

The case of celiac disease

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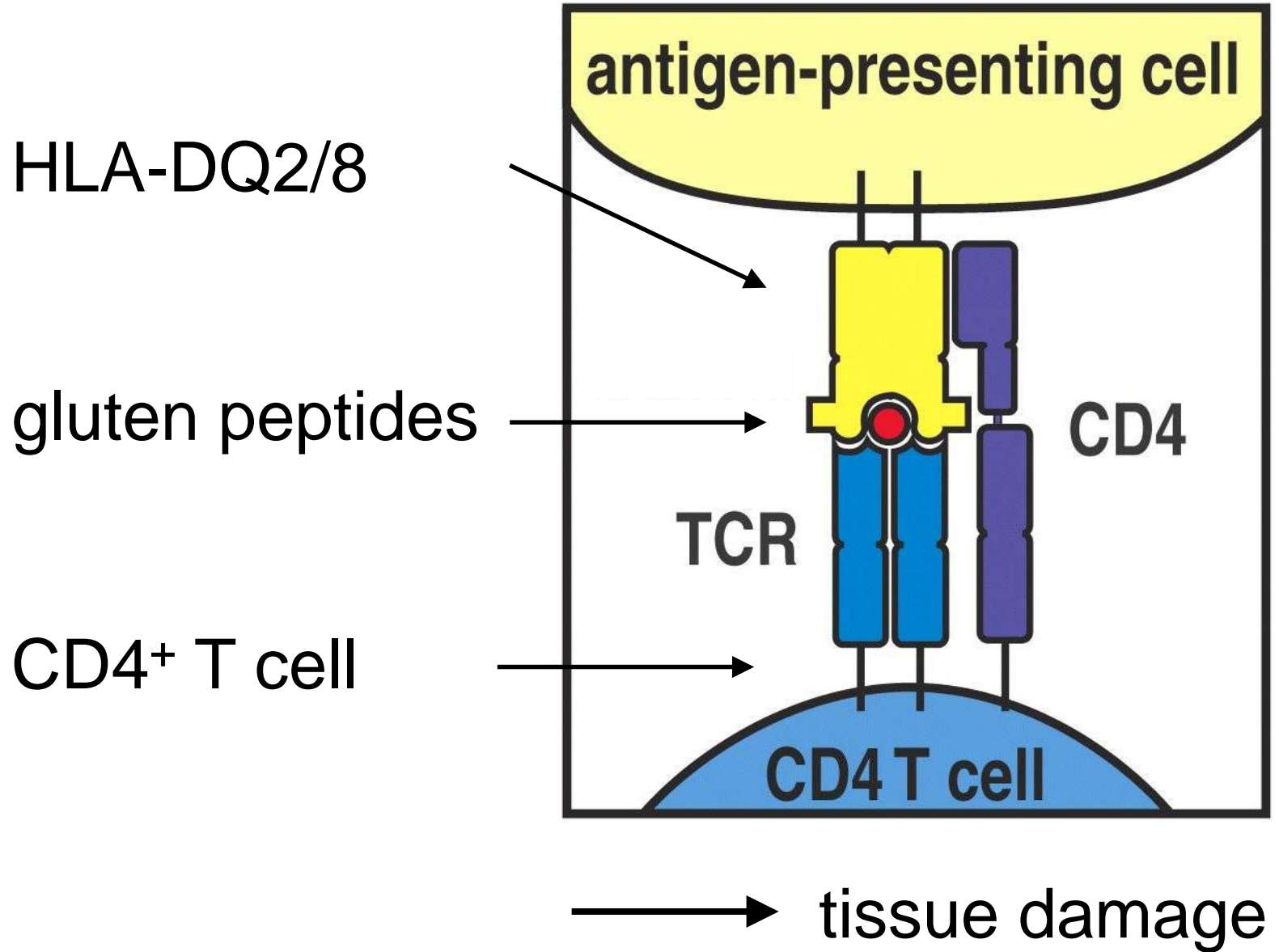
I have nothing to disclose

