Identifying autoimmune beta-cell epitopes in type 1 diabetes by HLA peptidomics

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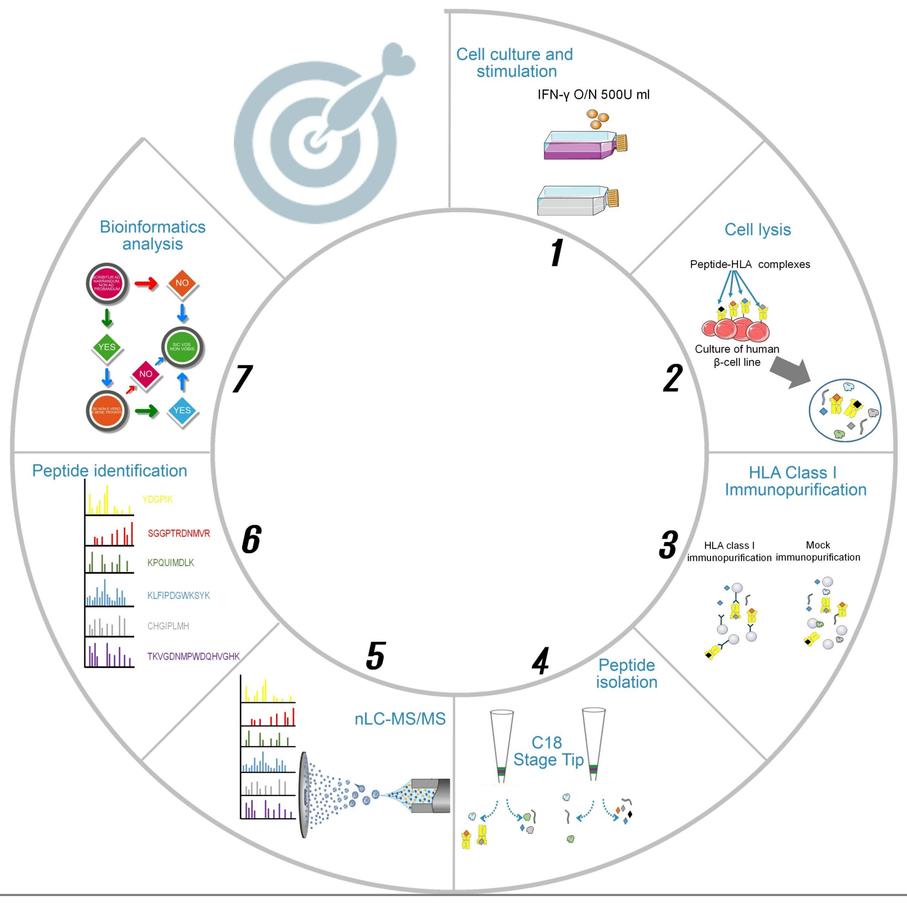
1. Introduction

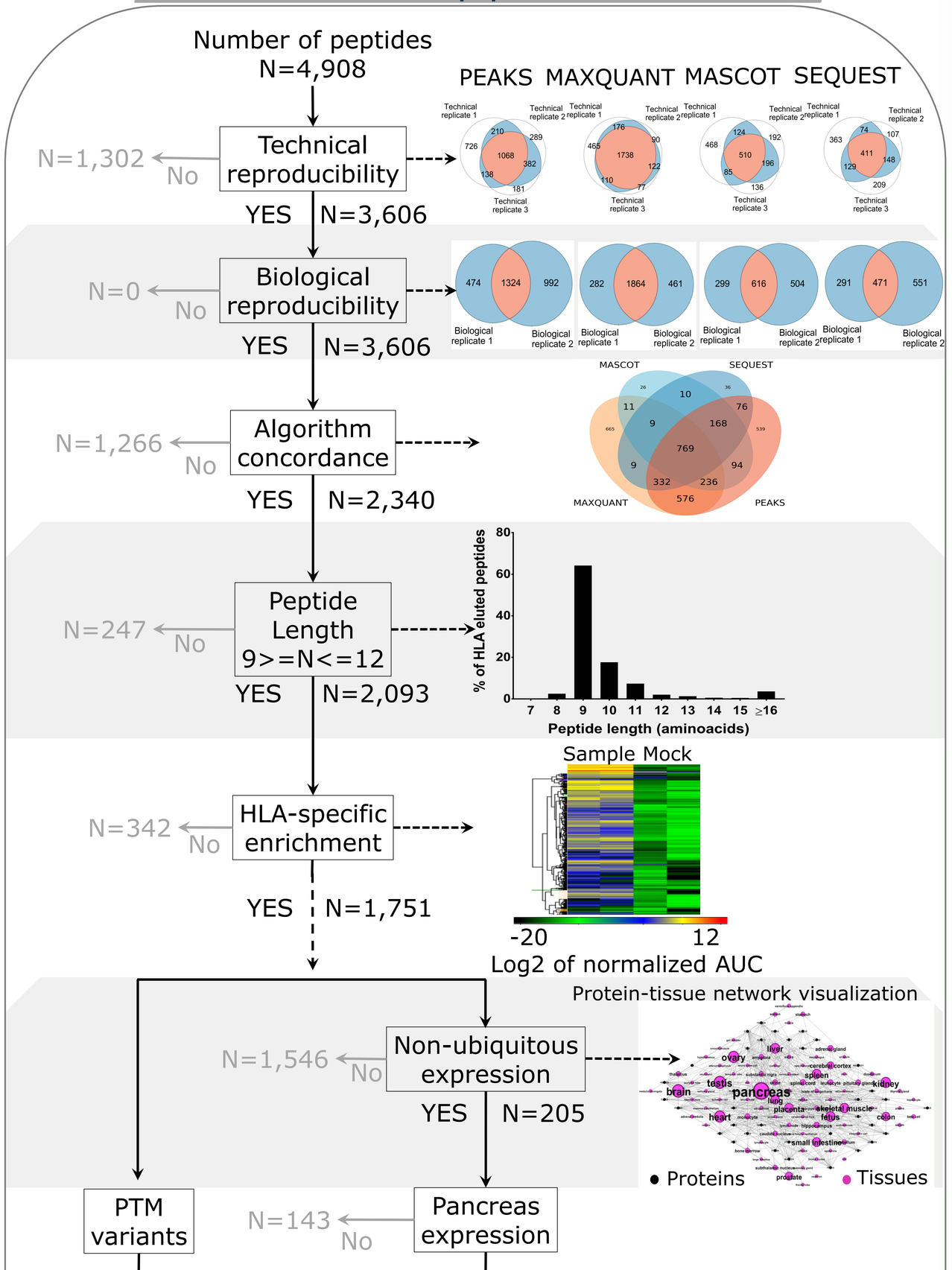
Type 1 diabetes (T1D) is an autoimmune disease in which autoreactive CD8+ T cells destroy pancreatic β cells. This destruction is triggered by the recognition of peptide fragments (epitopes), which are derived from protein antigens and presented at the β-cell surface in the pocket of HLA class I molecules.

