Improved bioconjugation reaction for antibody drug conjugates

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BRIEF DESCRIPTION

Antibody drug conjugates (ADCs) are a quickly developing class of oncology therapeutics. Current synthetic methods and chemical linkages produce ADCs that are reversible at physiological conditions and have varying amounts of drug per targeting antibody. These weakly held conjugates result in diminished antitumor activity and increased toxicity. Researchers at UCI have developed new conjugation chemistry to generate stable and uniform ADCs.

SUGGESTED USES

- Reaction to produce specific, sensitive, reproducible antibody drug conjugates
- Reaction to conjugate contrast agents for magnetic resonance and nuclear imaging, as well as optical imaging

FEATURES/BENEFITS

- Increased stability and selectivity: newly employed chemistry is stable in physiological conditions and establishes a permanent bond, affording more control delivering payloads in vivo
- Flexible scaffold: scaffold is exceptionally malleable chemically which allows bioconjugation of additional molecules
- Consistent product: newly employed chemistry allows thermodynamic control reactions, which allows much more consistent, reproducible stoichiometry of antibody to drug than kinetic control reactions

TECHNOLOGY DESCRIPTION

Antibody drug conjugates (ADCs) are a class of drugs designed for cancer treatment that specialize in targeting cancerous cells while sparing healthy cells. ADCs are synthesized using bioconjugation and consist of three vital components: 1) recombinant monoclonal antibodies, 2) a linker, and 3) a drug.

Current conjugation chemistry that employs succinimide or maleimide linkers, which can react with other thiols (sulfur analogue of alcohols), results in heterogeneously-substituted antibodies. Additionally, the drug-antibody bonds that are formed are relatively weak and degrade at physiological conditions, leading to toxicity and premature release of the therapeutic drug.

UCI researchers have developed a novel bioconjugation reaction which produces a more stable, consistent linker, decreasing likelihood of mistimed drug release and maximizing drug effect. This innovative conjugation chemistry has a flexible scaffold and thermodynamic control reactions that which insures uniform attachment numbers. This reaction uses pyrocinchonimide, which has been mentioned in literature in reference to a variety of uses including photochemically cross-linked polymers and antimicrobials. The scientists at UCI found that pyrocinchonimide was far less reactive towards thiols than maleimide, greatly increasing selectivity for therapeutic bioconjugates. The consistency and versatility of this chemistry make it valuable not only for new oncology therapeutics, but also for contrast agents for magnetic resonance and nuclear imaging.

STATE OF DEVELOPMENT

Researchers have completed conjugation experiments with insulin and the cancer-targeting antibody Herceptin demonstrating an improved drug to antibody ratio.

RELATED MATERIALS

- Richardson et al. “Pyrocinchonimides conjugate to amine groups on proteins via imide transfer”. Bioconjugate Chemistry 2020 - 04/17/2020