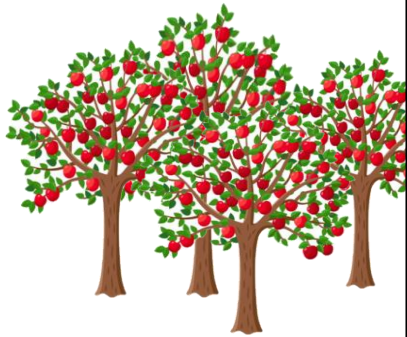


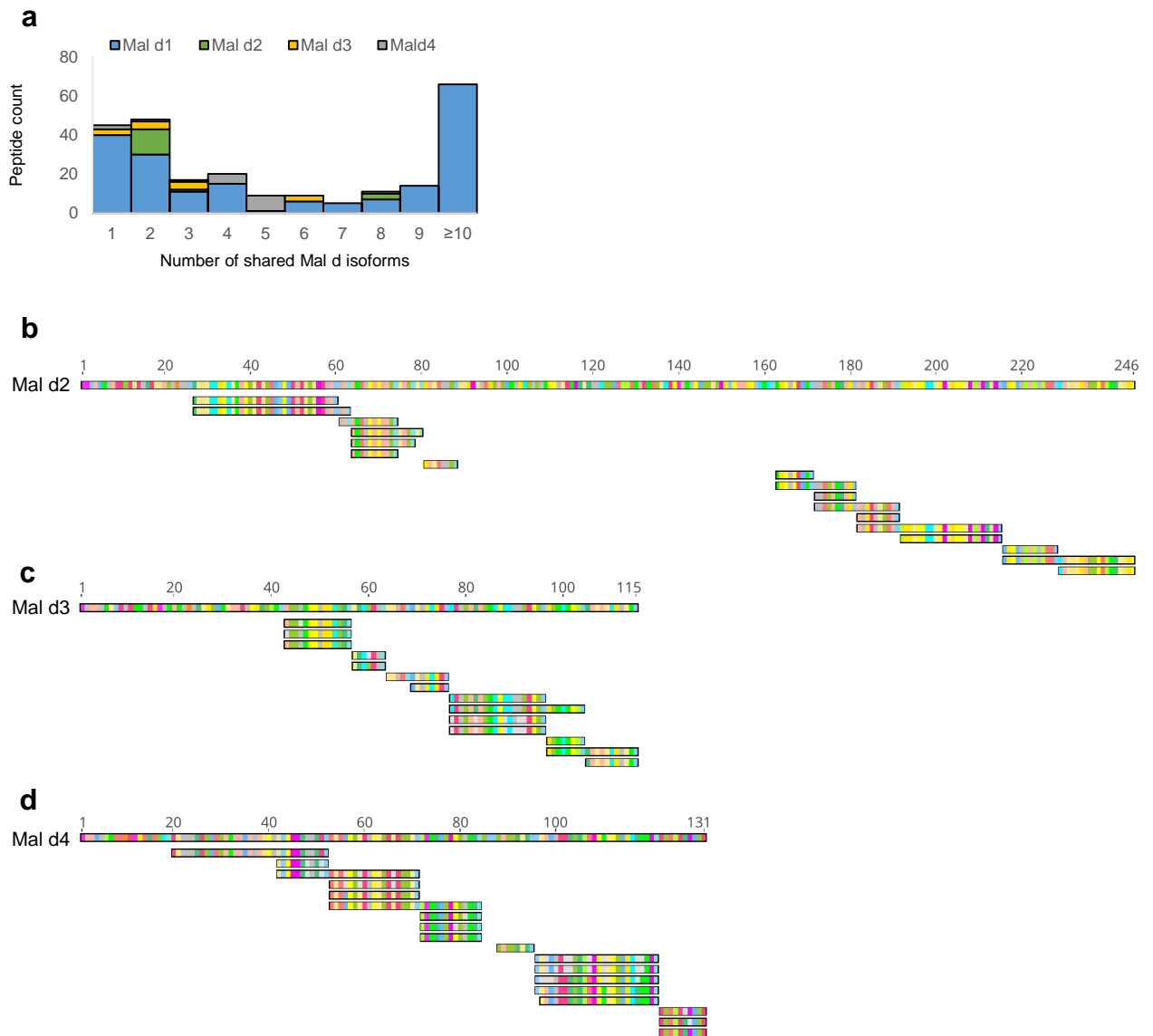
Supplementary Figure S1. Boxplot presentation of the recorded symptom scores for each genotype tested in the human study of the consecutive harvest years 2017 (Romer et al., 2020), 2018 (Romer et al., 2020) and 2019. Boxplots indicate the median (horizontal line in the box), the 25th and 75th percentile (box), the 10th and 90th percentile (whiskers) and remaining outliers (dots).