We aimed at identifying these peptides by HLA peptidomics. This strategy consists in purifying the peptide-HLA complexes from β cells and to analyze the eluted peptides by mass spectrometry.

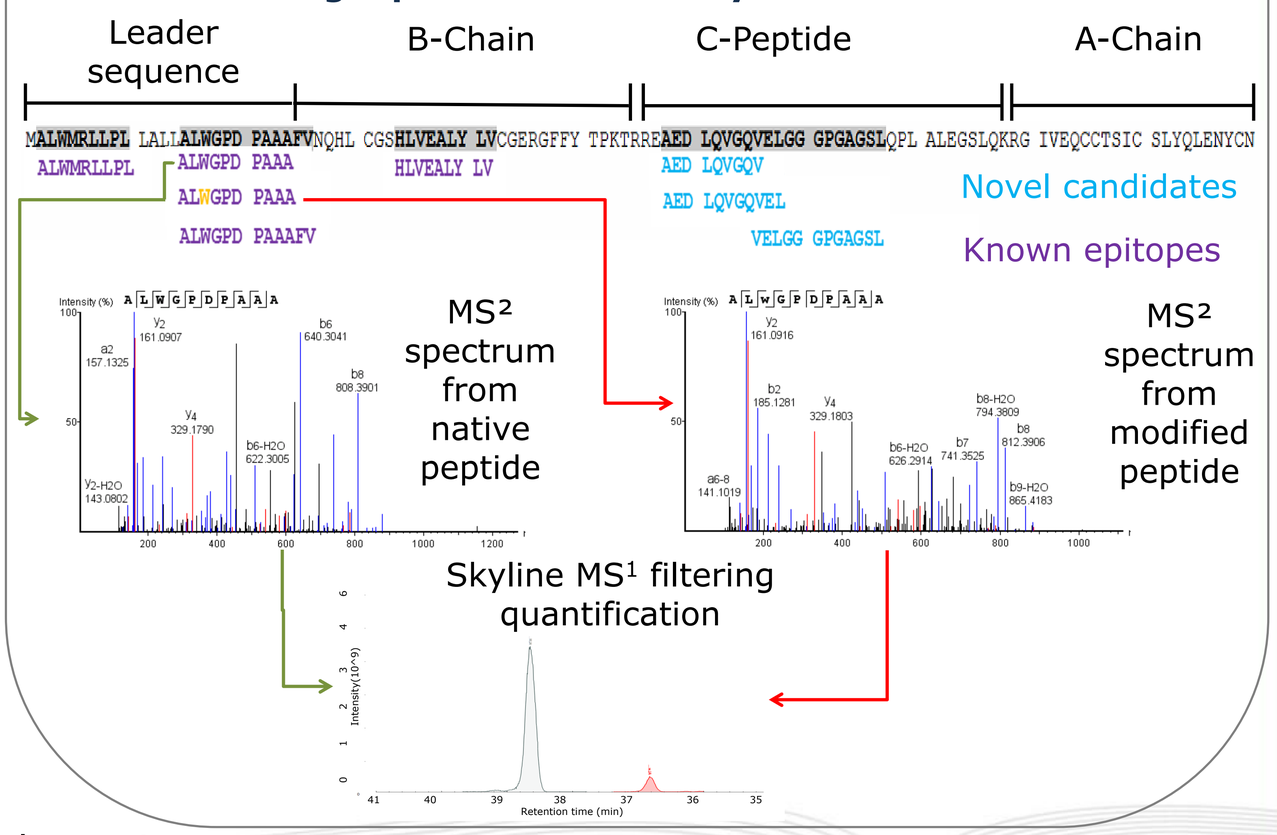
2. Material and methods



3. Bioinformatic pipeline and results



102 peptides identified, 16 are derived from preproinsulin including 9 post-translationally modified variants



4. Conclusions

HLA peptidomics identified preproinsulin sequences already described as major CD8+ T-cell epitopes, thus directly **validating our approach.**

Some of these peptides are **post-translationally modified** and could thus behave as **neo-antigens.**

Major T1D associated CD8+ T cell epitope PPI_{15-24} (ALWGPDPAAA) has been identified, both under unmodified and modified (trp->Kynurenin) forms.

95 additional candidate epitopes derived from 52 unique proteins are under study.

Acknowledgments

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