGQP ^G AKGE ^p GDAGAKGDAG ^P G ^p	Collagen alpha-1 (I) chain [820-843]	CO1A1_HUMAN
164	NGE ^p GGKGERG ^A pGEKGE ^G GP ^p G	Collagen alpha-1 (III) chain [818-840]	CO3A1_HUMAN
165	NSGE ^p G ^A pGSKGDTGAKGE ^p GP ^V G	Collagen alpha-1 (I) chain [432-455]	CO1A2_HUMAN
166	AEG ^S pGRDG ^S pGAKGDRGET ^G P ^A	Collagen alpha-1 (I) chain [1020-1042]	CO1A1_HUMAN
167	AG ^P pGEAGkPGEQGVPGDLGAP ^G p	Collagen alpha-1 (I) chain [646-669]	CO1A1_HUMAN
168	AG ^P pGEAGK ^p GEQGVpGDLGAP ^G P	Collagen alpha-1 (I) chain [646-669]	CO1A1_HUMAN
169	ADGQP ^G AKGE ^p GDAGAKGDAG ^P GP ^p	Collagen alpha-1 (I) chain [819-843]	CO1A1_HUMAN
170	NGDDGEAGK ^p GR ^p GERGPPG ^p Q	Collagen alpha-1 (I) chain [229-250]	CO1A1_HUMAN
171	NDG ^P pGRDGQpGHKGERGY ^p G	Collagen alpha-2 (I) chain [932-952]	CO1A2_HUMAN
172	ADGQP ^G AKGE ^p GDAGAKGDAG ^P GP ^p	Collagen alpha-1 (I) chain [819-843]	CO1A1_HUMAN
173	NGA ^p GNDGAKGDAGApGApGS ^Q GAp ^G	Collagen alpha-1 (I) chain [700-725]	CO1A1_HUMAN
174	LRTL ^N QPSQLQLTTGNGLF	Alpha-1-antitrypsin [124-143]	A1AT_HUMAN
175	GNSGE ^p GApGSKGDTGAKGE ^p G ^P VG	Collagen alpha-1 (I) chain [431-455]	CO1A1_HUMAN
176	NGDDGEAGK ^p GR ^p GERGPPG ^p Q ^G	Collagen alpha-1 (I) chain [229-251]	CO1A1_HUMAN
177	GKNGDDGEAGK ^p GR ^p GERGPP ^G p	Collagen alpha-1 (I) chain [227-249]	CO1A1_HUMAN
178	GRTGDAGPVGPPG ^p PpGppGpPGP ^{PS}	Collagen alpha-1 (I) chain [1169-1193]	CO1A1_HUMAN
179	GADGQP ^G AKGE ^p GDAGAKGDA ^G PpGP	Collagen alpha-1 (I) chain [818-843]	CO1A1_HUMAN
180	GKNGDDGEAGK ^p GR ^p GERGPP ^G p	Collagen alpha-1 (I) chain [227-249]	CO1A1_HUMAN
181	GE ^p GDDG ^p SGAEGPPG ^p QGLAG ^{QR}	Collagen alpha-1 (II) chain [957-980]	CO2A1_HUMAN
182	IEQNTKSP ^L FMGKVVNPTQK	Alpha-1-antitrypsin [399-418]	A1AT_HUMAN
183	GADGQP ^G AKGE ^p GDAGAKGDA ^G PpGP	Collagen alpha-1 (I) chain [818-843]	CO1A1_HUMAN
184	KGDAGApGApGGKGDAGApGE ^R Gp ^G	Collagen alpha-1 (III) chain [662-687]	CO3A1_HUMAN
185	QNGE ^p GGKGERG ^A pGEKGE ^G GP ^p G	Collagen alpha-1 (III) chain [817-840]	CO3A1_HUMAN
186	ADGQP ^G AKGE ^p GDAGAKGDAG ^P pGPA	Collagen alpha-1 (I) chain [819-844]	CO1A1_HUMAN
187	ADGQP ^G AKGE ^p GDAGAKGDAG ^P pGpA	Collagen alpha-1 (I) chain [819-844]	CO1A1_HUMAN
188	ADGQ ^p GAKGE ^p GDAGAKGDAG ^P pGpA	Collagen alpha-1 (I) chain [819-844]	CO1A1_HUMAN
189	LREGETKAVKTVRTPGAAANLE	Alpha-1B-glycoprotein [435-456]	A1BG_HUMAN

190	GQNGEpGGKGERGApGEKGE GpG	Collagen alpha-1 (III) chain [816-840]	CO3A1_HUMAN
