A combined prediction strategy increases identification of peptides bound with high affinity and stability to porcine MHC class I molecules SLA-1*04:01, SLA-2*04:01, and SLA-3*04:01 - DTU Orbit (08/11/2017)

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Affinity and stability of peptides bound by major histocompatibility complex (MHC) class I molecules are important factors in presentation of peptides to cytotoxic T lymphocytes (CTLs). In silico prediction methods of peptide-MHC binding followed by experimental analysis of peptide-MHC interactions constitute an attractive protocol to select target peptides from the vast pool of viral proteome peptides. We have earlier reported the peptide binding motif of the porcine MHC-I molecules SLA-1*04:01 and SLA-2*04:01, identified by an ELISA affinity-based positional scanning combinatorial peptide library (PSCPL) approach. Here, we report the peptide binding motif of SLA-3*04:01 and combine two prediction methods and analysis of both peptide binding affinity and stability of peptide-MHC complexes to improve rational peptide selection. Using a peptide prediction strategy combining PSCPL binding matrices and in silico prediction algorithms (NetMHCpan), peptide ligands from a repository of 8900 peptides were predicted for binding to SLA-1*04:01, SLA-2*04:01, and SLA-3*04:01 and validated by affinity and stability assays. From the pool of predicted peptides for SLA-1*04:01, SLA-2*04:01, and SLA-3*04:01, a total of 71, 28, and 38 % were binders with affinities below 500 nM, respectively. Comparison of peptide-SLA binding affinity and complex stability showed that peptides of high affinity generally, but not always, produce complexes of high stability. In conclusion, we demonstrate how state-of-the-art prediction and in vitro immunology tools in combination can be used for accurate selection of peptides for MHC class I binding, hence providing an expansion of the field of peptide-MHC analysis also to include pigs as a livestock experimental model.

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