Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Molecular mimicry between SARS-CoV-2 and human proteins

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To the Editor,

COVID-19 resemble immune dysregulation conditions, with hyper-activated immune system and cytokine storm [1,2]. In relation, molecular mimicry is drawing attention among possible mechanisms of autoimmune phenomena in COVID-19 [3–10]. Kanduc and Shoenfeld [11–16] searched related potential adverse events and peptide sharing between proteins of human and such pathogens, including SARS-CoV-2 [12–14]. In line with those studies, here it is aimed to draw attention to 7–9 residue matches in several known human proteins with a 15mer palindromic SARS-CoV-2 peptide (Table 1). Respective aligned sequences are predicted to contain peptides that both bind strongly to the same MHC supertype representative, based on predictions by NetMHCcons 1.1 and/or NetCTLpan 1.1 tools [17,18].

Associated diseases of some of those proteins listed in Table 1 are obtained from the human gene database GeneCards [20]. Accordingly, associated diseases of neuronal acetylcholine receptor subunit alpha-2 associated diseases involve Epilepsy and Nocturnal Frontal Lobe, 4, and Autosomal Dominant Nocturnal Frontal Lobe Epilepsy; that of Arginyl-tRNA synthetase-like involve Pontocerebellar Hypoplasia 6, Type 6 and Type 1; that of Tsukushin involve Barre-Lieou Syndrome and Spondylolisthesis; that of Golgi pH regulator B involve Chromosome 1Q21.1 Deletion Syndrome, 1.35-Mb and Hemochromatosis, Type 2A; that of Phospholipid phosphatase-related protein type 5 involve deafness, Autosomal Dominant 1, and Bardet-Biedl Syndrome 10; that of Solute carrier family 15 member 5 involve Dicarboxylic Aminoaciduria and Hydranencephaly; that of Adenosine receptor A2b involve Priapism and Cholera; that of Slit homolog 2 protein involve Cakut and Crohn's Colitis; that of Solute carrier family 35 member B1 involve Dicarboxylic Aminoaciduria and Hydranencephaly; that of Metabotropic glutamate receptor 5 involve Fragile X Syndrome and Fragile X-Associated Tremor/Ataxia Syndrome; that of Protein crumbs homolog 1 involve Leber Congenital Amaurosis 8 and Retinitis Pigmentosa 12. Relationships of those proteins with autoimmunity can be mentioned further. E.g., plasminogen activation system has important functions, and its deregulation is connected to pathological conditions like cancer, bacterial infection, fibrosis, neurogenerative diseases, muscular dystrophy, and rheumatoid arthritis [21]. Besides, elevated plasmin(ogen) was suggested to be a risk factor for COVID-19 susceptibility [22]. Plasminogen receptor KT is a membrane protein, expression of which increases on the surface upon inflammatory stimuli, like in case of several other plasminogen receptors [21]. Its contribution to the inflammatory diseases, together with the cell-surface associated plasmin activity, is yet to be elucidated, particularly in conditions where macrophages play a preeminent role in the pathogenesis, for being highly expressed at the proinflammatory macrophages [21]. Examples of such diseases are microglial cells and neuroinflammatory disease, Kupfer cells and hepatotoxic injury, Mi-type adipose tissue macrophage and obesity [21]. Another one, adenosine receptor A2b was suggested to play a role in inflammation [23], and immunoglobulin heavy chain variable 5–51, was reported to be among the modulated-genes in the patients with systemic sclerosis, which is characterized by immune system alterations, for being an autoimmune connective tissue disease [24]. Immunoglobulin heavy chain variable 5–51 is also among the 115 genes that are co-occurring with the disease autoimmune hemolytic anemia, in the abstracts of biomedical publications from the DISEASES Text-mining Gene-Disease Association Evidence Scores dataset [25]. Last, antibodies against metabotropic glutamate receptor 5 is among the antibodies that are possibly associated with autoimmune encephalitis [26,27]. Inhibitors of metabotropic glutamate 5 receptor were offered as a therapeutic strategy to fight against COVID-19 [28], and it was suggested that the therapeutic effect would be acting through interfering with the viral hijacking of the host protein synthesis [28]. It is worth to mention in the end that, other than one immunoglobulin heavy chain junction region (sequence ID MCG41834.1), the highest statistical significance in the alignments are observed for the peptides of slit homolog 2 protein and the solute carrier family proteins, among the proteins that are mentioned above.