191	KGNSGEpGApGSKGDTGAKGEp GPVG	Collagen alpha-1 (I) chain [430-455]	CO1A1_HUMAN
192	DAHKSEVAHRFKDLGEENFK	Serum albumin [25-44]	ALBU_HUMAN
193	GKNGDDGEAGKpGRpGERGpP GPQ	Collagen alpha-1 (I) chain [227-250]	CO1A1_HUMAN
194	GKNGDDGEAGKpGRpGERGpP PQ	Collagen alpha-1 (I) chain [227-250]	CO1A1_HUMAN
195	MIEQNTKSPLFMGKVVNPTQK	Alpha-1-antitrypsin [398-418]	A1AT_HUMAN
196	mIEQNTKSPLFmGKVVNPTQK	Alpha-1-antitrypsin [398-418]	A1AT_HUMAN
197	LDGAKGDAGPAGpKGEpGSpGE NGApG	Collagen alpha-1 (I) chain [273-299]	CO1A1_HUMAN
198	DAHKSEVAHRFKDLGEENFKA	Serum albumin [25-45]	ALBU_HUMAN
199	ADGQPGAKGEpGDAGAKGDAG PpGPAGP	Collagen alpha-1 (I) chain [819-846]	CO1A1_HUMAN
200	ADGQpGAKGEpGDAGAKGDAG pPGPAGP	Collagen alpha-1 (I) chain [819-846]	CO1A1_HUMAN
201	TGPIGPpGPAGAPGDkGESGPS PAGPTG	Collagen alpha-1 (I) chain [766-794]	CO1A1_HUMAN
202	pPGADGQPGAKGEpGDAGAKG DAGPPGp	Collagen alpha-1 (I) chain [816-843]	CO1A1_HUMAN
203	GADGQpGAKGEpGDAGAKGDA GpPGPAGP	Collagen alpha-1 (I) chain [818-846]	CO1A1_HUMAN
204	LmIEQNTKSPLFMGKVVNPTQK	Alpha-1-antitrypsin [397-418]	A1AT_HUMAN
205	GPPGADGQpGAKGEpGDAGAK GDAGpPGP	Collagen alpha-1 (I) chain [815-843]	CO1A1_HUMAN
206	DAHKSEVAHRFKDLGEENFKA L	Serum albumin [25-46]	ALBU_HUMAN
207	GPpGADGQpPGAKGEpGDAGA KGDAGpPGP	Collagen alpha-1 (I) chain [815-843]	CO1A1_HUMAN
208	DEAGSEADHEGTHSTKRGHAK SRP	Fibrinogen alpha chain [605-628]	FIBA_HUMAN
209	GApGQNGEpGGKGERGApGEK GEGGPpG	Collagen alpha-1 (III) chain [815-840]	CO3A1_HUMAN
210	DDILASPPRLPEPQYPGAPHHS S	Collagen alpha-1 (XVIII) chain [1296-1319]	CO1A1_HUMAN
211	AGPpGApGApGAPGPVGPAGKS GDRGETGP	Collagen alpha-1 (I) chain [1042-1071]	CO1A1_HUMAN
212	AGPpGApGApGApGPVGPAGKS GDRGETGP	Collagen alpha-1 (I) chain [1042-1071]	CO1A1_HUMAN
213	GPpGADGQpGAKGEpGDAGAK GDAGpPGPA	Collagen alpha-1 (I) chain [815-844]	CO1A1_HUMAN
214	DAHKSEVAHRFKDLGEENFKA LV	Serum albumin [25-47]	ALBU_HUMAN
215	QGpPGPSGEEGKRGNPGEAGSA GPPGppG	Collagen alpha-2 (I) chain [369-397]	CO1A2_HUMAN
216	ERGEAGIpGVpGAKGEDGKDGS pGEpGA	Collagen alpha-1 (III) chain [448-475]	CO3A1_HUMAN
217	YQHLADSKNDNDNIFLSPLSIST	Antithrombin-III [95-118]	ANT3_HUMAN

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218	NRGERGSESPGHPGQPpGpp GApGP	Collagen alpha-1 (III) chain [1168-1195]	CO3A1_HUMAN
219	NRGERGSESPGHPGQPpGpp PGApGP	Collagen alpha-1 (III) chain [1168-1195]	CO3A1_HUMAN
220	KDGEAGAQQpGPAGPAGERG EQGPAGSpG	Collagen alpha-1 (I) chain [612-641]	CO1A1_HUMAN