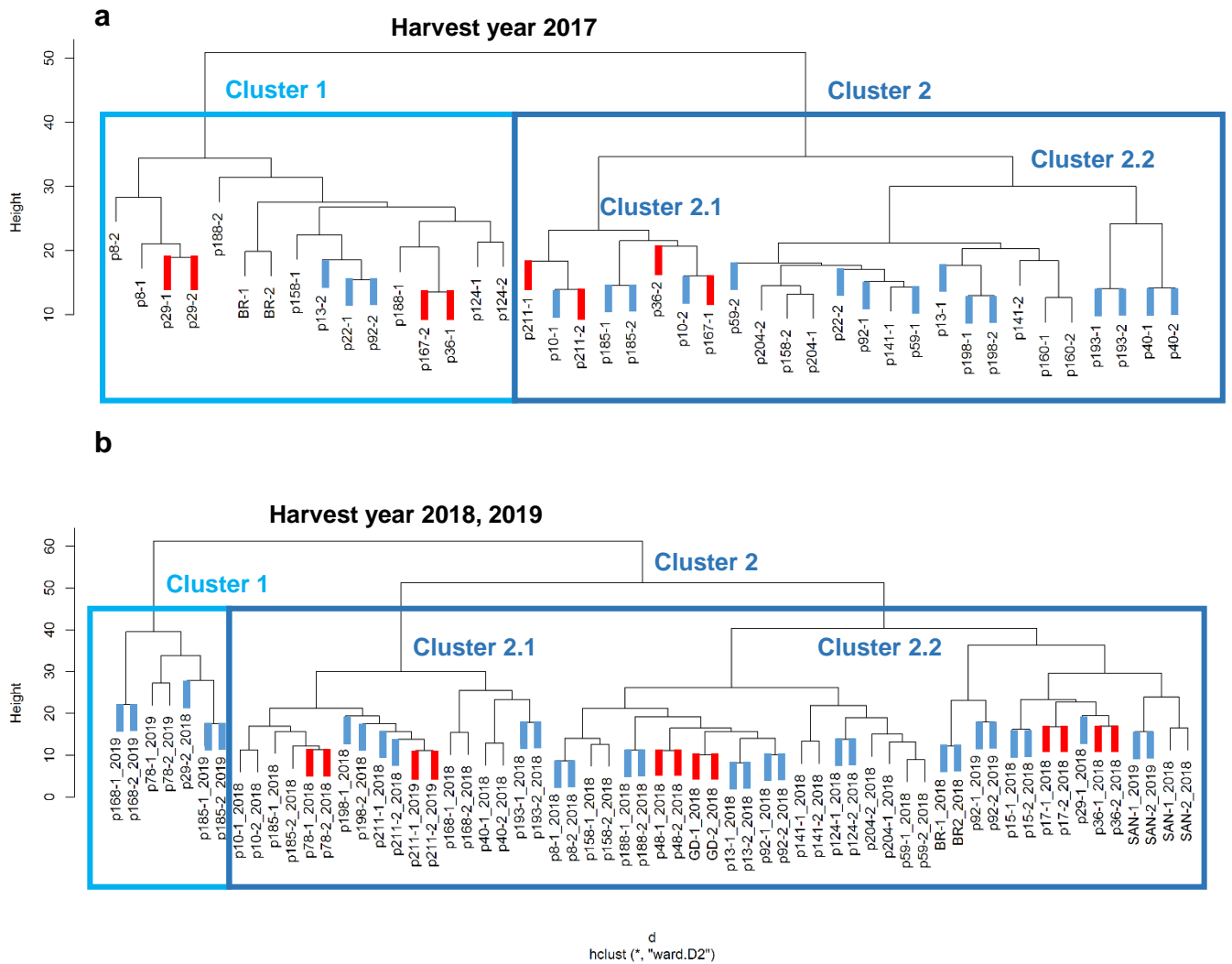
	Group I	Group II	Group III
2017	p10 p22 p92 p13 p40 p185 p59 p193 p198	BR* p158 p204 p141 p8 p188 p124	p211 p167 p36 p29 p160
2018	p10 p15 BR* p13 p185 p204 p124 p211 p8 p193 p188 p141 p198 p92	P40 p29 p59 P158 SAN p168	p78 p17 p36 p48 GD*
2019	p168 p92 p185 SAN*	p78	p211

*BR- Braeburn, SAN- Santana, GD- Golden Delicious

Supplementary Figure S2. The apple genotypes used in this study were classified according to their tolerability (refer to Materials and Methods). Genotypes in green, yellow, and red boxes indicate a symptom score below 1.4, between 1.4 and 1.7, and above 1.7 and are considered as well-tolerated, moderately tolerated, and as allergenic, respectively.