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Table 1
Human proteins that align with SARS-CoV-2 peptide CFLGYFCTCYFGLFC [19] with more than 7 residue matches. They are predicted to contain epitopes with at least 5 residue matches to the respective epitope regions in the query. Alignments are displayed as they are presented in the original file, but matching residues are written bold. Those residues in the predicted epitope parts are still bold if present. Yet they are further underlined if present in both query and subject epitopes. Gaps in the alignments are not shown in the epitopes. Numbers in front of the epitope pairs indicate the HLA allele and the predictor, as specified at the title row. However, only the epitopes predicted by NetMHCcons are displayed when significant predictions that are indicated at both 1 and 2, or 3 and 4, are present.

Alignments, top: query	1	HLA-A*24:02, NetMHCcons	3	HLA-A*02:01, NetMHCcons	Protein name
(Matches in bold)	2	HLA-A*24:02, NetCTLpan	4	HLA-A*01:01, NetCTLpan	Sequence ID (only the 1st)
CFLG**YF**CTCY**F**G**LFC**	1	CFLGYFCTCYFGLF			**hCG1995581, partial**
CFSS**YF**—**FLLFC**	2	CFSSYFFLLF			EAW57092.1
CFLG**Y**FCTC**YFGLF**	1	CFLGYFCTCYFGLF			**Immunoglobulin heavy chain junction region**
CFVG—**SC**-**FGLF**	2	CFVGSCFGLF			MON77051.1
CFLGYFC**T**CYF**GLF**	1	CFLGYFCTCYFGLF			**Neuronal acetylcholine receptor subunit alpha-2**
CFLG—**T**-I**GLF**	2	CFLGTIGLF			NP_001334636.1
CFLGY**F**CTC**YFGLF**	1	CFLGYFCTCYFGLF	3	FLGYFCTCYFGL	**arginyl-tRNA synthetase-like, isoform CRA_b, partial**
CFL-**F**I-**YF**I**LF**	2	CFLFIYFILF		FLFIYFI**LF**	EAW48585.1
FLGYFCT—**CYFGLFC**			4	FLGYFCTCY	**immunoglobulin heavy chain variable region, partial**
FIGY- **CSSTS****CYTGGFC**				FIGYCSSTSCY	CEF94348.1
CFLGYFC**T**C—**YFGLF**	1	CFLGYFCTCYFGLF			**unnamed protein product; E2IG4; tsukushin isoform b precursor**
CFPG-**CQC**EVET**FGLF**		CFPGCQCEVETFGLF			BAG52371.1; AAF09483.1; NP_001245139.1
FLGYFCTCY**F**GLF**C**			3	FLGYFCTCYFGL	**G protein-coupled receptor 89C, partial; Golgi pH regulator B; unnamed protein product; Golgi pH regulator A**
FLGYF—**F**SIY**C**			4	FLGYFFSI	CAI17085.1; NP_001337112.1; BAG63613.1; NP_001091082.2
FLG-**Y**FC**T**CY**FGLF**			3	FLGYFCTCYFGL	**unnamed protein product; PAP2D protein, partial; Phospholipid phosphatase-related protein type 5**
FLGIY-**T**-**FGLF**				FLGIYTFGL	BAG58540.1; AAH40174.1; XP_011539140.1
FLGYFCTCYFG**LF**	1	GYFCTCYFGLF			**Solute carrier family 15 member 5**
FLEYFSTC—**LF**	2	EYFSTCLF			NP_001164269.1