Celiac Disease

Gene: HLA-DQ2/8

Environment: Gluten

Effector: T cells

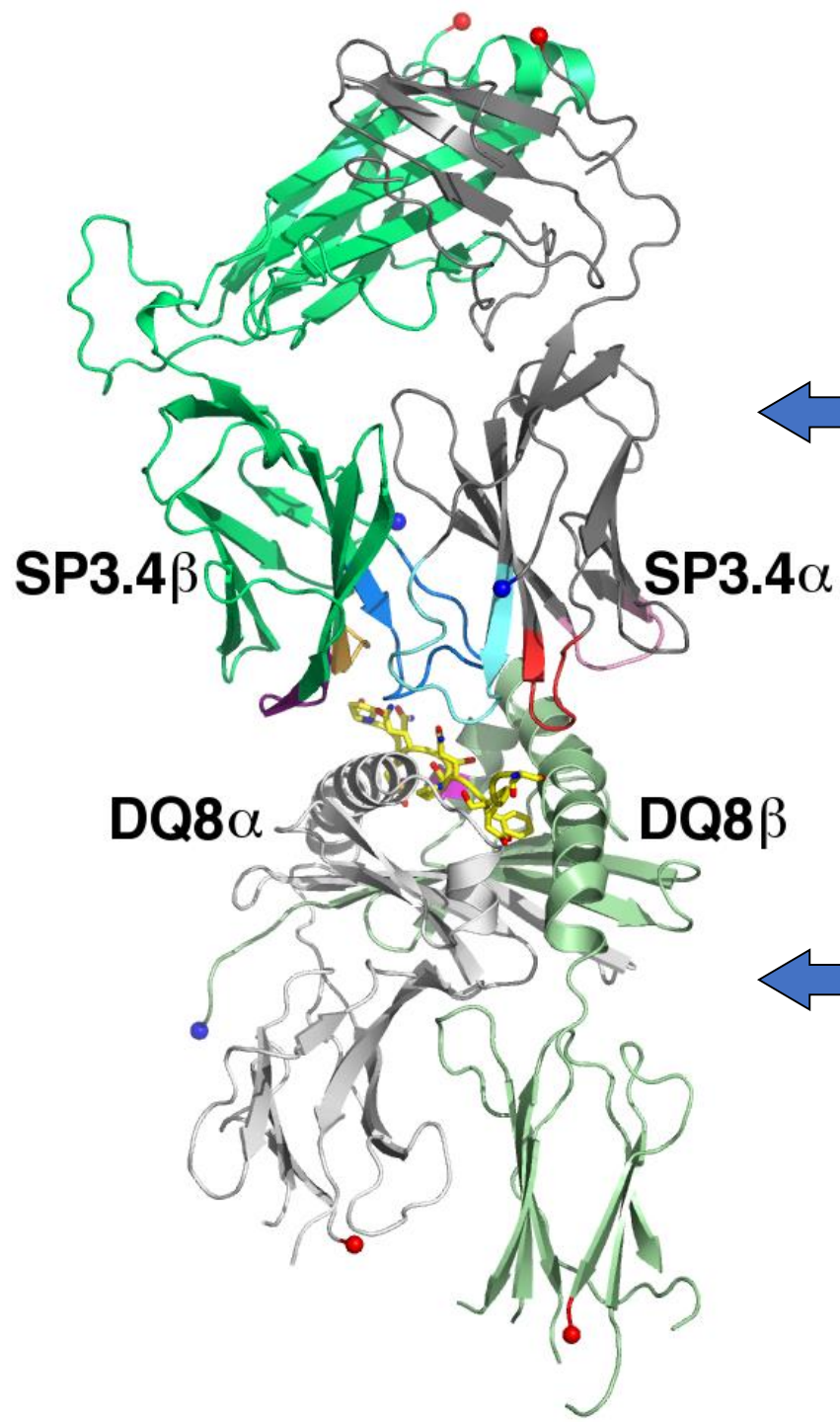


**Structure of complex
between**

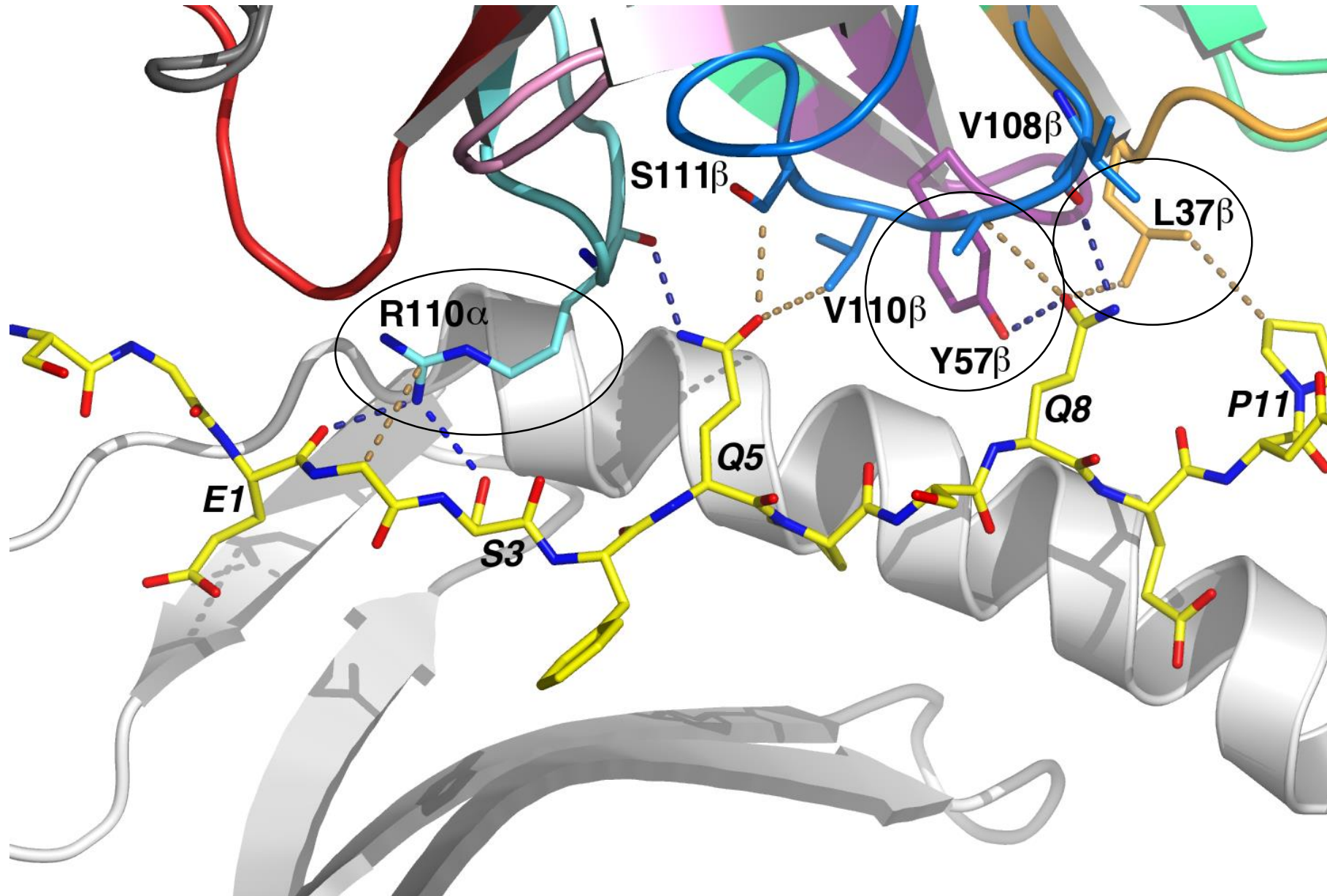
T cell receptor

and

HLA-DQ8-gliadin



TCR-DQ8-gliadin interface



DQ2 restricted epitopes

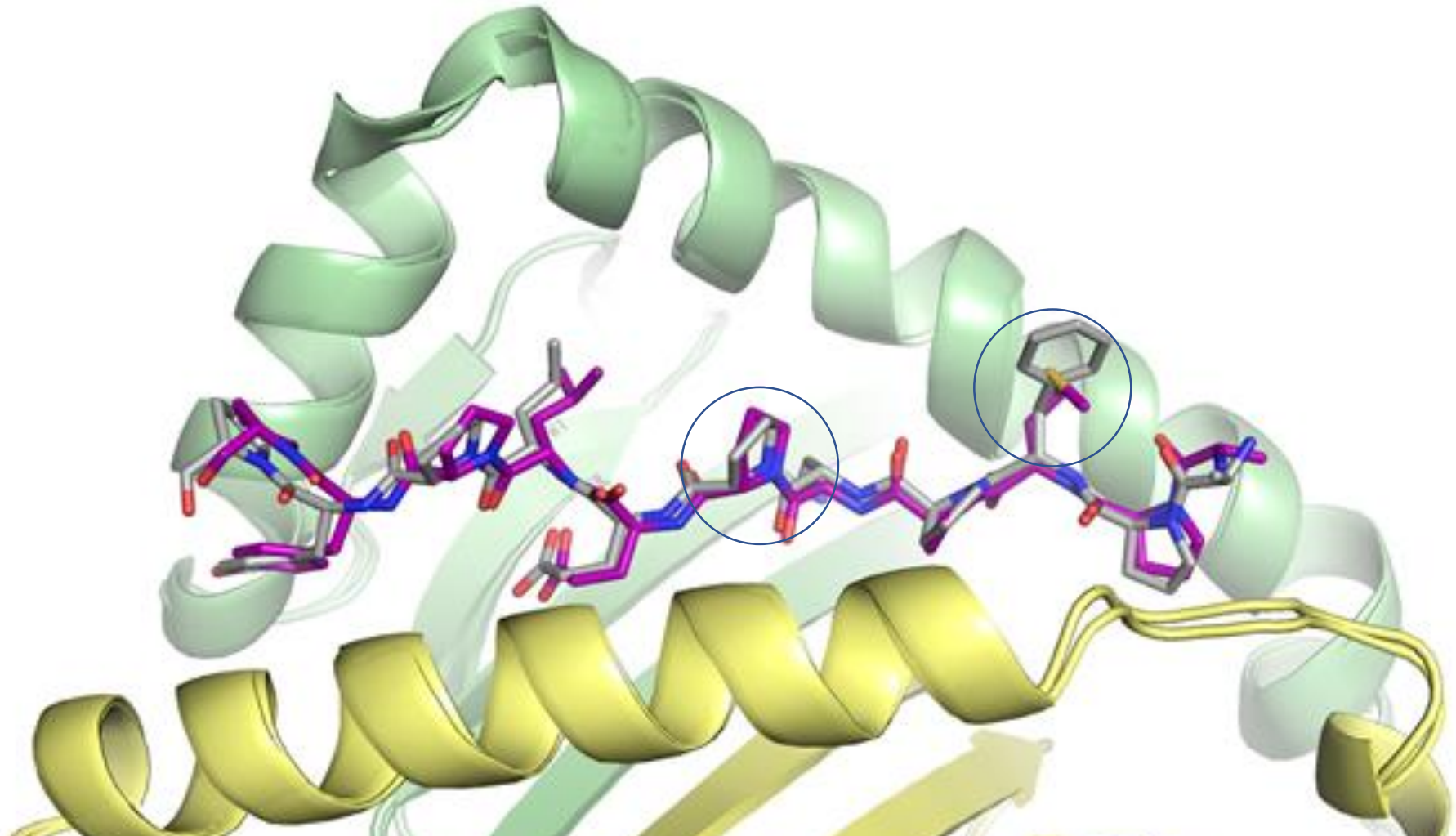
Epitope	Motif	Reference
DQ2.5-glia- α 1a	P F P Q P Q L P Y	Arentz-Hansen et al. (2000)
DQ2.5-glia- α 1b	P Y P Q P Q L P Y	Arentz-Hansen et al. (2002)
DQ2.5-glia- α 2	P Q P Q L P Y P Q	Arentz-Hansen et al. (2000)
DQ2.5-glia- α 3	F R P Q Q P Y P Q	Vader et al. (2002b)
DQ2.5-glia- γ 1	P Q Q S F P Q Q Q	Sjöström et al. (1998)
DQ2.5-glia- γ 2	I Q P Q Q P A Q L	Qiao et al. (2005), Vader et al. (2002b)
DQ2.5-glia- γ 3	Q Q P Q Q P Y P Q	Arentz-Hansen et al. (2002)
DQ2.5-glia- γ 4a	S Q P Q Q Q F P Q	Arentz-Hansen et al. (2002)
DQ2.5-glia- γ 4b	P Q P Q Q Q F P Q	Qiao et al. (2005)
DQ2.5-glia- γ 4c	Q Q P Q Q P F P Q	Arentz-Hansen et al. (2002)
DQ2.5-glia- γ 4d	P Q P Q Q P F C Q	Qiao (unpublished)

