

Lead Inventors

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Background

Multispecific antibodies represent a paradigm shift in biotherapeutics, moving beyond the traditional “one target, one antibody” model of monoclonal antibodies (mAbs). By enabling a single therapeutic molecule to bind two or more distinct antigens or epitopes, multispecific antibodies can engage complex biological networks with a level of precision unattainable by monospecific mAbs. Among these, bispecific antibodies (bsAbs) are the most mature and commercially successful modality, with more than 15 approvals worldwide. BsAbs simultaneously bind two targets, enabling novel mechanisms of action such as redirecting immune effector cells to tumor cells, blocking redundant signaling pathways to overcome drug resistance, or enhancing tissue specificity. These capabilities have established bsAbs as a cornerstone of modern therapeutic strategies, particularly in oncology, autoimmune diseases, and infectious disorders.

Despite their promise, bsAb development and manufacturing remain technically challenging. A central obstacle is the chain-association problem, which arises from the need to correctly pair specific heavy and light chains during expression. Random assembly frequently produces mis-paired or inactive species, complicating purification, reducing yield, and increasing immunogenic risk. In addition, bsAb optimization requires careful balancing of dual binding affinities, molecular geometry, stability, and pharmacokinetic properties that are comparable to those of conventional mAbs.

In parallel, antibody–drug conjugates (ADCs) have transformed targeted cancer therapy by combining antibody specificity with the cytotoxic potency of small-molecule drugs. The antibody serves as a delivery vehicle, selectively targeting tumor antigens and enabling intracellular release of the payload, thereby expanding the therapeutic window relative to conventional chemotherapy. Clinical successes such as trastuzumab emtansine have validated this approach. However, ADCs face their own challenges, including control of the drug–antibody ratio, conjugation-induced heterogeneity, payload-driven aggregation, and altered pharmacokinetics.

To overcome these limitations, a novel therapeutic platform developed at Saint Joseph's University aims to integrate the precision of multispecific targeting with improved molecular stability, manufacturability, and safety, addressing key bottlenecks in both bsAb and ADC development.

Opportunities

To address the manufacturing and stability challenges inherent in current bispecific and ADC technologies, Dr. Li and his colleagues have invented a novel therapeutic platform. This approach exploits the inherent stability and predictable assembly of proprietary dimeric constructs to generate bispecific or multispecific proteins. Each monomer within the dimer can be engineered to carry a specific targeting or therapeutic moiety. This modular design allows for a flexible combination of functionalities and simplifies manufacturing, potentially leading to more efficient, cost-effective production of bsAb-like therapeutics. A distinct advantage of this system is that the two monomers combine spontaneously and effectively eliminate homodimerization.

The versatility of this platform is further demonstrated by its capacity to deliver targeted therapeutics through varied mechanisms. The inventors theorize that one targeting component of the dimerized protein can carry a therapeutic partner, either a protein/peptide fused to the dimerizing motif or a drug conjugated to the motif.

Expanding on this delivery potential, one of the protein monomers has been engineered to incorporate Human Serum Albumin (HSA) to adjust pharmacokinetics and enhance drug delivery. This modification enables the use of fatty acid-linked molecules (small molecules, peptides, and nucleotides) that bind to the HSA construct to effectively deliver therapeutic moieties. This mechanism not only facilitates drug delivery but also supports the development of advanced *in vitro* and *in vivo* imaging reagents. The scaffold readily accommodates the covalent conjugation of small molecule imaging probes (such as fluorophores or radioisotopes) or the non-covalent binding of fatty acid-linked imaging agents.

Finally, to ensure precise biodistribution, the architecture supports the simultaneous integration of multiple targeting moieties, such as nanobodies or affibodies. By utilizing two or more of these compact binding domains, the platform facilitates multi-epitope or multi-antigen recognition. This approach significantly enhances targeting specificity through avidity effects, allowing for the precise detection and treatment of malignant tissues while minimizing background signal in healthy organs.

Unique Attributes

- **Cost-Effective:** The platform is designed to be more cost-effective than traditional antibody-based approaches, reducing the financial burden of research and development.
- **Efficient Production:** Enables faster, spontaneous, and more efficient production of functional proteins, allowing for accelerated development and commercialization of new products.
- **Increased Versatility:** Flexibility to make changes by disease requirement, as well as control over the dimerization process, makes it versatile.

Clinical Applications

Allows the development of a diverse range of therapeutic applications beyond the scope of traditional bsAbs and ADC through site-specific drug conjugation. These can include, but are not limited to, cancer immunotherapy, autoimmune disease management, infectious disease control, and diagnostic tools. This broad potential can significantly expand the impact of this innovative technology across multiple sectors.

Intellectual Property

Provisional patent application filed June 2025.

Collaboration or Licensing Opportunity

Actively seeking a licensee for commercialization or collaboration / sponsorship to complete preclinical studies.

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