

The identification of new peptide sequences that would be added to the list published by Sollid et al., 2020¹ and result in the 2021 celiac disease peptide sequence collection was initiated in November 2020 by conducting three publication searches.

- A search of the Core Collection of Web of Science and Medline using the term:

TS=((celiac* or coeliac* or ((gluten or glutenin or gliadin) near/3 (intoleran* or sensiti*))) AND (wheat or barley or spelt or rye or oat or gliadin or gluten*) and (peptid* or epitop* or motif) AND (t-cell-epitop* OR t-cell-receptor OR t-cell-response or tcell or TCR or MHC or HLA-DQ2 OR HLA-DQ8) AND (activat* or recogn* or stimulat* or response*))

- And searches to identify publications that cited either Sollid et al., 2020¹ or Sollid et al., 2012².

All three searches were confined to a timeframe between January 1, 2019 through November 2, 2020. Publications identified by the three searches were collated, yielding a total of 106 publications after removal of duplicates.

[See publication list](#)

The 106 publications were divided into four approximately equal sized groups and each group was assigned to two reviewers such that each of the 106 publications received two independent reviews.

The reviewers were tasked with identifying whether the publication contained one of two classes of information that identified novel peptides that were not listed in the Table 1 of Sollid et al., 2020¹.

- Did the publication feature structural data of a complex composed of an HLA-DQ molecule, a peptide and a T-Cell receptor?
- Did the publication fulfill the criteria described in Sollid et al., 2012².
 - Reactivity against the epitope must have been defined by at least one specific T-cell clone.
 - The HLA-restriction element involved must have been unequivocally defined.
 - The nine-amino acid core of the epitope must have been defined either by an analysis with truncated peptides and/or HLA-binding with lysine scan of the epitope or comparable approach.

¹ Sollid, L. M., Tye-Din, J. A., Qiao, S.-W., Anderson, R. P., Gianfrani, C., and Konig, F. (2020). Update 2020: nomenclature and listing of celiac disease relevant gluten epitopes recognized by CD4+ T cells. *Immunogenetics* 72, 85–88.

² Sollid L, Qiao SW, Anderson R, Gianfrani C, Koning F (2012) Nomenclature and listing of celiac disease relevant gluten T-cell epitopes restricted by HLA-DQ molecules. *Immunogenetics* 64: 455–460.

Using this approach four publications containing information regarding peptides not listed in the Table 1 of Sollid et al., 2020¹ were identified.

Publication	Notes
Ruiz-Carnicer, A., et al. (2019). "Celiac Immunogenic Potential of alfa-Gliadin Epitope Variants from Triticum and Aegilops Species." <i>Nutrients</i> 11(2): 13.	DQ2.5-glia- α 3 variant, FLP <u>Q</u> LPYPQ This peptide is one of several DQ2.5-glia- α 3 epitope variants that were assayed and exceeds the respective canonical positive control in both the T-cell assay and mAb-binding testing as shown in Figure 6c. No other epitope variants in the publication meet or exceed their respective canonical control in both the T-cell and mAb-binding assay.
Pilolli, R., et al. (2019). "Scouting for Naturally Low-Toxicity Wheat Genotypes by a Multidisciplinary Approach." <i>Scientific Reports</i> 9: 15.	While several new peptides were presented, none were evaluated by T-cell activation assays or amino acid scanning. Rather peptides were identified by mass spectrometry of proteolytic digests of wheat protein extract and peptides were then assigned a restricted core epitope using bioinformatics.
Petersen, J., et al. (2020). "T cell receptor cross-reactivity between gliadin and bacterial peptides in celiac disease." <i>Nature Structural & Molecular Biology</i> 27(1): 49-+.	<p>DQ2-P.fluor-α1a PMPMP<u>E</u>LPY DQ2-P.fluor-α1b PMPLP<u>D</u>LPY DQ2-E.cloac-ω1a PFPEGE<u>E</u>QPF DQ2-P.fluor-α2a PMP<u>E</u>LPYPA DQ2-P.fluor-α2b PLP<u>E</u>LPYPA DQ2-B.copro-α2a PLP<u>D</u>LPYPV DQ2-P.aerug-α2a VQSE<u>E</u>LPYPE</p> <p>Upon review of the data seven peptides were identified, each was trimmed to a core of nine amino acids. For peptides containing a critical "E", both "E" and "Q" containing versions of the peptides should be used for searches as this amino acid is likely subject to transamidation. For peptides containing "D", only use "D" containing versions should be used in searches. This stance is subject to modification if and when evidence of transamidation of this residue is published. DQ2-<u>E</u>.copro-α2a will be renamed to DQ2-<u>E</u>.copro-α2a to reflect the likely source of the peptide, <i>Phocaeicola coprophilus</i>. Trimming of two amino acids from the amino terminus of DQ2-P.aerug-α2a was performed to retain the proline and charged glutamic acid at the carboxy terminus.</p>
Sanchez-Leon, S., et al. (2019). "Stimulatory Response of Celiac Disease Peripheral Blood Mononuclear Cells Induced by RNAi Wheat Lines Differing in Grain Protein Composition." <i>Nutrients</i> 11(12): 16.	While this publication contains new peptide sequences, it was not possible to verify the reliability of the data because the references cited in the supplementary data were not reflected in the bibliography. Attempts to contact the lead author to identify these citations were unsuccessful.

Therefore, the following newly identified peptides will be added to those sequences listed in Table 1 of Sollid et al., 2020.

DQ2.5-glia- α 3var	FLP <u>Q</u> LPYPQ
DQ2.5-glia- α 3var*	FLP <u>E</u> <u>Q</u> LPYPQ
DQ2-P.fluor- α 1a	PMPMP <u>E</u> LPY
DQ2-P.fluor- α 1a*	PMPMP <u>Q</u> LPY
DQ2-P.fluor- α 1b	PMPLP <u>D</u> LPY
DQ2-E.cloac- ω 1a	PFPEGE <u>E</u> QPF
DQ2-E.cloac- ω 1a*	PFPEGE <u>Q</u> QPF
DQ2-P.fluor- α 2a	PMP <u>E</u> LPYPA
DQ2-P.fluor- α 2a*	PMP <u>Q</u> LPYPA
DQ2-P.fluor- α 2b	PLP <u>E</u> LPYPA
DQ2-P.fluor- α 2b*	PLP <u>Q</u> LPYPA
DQ2-P.copro- α 2a	PLP <u>D</u> LPYPV
DQ2-P.aerug- α 2a	VQS <u>E</u> LPYPE
DQ2-P.aerug- α 2a*	VQS <u>Q</u> LPYPE

A complete selection of 2021 celiac peptides (updated from the 2020 celiac peptide table as described), including transamidations can be found [here](#)

A complete selection of 2020 celiac peptides (from Sollid et al., 2020), including transamidations can be found [here](#)