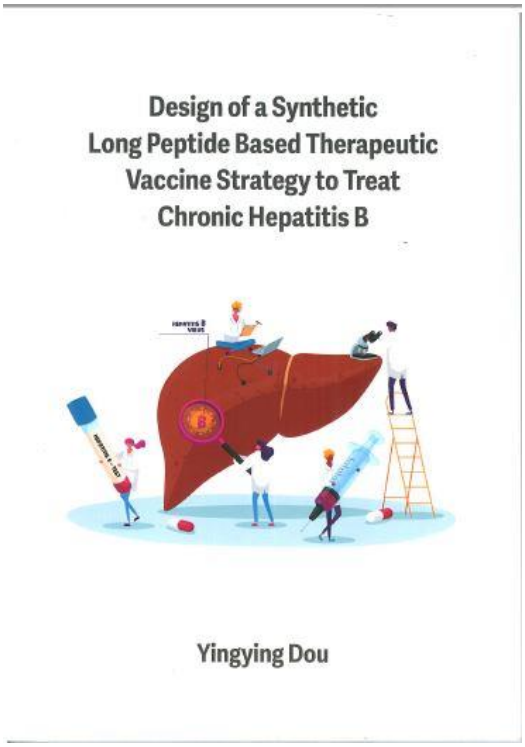


**Samenvatting van het proefschrift**

Y. Dou
*"Design of a Synthetic Long Peptide Based Therapeutic Vaccine Strategy to Treat Chronic Hepatitis B"*

**Promotiedatum:** 22 maart 2023
**Universiteit:** Erasmus Universiteit Rotterdam

**Promotor:**
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Facing the chronic hepatitis B (CHB) disease burden and treatment challenges, this thesis focuses on utilizing dendritic cell (DC)'s unique role in HBV antigen presentation and HBV-T cell activation for the development of a therapeutic vaccine strategy to treat CHB. In addition, soluble CD14 is explored as a novel biomarker.

The studies started from a proof-of-concept investigation of using a prototype HBV-derived synthetic long peptide (SLP) to boost both HBV-specific CD8+ and HBV-specific CD4+ T cells. DC cross-presentation of an HBV-SLP derived epitope was for the first time demonstrated in vitro on CHB material, both adjuvant and checkpoint inhibitor were tested along with SLP.

In order to improve the efficacy of a therapeutic vaccine in vivo by physically linking it to an adjuvant, this thesis further studied various TLR-2L-SLP conjugates and tested on patient material in vitro. The results of this study provided insight into how SLP-conjugates may be best designed for a therapeutic SLP-based vaccine to cure chronic HBV.

Besides, this thesis studied soluble CD14 elevation upon PEG-IFN treatment of HBeAg+ CHB patients as an early biomarker to identify CHB patients who likely respond to this drug.

Finally, all attempts to develop a therapeutic vaccine to cure HBV thus far were summarized and reviewed, where it combined the lessons learned from past studies on HBV antigen presentation, T cell responses, vaccine composition and treatment effects with our vision on the design of the next generation therapeutic vaccines to cure CHB.

This thesis now paves the way for an SLP-based vaccination strategy, utilizing DC to boost HBV-directed T cells to cure HBV and provides an early-on biomarker with the potential to monitor effective HBV immune response during treatment.