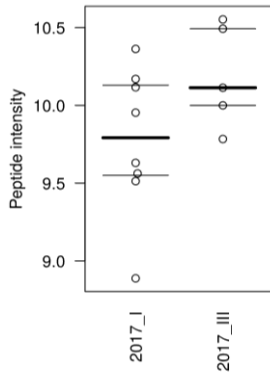
Supplementary Figure S3. General sequence information of identified Mal d2, d3, and d4 peptides from all samples. Peptide count of isoform-specific and shared peptides between Mal d isoforms (a). Peptide position within Mal d2 (NP_001315714.1) (b), 3 (AAV64878.1) (c), and 4 (AAD29414.1) protein sequences (d) (Image was generated with Geneious Prime (v. 2021.1.1) (<https://www.geneious.com>)).



Supplementary Figure S4. Cluster dendrogram obtained via hierarchical clustering of the detected Mal d1-4 peptides for each analyzed genotype. The distances were calculated using the ward.D2 method. Rectangles mark the clusters and sub-clusters identified. From left to right: Cluster 1, Cluster 2 (subdivided into Clusters 2.1 and 2.2). Allergenic genotypes and well tolerated genotypes are marked red and blue, respectively. Genotypes of the harvest year 2017 (a). Genotypes of the harvest years 2018 and 2019 (b).

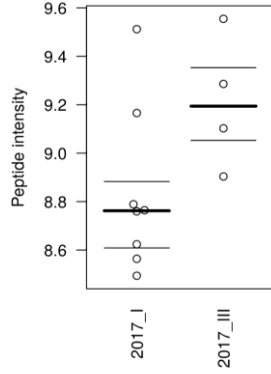
TVEILEGDDGGVGTIKK:
Mal d1.06 (27 isoforms)

fold change = 2.6 p-value = 0.09



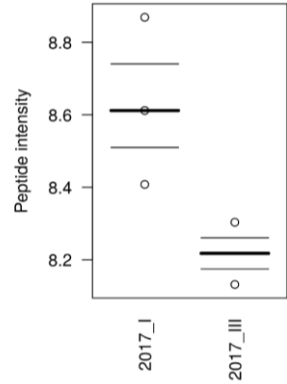
LYNAFVLADADNLIPK:
Mal d1.03 and Mal d1.07 (13 isoforms)

fold change = 2.4 p-value = 0.076



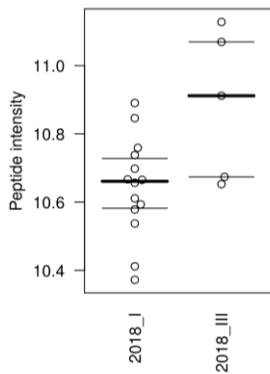
GDVEINEEHLK:
Mal d1.08 (CBL94177.1)

