

5 April 2019



# Exclusion criteria for the safety assessment of proteins regarding their capacity to cause celiac

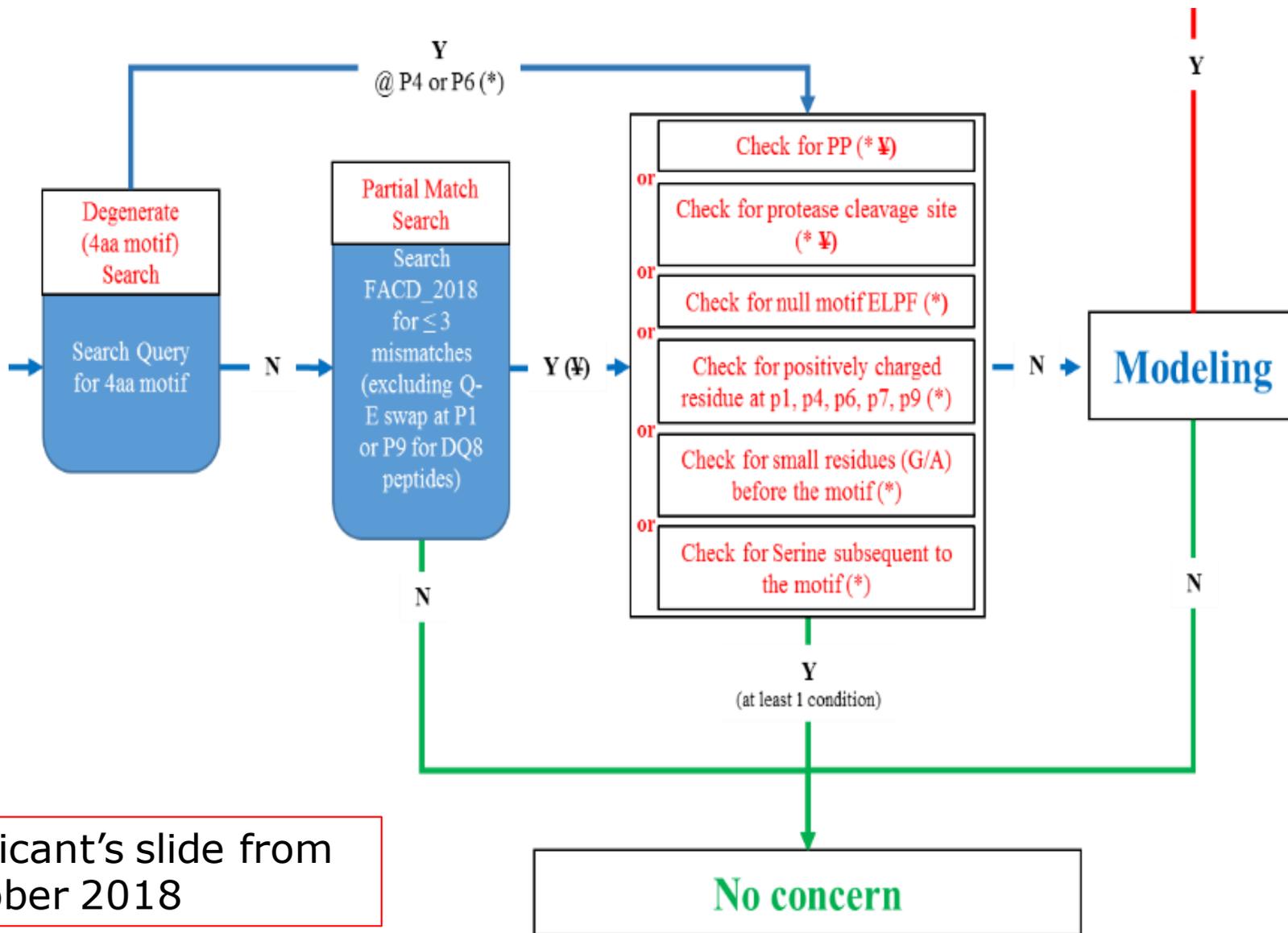
Trusted science for safe food

## EXCLUSION CRITERIA

### Main aspects to highlight

- Positively charge amino acids at positions p1, p4, p6, p7 and p9
- P-P not present in T-cell epitopes
- P-X-P in addition to the motif is associated with the most immunogenic epitopes
- Examples on the safety assessment of peptides requiring additional investigations in Annex A-2
- Any interest in EFSA proving additional examples? Can this serve to produce supplementary exclusion criteria?