Q/E-X1-P-X2

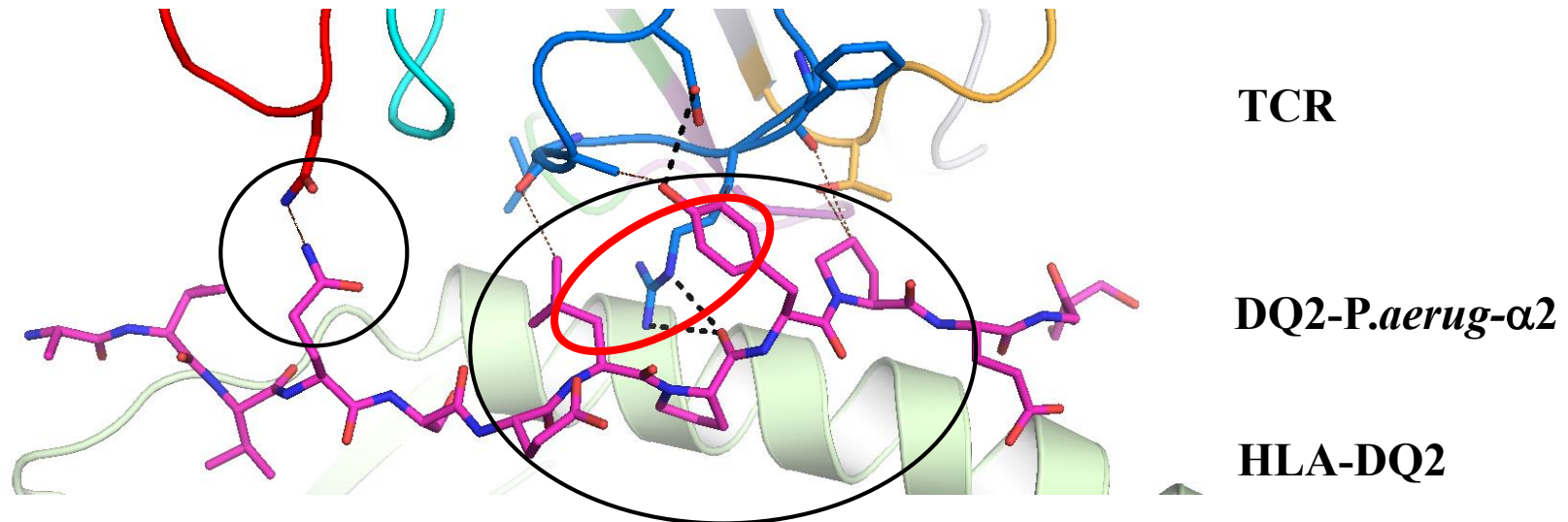
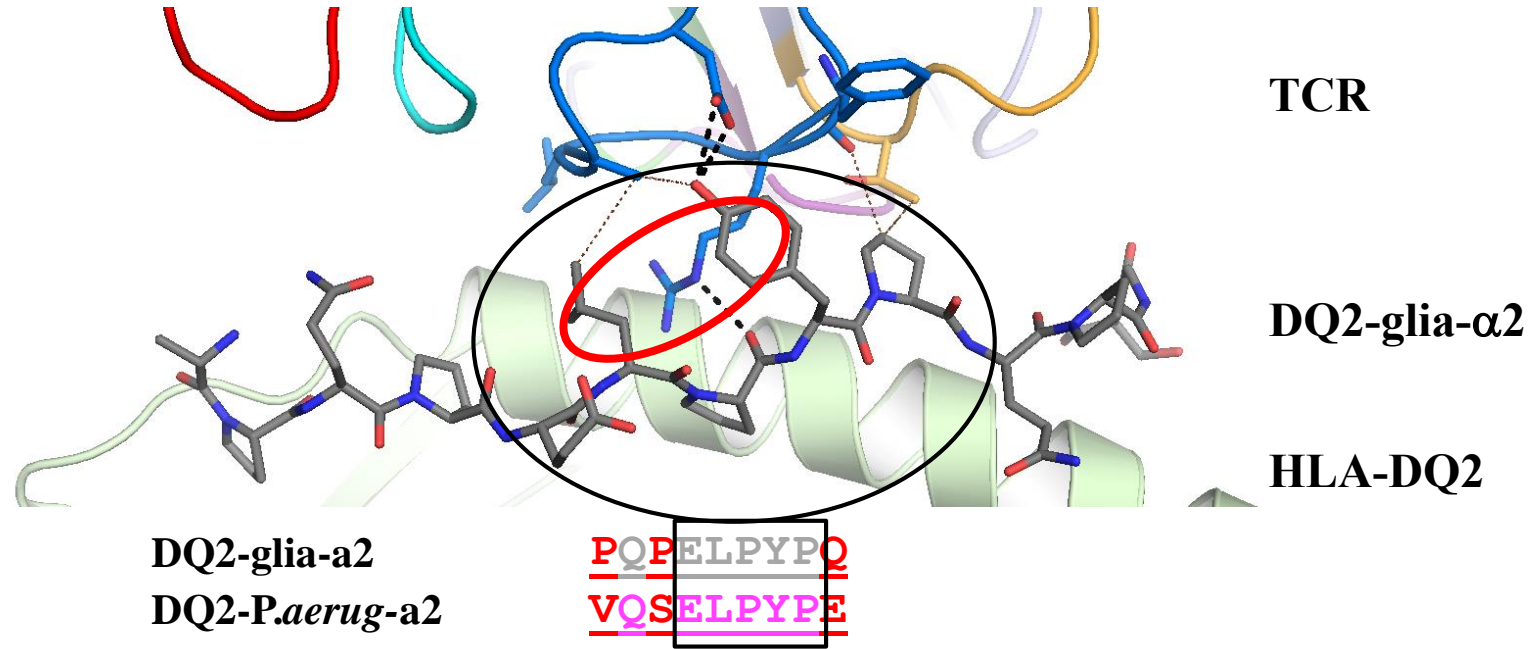
Bacterial peptides that resemble gluten peptides

Glia- α 1	PFPQPELPY
Pseudomonas	PMMPPELPY
Bordetella	PYTLPELPY
Glia- α 2	PQPELPYPQ
Pseudomonas	PMPELPYPA
Bordetella	VQSELPYPE

DQ2.5-glia- α 1 vs. DQ2.5-pseudoA1.1
PFQPELPY PMPMPELPY



T cell cannot discriminate between gluten and bacterial peptides!



Conclusions

- We know which gluten sequences are harmful
- We know why gluten sequences are harmful
- We know what is required for binding to HLA-DQ and what is required for the T cell receptor to respond
- We know that microorganisms can encode gluten-like epitopes

- Therefore, we can and should screen any GMO protein for potentially harmful sequences
- In silico tools:
 - Q/E-X1-P-X2 motif
 - Critical amino acids for binding to HLA-DQ and T cell receptor
 - Molecular docking

Thank you!

This work was performed in collaboration with

Dr. Jan Petersen

Dr. Hugh Reid

Prof. Dr. Jamie Rossjohn

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