221	LLKNGERIEKVEHSDLSFSKDW S	Beta-2-microglobulin [59-81]	B2MG_HUMAN
222	KNGETGPQPPGPTGPGGDKGD TGPpGpQG	Collagen alpha-1 (III) chain [610-639]	CO3A1_HUMAN
223	DAHKSEVAHRFKDLGEENFKA LVL	Serum albumin [25-48]	ALBU_HUMAN
224	ERGSpGPAGPKGSpGEAGRpGE AGLpGAKG	Collagen alpha-1 (I) chain [510-539]	CO1A1_HUMAN
225	KEGGKGPpRGETGPAGRpGEVGP pGppGPAG	Collagen alpha-1 (I) chain [903-932]	CO1A1_HUMAN
226	GPPGADGQpGAKGepGDAGAK GDAGppGPAGP	Collagen alpha-1 (I) chain [815-843]	CO1A1_HUMAN
227	IPVKQADSGSSEEKQLYNKYPD AVAT	Osteopontin [17-42]	OSTP_HUMAN
228	LkGQpGApGVkGepGApGENGTp GQTGARG	Collagen alpha-2 (I) chain [188-217]	CO1A2_HUMAN
229	ESGREGAPGAEGSpGRDGSpGA KGDRGETGP	Collagen alpha-1 (I) chain [1011-1041]	CO1A1_HUMAN
230	ESGREGApGAEGSpGRDGSpGA KGDRGETGP	Collagen alpha-1 (I) chain [1011-1041]	CO1A1_HUMAN
231	GESGREGApGAEGSpGRDGSpG AKGDRGETGP	Collagen alpha-1 (I) chain [1010-1041]	CO1A1_HUMAN
232	LTGSpGSpGPDGkTGPPGPAGQD GRPGppGppG	Collagen alpha-1 (I) chain [537-569]	CO1A1_HUMAN
233	ESGREGApGAEGSpGRDGSpGA KGDRGETGPA	Collagen alpha-1 (I) chain [1011-1042]	CO1A1_HUMAN
234	DGVSGGEGKGGSDGGGSHRKE GEEADAPGVIPG	CD99 antigen [97-129]	CD99_HUMAN
235	DAAQKTDTSHHDQDHPTFNKIT PNLAE	Alpha-1-antitrypsin [30-56]	A1AT_HUMAN
236	ADGQPGAKGEPGDAGAKGDA GPPGpAGPAGPPGPIG	Collagen alpha-1 (I) chain [819-854]	CO1A1_HUMAN
237	ADGQPGAKGEPGDAGAKGDA GPPGPAGpAGpPGPIG	Collagen alpha-1 (I) chain [819-854]	CO1A1_HUMAN
238	ADGQpGAKGepGDAGAKGDA GpPGPAGPAGPPGpIG	Collagen alpha-1 (I) chain [819-854]	CO1A1_HUMAN
239	GADGQPGAKGEPGDAGAKG DAGPPGPAGpAGpPGPIG	Collagen alpha-1 (I) chain [818-854]	CO1A1_HUMAN
240	GADGQPGAKGEPGDAGAKGD AGPPGPAGPAGPpGpIG	Collagen alpha-1 (I) chain [818-854]	CO1A1_HUMAN
241	GERGSpGGpGAAGFpGARGLp GpPGSNGNPGpGp	Collagen alpha-1 (III) chain [861-895]	CO3A1_HUMAN
242	GEpGRDGVpGGpGMRGmpGSp GGpGSDGKpGppG	Collagen alpha-1 (III) chain [522-555]	CO3A1_HUMAN

243	PPGESGREGApGAEGSpGRDG SpGAKGDRGETGP	Collagen alpha-1 (I) chain [1008-1041]	CO1A1_HUMAN
244	PpGESGREGApGAEGSpGRDG SpGAKGDRGETGP	Collagen alpha-1 (I) chain [1008-1041]	CO1A1_HUMAN
245	TVNFGDTEEAKKQINDYVEK GTQGKIVDL	Alpha-1-antitrypsin [168-196]	A1AT_HUMAN
246	RTGEVGA VGpPGFAGEKGPSG EAGTAGPPGTpGpQG	Collagen alpha-2 (I) chain [830-865]	CO1A2_HUMAN
247	ENGKPGEpGpKGDAGApGApG GKG DAGApGERGpPG	Collagen alpha-1 (III) chain [652-687]	CO3A1_HUMAN
248	RTGEVGA VGpPGFAGEkGPSG EAGTAGPPGTpGpQG	Collagen alpha-2 (I) chain [830-865]	CO1A2_HUMAN