# EXCLUSION CRITERIA BY APPLICANTS



Applicant's slide from October 2018

Molecular mimicry?

Cross-reactivity between microbial antigens and gluten epitopes?

**Glia- $\alpha$ 1**

**PFPQPELPY**

**Bacterial peptide 1**

**6 matches**

**Bacterial peptide 2**

**5 matches**

**Glia- $\alpha$ 2**

**PQPELPYPQ**

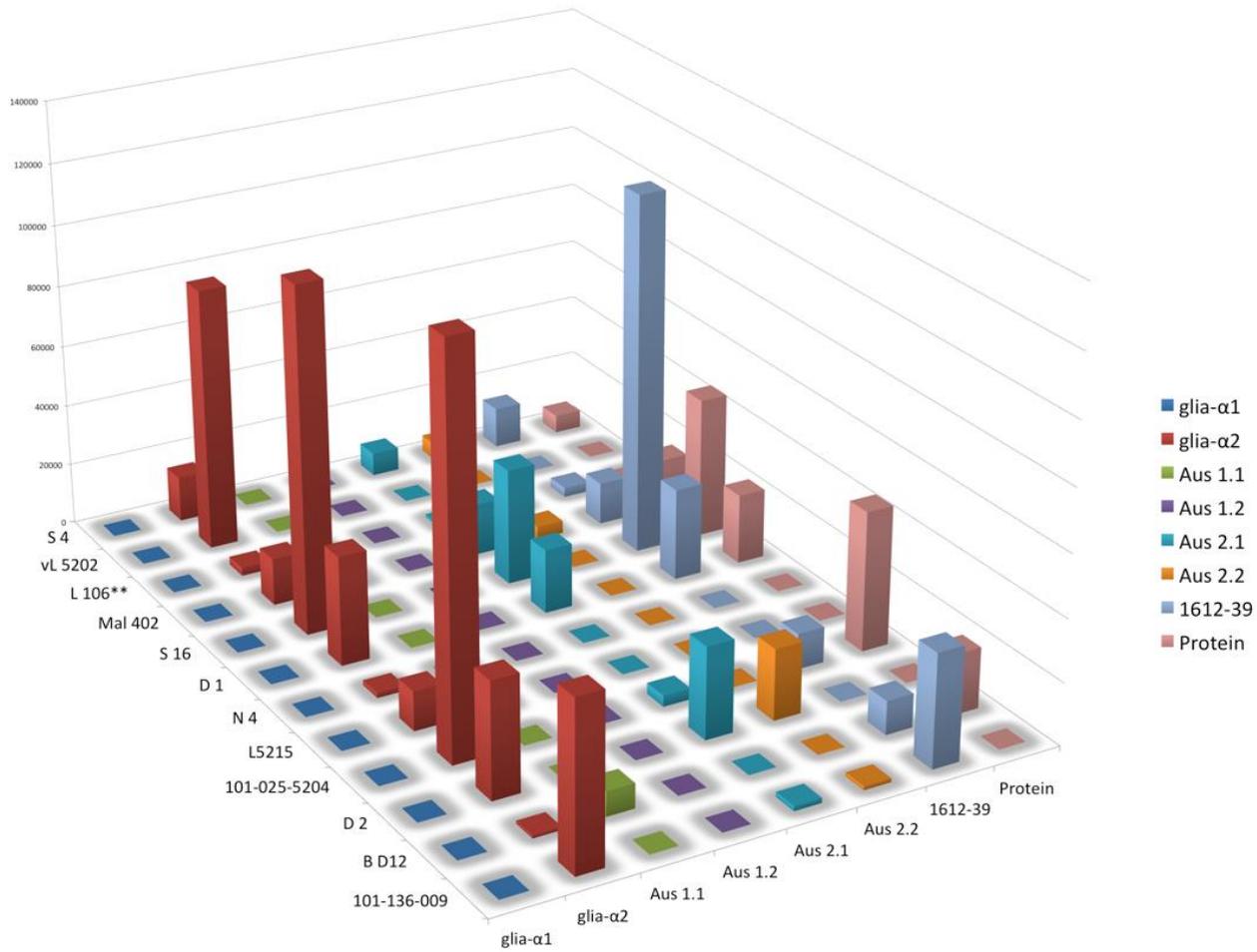
