



## **P5 HER2/neu-derived peptide conjugated to pH-sensitive liposomes containing MPL adjuvant as a vaccine against breast cancer**

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### **Abstract:**

Vaccines containing synthetic peptides derived from tumor-associated antigens (TAA) can elicit potent cytotoxic T lymphocyte (CTL) response if they are formulated in an optimal vaccine delivery system. The purpose of this study was to induce effective anti tumor immune responses in BALB/c mice using P5 peptide coupled to pH-sensitive nanoliposomes containing MPL. P5 peptide is a synthetic, hydrophobic peptide derived from rat HER2/neu protein. Since in tumor immunotherapy, cytotoxic T lymphocytes (CTLs) have main role against tumors, we tried to induce an effective cytotoxic T lymphocyte (CTL) response against P5 peptide by employing the potential benefit of liposomes as a co-delivery vehicle and MPL as adjuvant.

P5 peptide was conjugated to - DSPE- mPEG2000- Maleimide lipid and incorporated into a pH-sensitive (DOPE) liposome containing Monophosphoryl lipid A (MPL) (pH-Lip-P5-MPL). Different liposome formulations were prepared and characterized for their physicochemical properties. To evaluate anti-tumoral efficacy, BALB/c mice were subcutaneously vaccinated with formulations containing 10 µg P5 peptide and 25 µg MPL per mouse three times with two weeks interval. On day 14 post last boosting, spleenocytes were collected for immunoassay. Released amount of IFN-γ and IL-4 were determined by ELISpot kits and flow cytometric analysis was used to identify IFN-γ producing cells. Moreover, tumor size and survival time were monitored in mice for a period of 130 days.

Mice immunized with pH-sensitive liposome-P5-MPL formulation had the most released IFN-γ and the highest CTL responses. These responses led to the lowest tumor size and the longest survival time among groups. The higher level of IFN-γ and the lower level of IL-4 in this group represented a shift toward Th1 immune response.

The encouraging results achieved by pH-Lip-P5-MPL formulation could make it a promising candidate in developing effective vaccines against Her2 positive breast cancers.

**Keyword:** pH-sensitive liposome; Peptide vaccine; CTL epitope; HER2/neu peptide; Breast cancer