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Synthesis of TLR7 Agonists Conjugated Iron Oxide Nanoparticles to Elicit Robust Cytotoxic T Cell Responses via DC Activation

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Recognition of pathogen-associated molecular patterns (PAMPs) is the first steps in immune therapy. Especially, Toll-like receptors (TLRs) in dendritic cell (DC) are representative pattern recognition receptors, which is critical for coordinating innate and adaptive immune responses. Imidazoquinolines, known as artificial compounds commercially available as TLR7 agonists, were attacked in aspect of efficiency because of their small size and short half-life in the bloodstream. Here, we synthesized covalent incorporation of imidazoquinoline moieties onto the surface of iron oxide nanoparticles to enhance their chemical stability, cellular uptake efficiency, and adjuvanticity. We utilized copper-catalyzed click reaction (CuAAC) to make novel conjugation between adjuvant and nanoparticles and these synthetic adjuvant-nanocomplexes showed powerful DC activation with lower nanomolar doses. Furthermore we checked unusually strong cytotoxic T lymphocyte responses, by the addition of ovalbumin, because conjugation to macromolecules could induce multivalency effect and efficient transport to endosomal TLR7.