**Bacterial peptide 3**

**7 matches**

**Bacterial peptide 4**

**5 matches**

**All have the Q/E-X1-P-X2 motif**



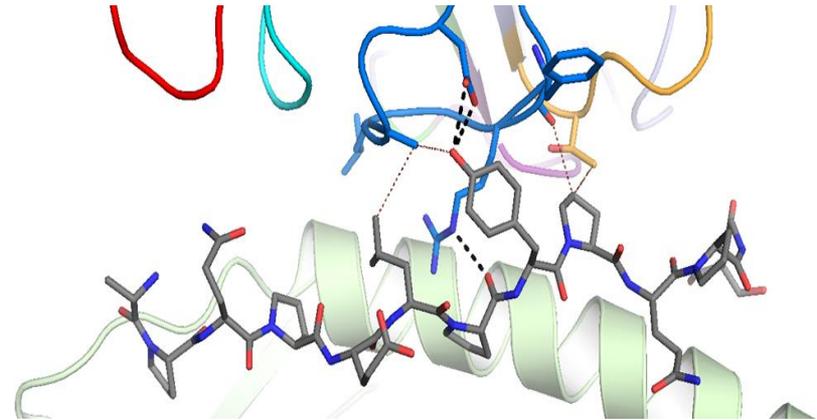
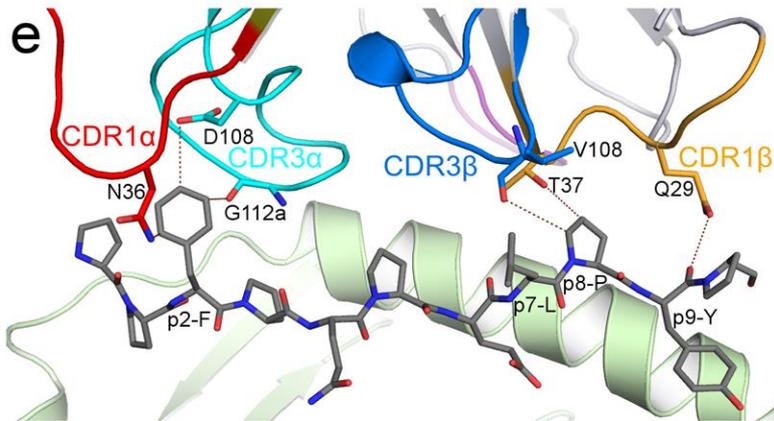
# Predicted protease cleavage sites, i.e. Trypsin

- Potential cleavage site does not automatically translate to actual cleavage site or 100% efficiency.
  - Glia- $\alpha$ 3 epitope: FRPQQPYPQ