CFLGYFC**TCYFGL**			3	FLGYFCTCYFGL	**Immunoglobulin heavy chain junction region**
CALG—**TCY**YGL				ALGTCYYGL	MOL37243.1
FLGYFCTC**Y**-**FGLF**			3	FLGYFCTCYFGL	**Phospholipid phosphatase-related protein type 2**
FLG—V**YSFGLF**				FLGVYSFGL	XP_024307423.1
CFLGYFCTC**YFGL**	1	CFLGYFCTCYFGLF	3	FLGYFCTCYFGL	**Immunoglobulin heavy chain junction region**
CYLGYW—**YFDL**	2	CYLGYWYFDL		YLGYWYFDL	MCC33910.1
CFLGYFCTC**YFGL**			3	FLGYFCTCYFGL	**Immunoglobulin heavy chain junction region**
CFLHY—**YYGL**				FLHYYYGL	MOQ87140.1
FLGYFCTC**YFGL**F	1	GYFCTCYFGLF			**Adenosine receptor A2b**
FLGY-MV**YFNFF**	2	GYMVYFNFF			EAX04485.1
FLGYFC**T**CYFG**LF**			3	FLGYFCTCYFGL	**[Protein ADP-ribosylarginine] hydrolase-like protein 1**
FLGSLCT—**ALF**				FLGSLCTAL	NP_954631.1
FLGYFCTCYFG**LF**	2	GYFCTCYFGLF	3	FLGYFCTCYFGL	**Transmembrane protein 250**
FLLYF-SC-S**LF**		LYFSCSLF		FLLYFSCSL	NP_001243455.1
FLGYFCTCYFGLF	1	GYFCTCYFGLF			**chromosome 9 open reading frame 46; Plasminogen receptor (KT)**
FLKYFGT-F**FGL**	2	KYFGTFFGL			EAW58764.1; XP_005251569.1
FL-**GYFCTCYFGL**	1	GYFCTCYFGLF	3	FLGYFCTCYFGL	**Immunoglobulin heavy chain junction region**
FLTGYYAT**PYFDL**	2	GYYATPYFDL	4	FLTGYYATPYFDL	MOM08080.1
LGYFCT—**CYFGLF**	1	GYFCTCYFGLF			**Immunoglobulin heavy chain junction region**
LGY-**CSSTSCYFGF**F	2	GYCSSTSCYFGFF			MCG41834.1
GYFCTC—**YFGLFC**	1	GYFCTCYFGLF			**Slit homolog 2 protein**
GYTCICPEG**YSGLFC**		GYTCICPEGYSGLF			XP_011512212.2
FLGYFCTC**YFGL**			3	FLGYFCTCYFGL	**Immunoglobulin heavy chain junction region**
FLGY—**YYGL**				FLGYYYGL	MOP50498.1
CFLGYFC**TCYF**	2	CFLGYFCTCYF	4	FLGYFCTCY	**unnamed protein product; Solute carrier family 35 member B1**
CFLGVF-**VCYF**		CFLGVFVCYF		FLGVFVCY	BAG58831.1; XP_011522481.1
LGYFCTCYFGL	2	GYFCTCYFGL			**Chain A, Metabotropic glutamate receptor 5, Lysozyme and Endolysin**
LGYLCT-F**XL**		GYLCTFXL			4OO9_A and 6FFH_A
LGYFCTCYFGL			4	FLGYFCTCY	**Immunoglobulin gamma 2 heavy chain variable region, partial**
LGTF-**TYYYGL**				LGTFTYYY	ADM43945.1
GYFCTCYFGLF	1	GYFCTCYFGLF			**hypothetical protein; Protein crumbs homolog 1**
GYSCLC-**FGNF**	2	GYSCLCFGNF			CAE45845.1; XP_011507671.1
GYFCTCYFGL	2	GYFCTCYFGL			**Immunoglobulin heavy chain junction region**
GYFY-**YFGL**		GYFYYFGL			MOL71978.1
GYFCTCYFGL	2	GYFCTCYFGL			**Immunoglobulin heavy chain junction region**
GYFTTGYFDL		GYFTTGYFDL			MOM22920.1
GYFCTCYF	1	GYFCTCYFGLF			**hCG2028737**
GYFCTNYF	2	GYFCTNYF			EAW73174.1

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