249	GPpGESGREGAPGAEGSpGRD GSpGAKGDRGETGp	Collagen alpha-1 (I) chain [1007-1041]	CO1A1_HUMAN
250	NTGApGSpGVSGPKGDAGQP GEKSPGAQGPpGApGp	Collagen alpha-1 (III) chain [910-946]	CO3A1_HUMAN
251	pPGESGREGApGAEGSpGRDG SpGAKGDRGETGPA	Collagen alpha-1 (I) chain [1008-1042]	CO1A1_HUMAN
252	GPpGESGREGApGAEGSpGRD GSpGAKGDRGETGPA	Collagen alpha-1 (I) chain [1007-1042]	CO1A1_HUMAN
253	EEKAVADTRDQADGSRASVD SGSSEEQGGSSRA	Polymeric-immunoglobulin receptor [607-639]	PIGR_HUMAN
254	pPGADGQPGA KGE PGDAGAK GDAGPPGPAGPAGPPGpIG	Collagen alpha-1 (I) chain [816-854]	CO1A1_HUMAN
255	EDPQGDAAQKTDTSHHDQDH PTFNKITPNL	Alpha-1-antitrypsin [25-54]	A1AT_HUMAN
256	VAWKADSSPVKAGVETTPS KQSNKYAASSY	Ig lambda chain C regions [39-70]	LAC_HUMAN
257	ARGNDGARGSDGQGPpGppG TAGFpGSpGAKGEVGP	Collagen alpha-1 (III) chain [319-355]	CO3A1_HUMAN
258	DLPETGVWPPEPPRTDPPQPP RPDDPWPAGP	Psoriasis susceptibility 1 candidate gene 2 protein [75-105]	PS1C2_HUMAN
259	NTGApGSpGVSGPKGDAGQP GEKSPGAQGPpGApGpLG	Collagen alpha-1 (III) chain [910-948]	CO3A1_HUMAN
260	NTGApGSpGVSGpKGDAGQpG EKSpGAQGPpPGAPGpLG	Collagen alpha-1 (III) chain [910-948]	CO3A1_HUMAN
261	FAEEKAVADTRDQADGSRAS VDSGSSEEQGGSSRA	Polymeric-immunoglobulin receptor [605-639]	PIGR_HUMAN
262	EDPQGDAAQKTDTSHHDQDH PTFNKITPNLAE	Alpha-1-antitrypsin [25-56]	A1AT_HUMAN
263	DQGPVGR TGEVGA VGPPGFA GEKGP SGEAGTAGppGTPGP	Collagen alpha-2 (I) chain [824-863]	CO1A2_HUMAN
264	GRPEAQPPPLSSEHKEPVAGD AVPGPKDGSAPVVRGA	Neurosecretory protein VGF [26-62]	VGF_HUMAN
265	DQGPVGR TGEVGA VGPPGFA GEKGPSGEAGTAGPpGTpGpQ G	Collagen alpha-2 (I) chain [824-865]	CO1A2_HUMAN
266	ANGApGNDGAKGDAGApGAp GSQGApGLQGMpGERGAAGL PGp	Collagen alpha-1 (I) chain [699-741]	CO1A1_HUMAN
267	ANGApGNDGAKGDAGApGAp	Collagen alpha-1 (I) chain [699-741]	CO1A1_HUMAN

	GSQGApGLQGMpGERGAAGL pGp		
268	ERGEQGPAGSpGFQGLpGpAG ppGEAGKpGEQGVPGDLGAPG PSG	Collagen alpha-1 (I) chain [630-674]	CO1A1_HUMAN
269	EEKAVADTRDQADGSRASVD SGSSEEQGGSSRALVSTLVPL G	Polymeric-immunoglobulin receptor [607-643]	PIGR_HUMAN
270	ARGNDGARGSDGQpGppGPPG TAGFPGSpGAKGEVGpAGSpG SNGApG	Collagen alpha-1 (III) chain [319-366]	CO3A1_HUMAN
271	ARGNDGARGSDGQpGpPGPpG TAGFpGSpGAKGEVGpAGSpG SNGApG	Collagen alpha-1 (III) chain [319-366]	CO3A1_HUMAN
272	LQGLpGTGGppGENGKpGEPG PkGDAGAPGAPGGkGDAGAP GERGppG	Collagen alpha-1 (III) chain [640-687]	CO3A1_HUMAN
273	LQGLPGTGGppGENGKpGEpG pKGDAGApGApGGKGDAGAp GERGpPG	Collagen alpha-1 (III) chain [640-687]	CO3A1_HUMAN