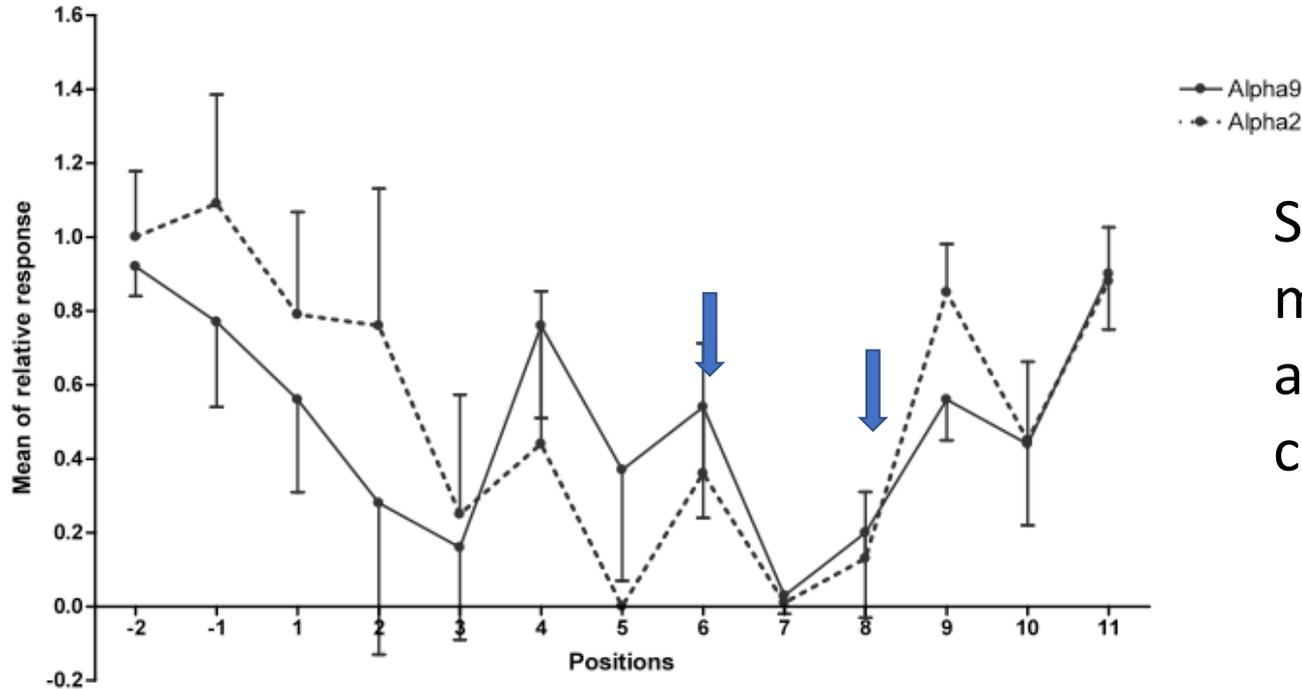
Cannot be used as exclusion criterium

# “Null” motif ELPF

- In PQPELPYPQ Y > F can affect T cell recognition
- In PFPQPELPY it does NOT



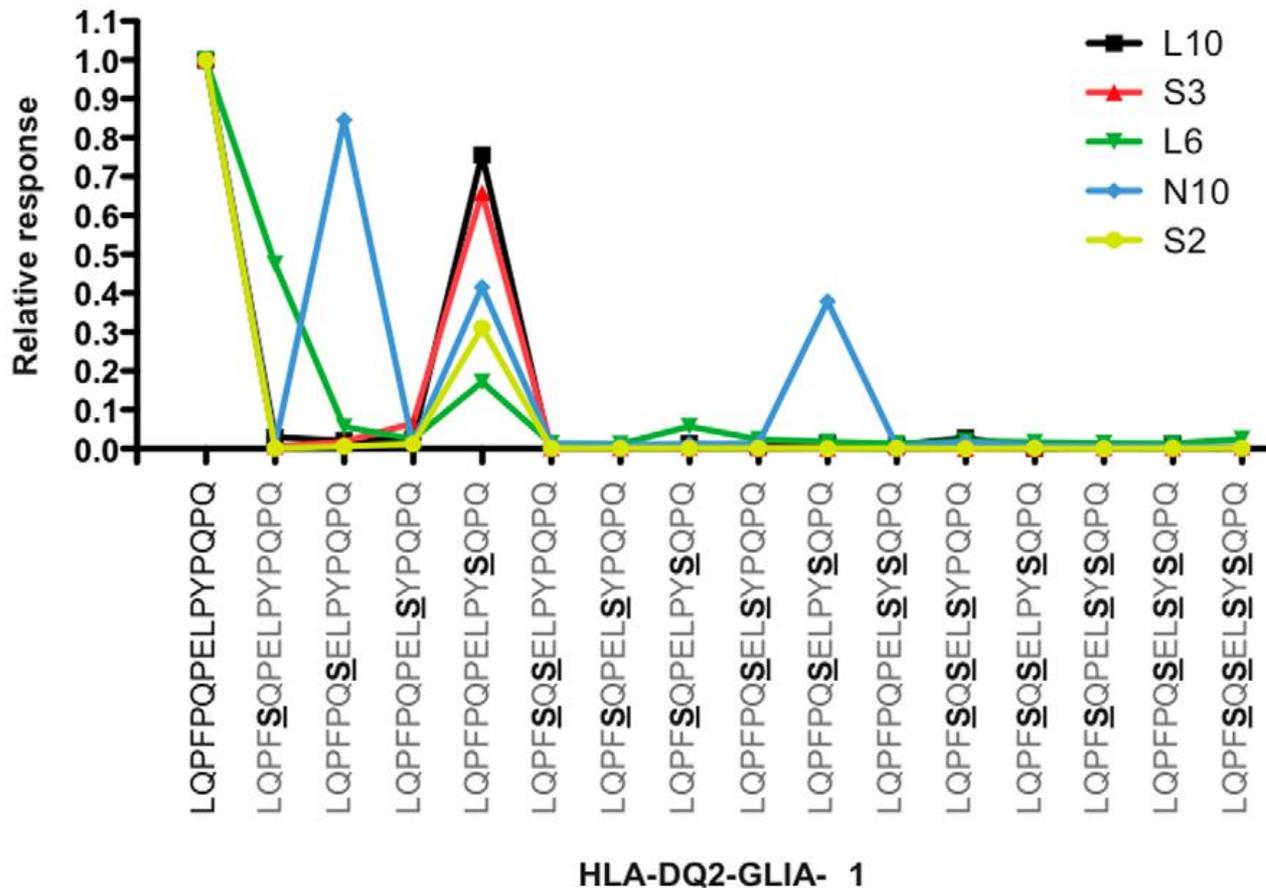
## Petersen et al. NSMB 2014: Alanine substitutions Glia- $\alpha$ 1 and - $\alpha$ 2



Small residue before motif cannot be used as exclusion criterium.

E L P Y

E L P Y



Serine after motif cannot be used as exclusion criterium.

## Partial matches: Q/E-X1-P-X2 motif is present

**PF****P****Q****P****Q****L****P****Y** and  
**AL****P****L****T****Q****L****P****A**

4 identical, two invisible, one  
conservative:

POTENTIAL HAZARD

**P****Q****P****Q****L****P****Y****P****Q** and  
**P****L****T****Q****L****P****A****S****R**

4 identical, one conservative BUT  
Y > A, P > S and Q > R prohibit recognition:

NO HAZARD

## Partial matches: Q/E-X1-P-X2 motif is NOT present

**QGSFQPSQQ** and

**EGSIQAGQQ**

5 identical, one conservative, one enhances binding:

**POTENTIAL HAZARD**

**QGSFQPSQQ** and

**QGLFSPSAQ**

6 identical BUT

Critical T cell receptor contact residues differ:

**NO HAZARD**



## Subscribe to

[www.efsa.europa.eu/en/news/newsletters](http://www.efsa.europa.eu/en/news/newsletters)  
[www.efsa.europa.eu/en/rss](http://www.efsa.europa.eu/en/rss)



## Engage with careers



## Follow us on Twitter

@efsa\_eu  
@plants\_efsa  
@methods\_efsa