

Bio-nanomolecules for Diagnostic and Therapy Applications

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Background We are developing novel bio-nanomolecules such as oligonucleotide-, peptide-, and protein-based materials, with knowledge gained from the life sciences. We seek to utilize the novel bio-nanomolecules to diagnostic and therapy of cancer, infection and immunological disease.

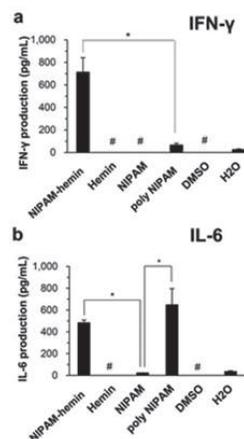
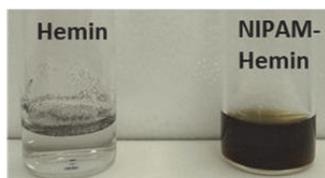
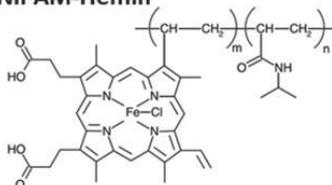
Aim Toll-like receptor 9 (TLR9) is one of innate immunity receptors recognizing single-stranded DNA derived from viruses and microorganisms, and hemozoin which is malaria-derived heme crystals. The ligands of TLR9 act as a molecule that immuno-activator or suppressor. We elucidated the interaction between TLR 9 and the natural ligand molecule, then developed novel ligand with superior function to natural ligand molecules.

Advanced Research Topics

Development of novel adjuvant molecules mimicking heme crystals of malaria parasite.

Hemozoin, a chemical analogue of a malarial pigment that can act as a potent Th1-type adjuvant, which strongly induces antibody production. However, the clinical applications of malarial hemozoin has limitations due to biosafety concerns and difficulties in the manufacturing process. Based on the premise that an analogue of the heme polymer might display immunostimulatory effects, we developed a heme-containing polymer.

NIPAM-Hemin



The polymer synthesized from heme and NIPAM showed good water solubility. NIPAM-Hemin induce interferon γ (IFN- γ) and interleukin 6 (IL-6), which promotes antibody production, in human peripheral blood mononuclear cells.

Publications

- Hoshi K, Yamazaki T, Yoshikawa C, Tsugawa W, Ikebukuro K, Sode K. Synthesis of a heme-containing copolymer as a novel immunostimulator that induces IFN-gamma production. *International Journal of Nanomedicine*, 13, pp4461-72 (2018)
- Q. Ji, T. Yamazaki et. Al. *ACS Applied Materials & Interfaces*, 9, 4509-4518 (2017)
- S. Hiromoto and T. Yamazaki. *Science and Technology of Advanced Materials*, 18, 96-109 (2017).

Summary

- We synthesized a heme-containing immunostimulator. Importantly, NIPAM-hemin does not affect cell viability, and induced the production of large amounts of IFN- γ in human PBMCs.

Research outcome

- The NIPAM-hemin copolymer shows potential as a new Th1-type adjuvant, which strongly induces antibody production.