fold change = 0.039 p-value = 0.061

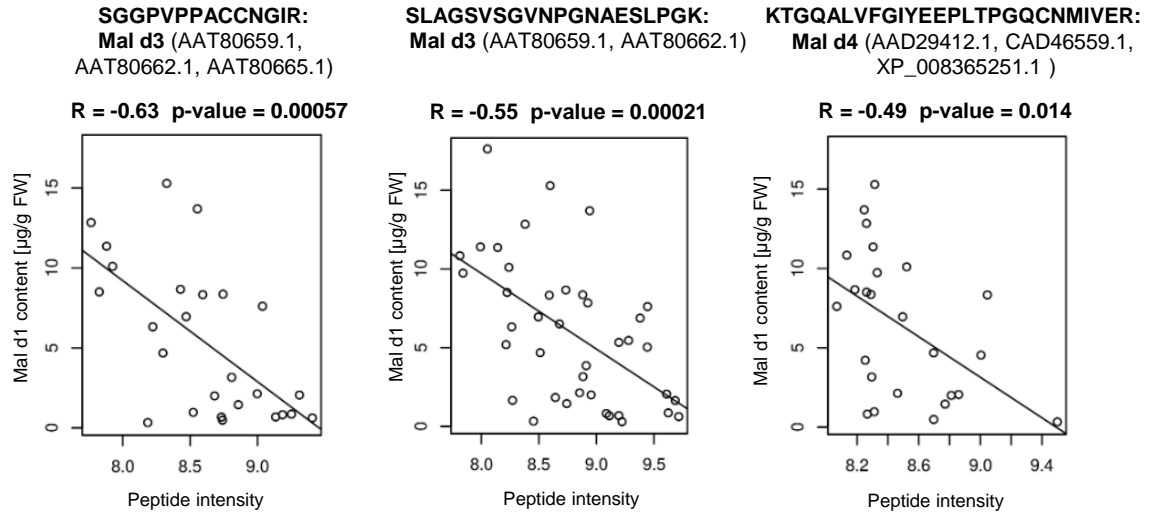
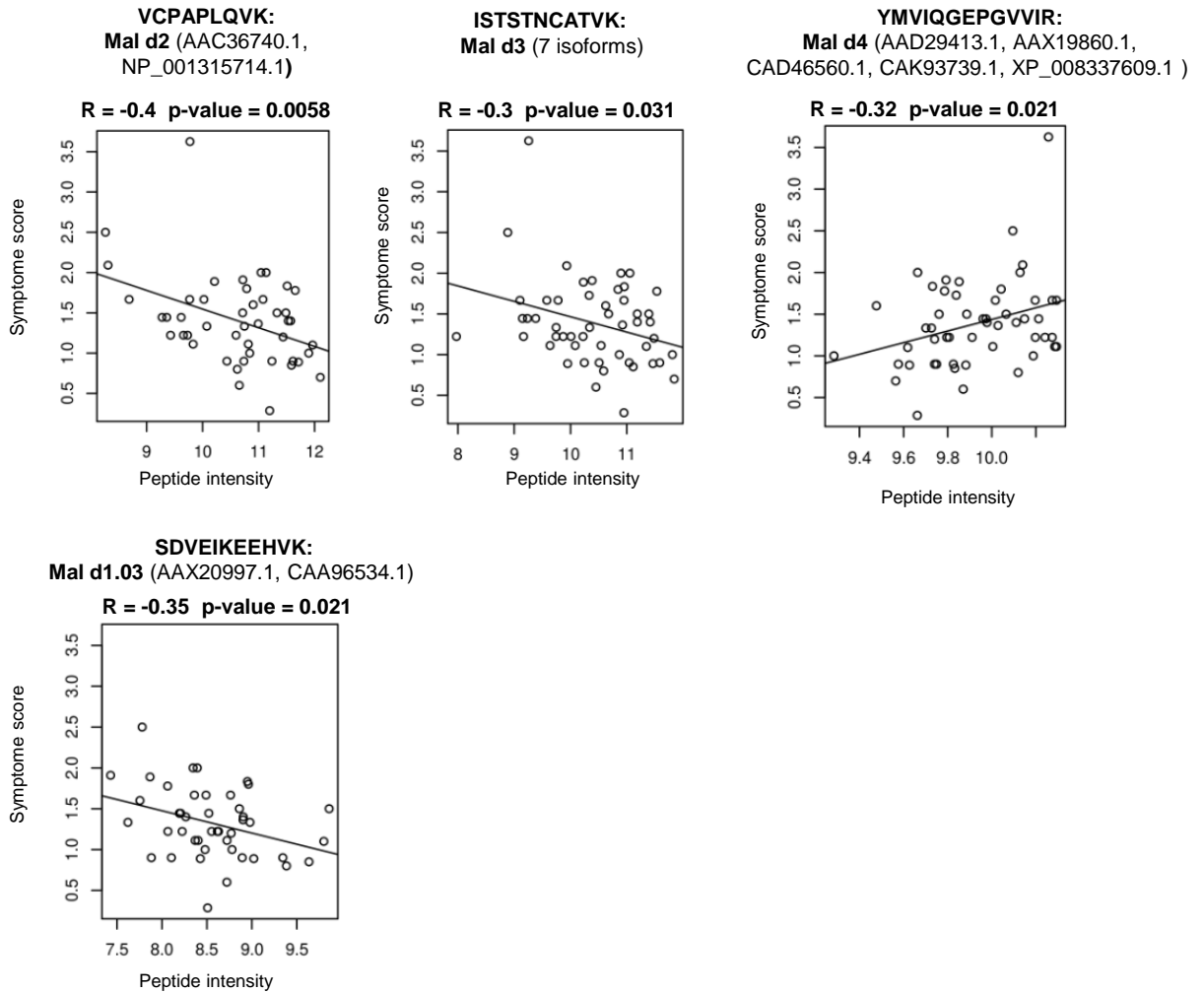


HAEILEGDDGGPGTIKK:
Mal d1.02
(7 isoforms)

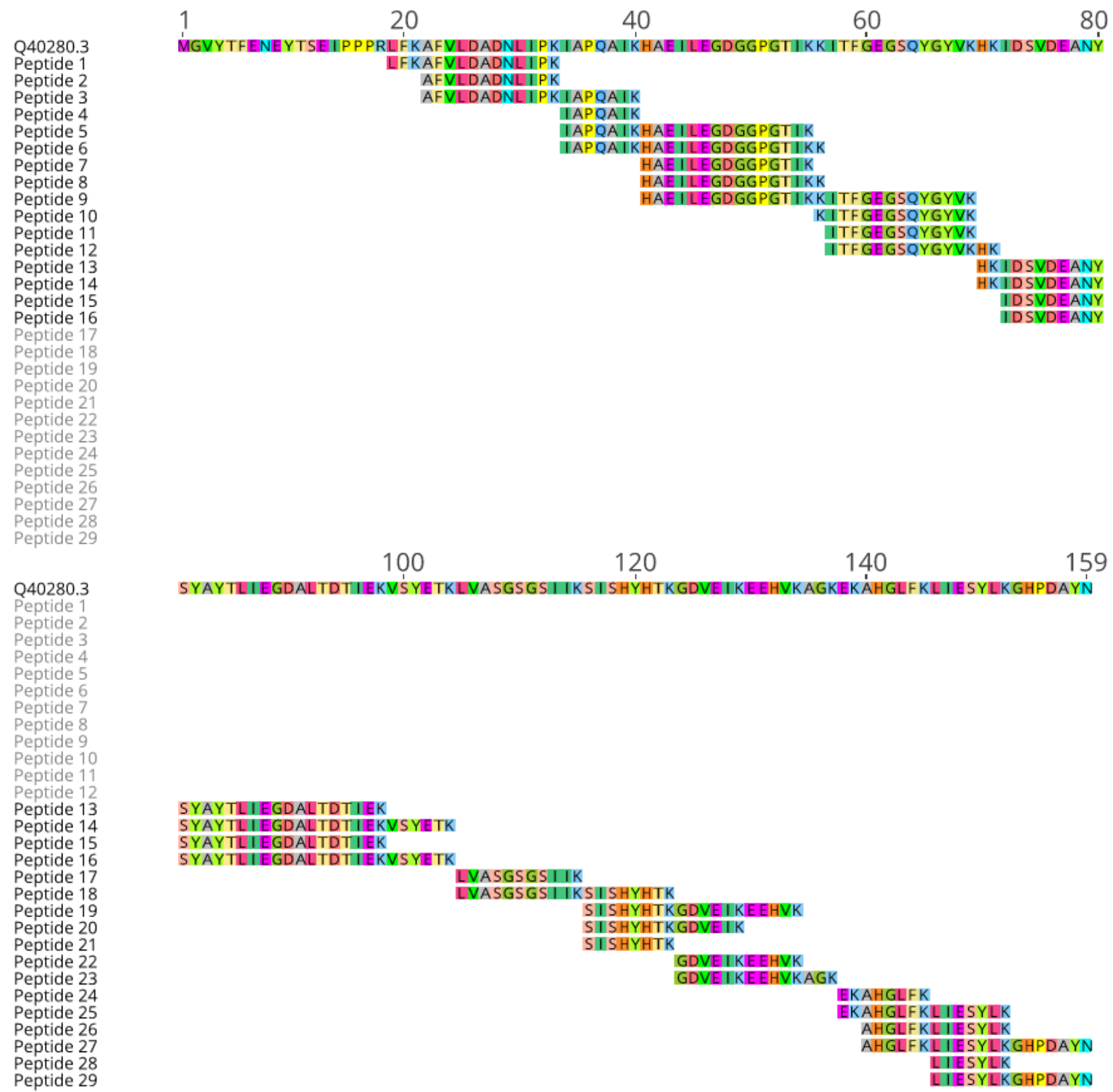
fold change = 1.7 p-value = 0.067



Supplementary Figure S5. Beeswarm Boxplot presentation of performed T-Test analysis between well-tolerated (group I) and allergenic genotypes (group III) of the harvest years 2017, 2018.

a**b**

Supplementary Figure S6. Correlation analysis showing the relationship between peptide intensity and the Mal d1 content (a). Correlation analysis showing the relationship between peptide intensity and the mean symptom value according to the human study with oral provocation tests (b).



Supplementary Figure S7. Sequence alignment of identified peptide sequences possibly derived from the Mal d1.02 isoform Q40280.3 (Image was generated with Geneious Prime (v. 2021.1.1) (<https://www.geneious.com>)).