ABZENA

What Are Antibody-Drug Conjugates (ADCs)?

ADCs are an iteration of a well-established concept: using antibodies to deliver toxic payloads directly to cells, serving as a molecular rifle-scope, targeting and killing tumour cells …but how do they work?

Cancer Treatment With ADCs

Developers have long since understood the power of specifically targeting harmful cells and delivering a cytotoxic payload with minimal systemic toxicity – particularly in the treatment of cancer. As a result, ADCs are one of the fastest growing anti-cancer therapeutic areas.

2000
Year of the first ADC approval

12
ADC drugs now approved for marketing worldwide

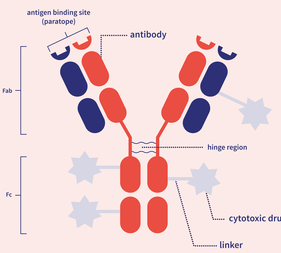
$22.87 Billion
Predicted ADC market size in 2030

How Do ADCs Work?

ADCs are comprised of three main components:

1. An **antibody** – typically a monoclonal antibody (mAb)
2. A **linker**
3. A **cytotoxic payload**

The mechanism of action of ADCs is complex, often requiring internalization, intracellular processing and payload release.



ANTIBODY

The antibody subunit provides specificity towards cancer cells by recognising antigens exclusive to, or highly expressed by, cancer cells. Upon recognition, the ADC enters the cell, and the linker is degraded, releasing the cytotoxic.

CYTOTOXIC DRUG

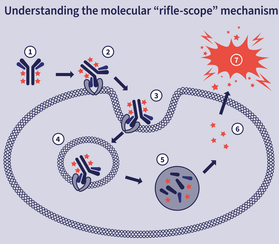
Most cytotoxic drug components are highly potent and belong to two major families: tubulin and DNA-damaging agents. Inappropriate release of these drugs can cause toxic effects, so the drug must remain attached to the antibody until internalization.

LINKER

The antibody and cytotoxic drug component are generally linked by a covalent linker. Peptide linkers are the most common type, offering stability and the ability to be selectively cleaved by lysosomal proteases following cell uptake.

ADCs in Action

Understanding the molecular "rifle-scope" mechanism



1. ADC administered to patient via intravenous injection
2. Antibody component specifically recognizes and binds to cancer cell receptor
3. Internalization via receptor-mediated endocytosis
4. ADC in endosome
5. Lysosomal proteases degrade ADC, releasing cytotoxic drug
6. Cytotoxic payload free to interact with internal targets
7. Cell undergoes apoptosis (programmed cell death)

Joining the Components: Conjugation

The method used to conjugate the components must be carefully considered to safeguard efficacy and safety.

The number of drug molecules attached to the ADC needs to be controlled. The type of conjugation will determine the amount of **heterogeneity** and the generation of **undesirable species** (e.g., antibodies with no drug attached or those with too many attached).

The ADC Revolution

Advances in molecular engineering techniques have translated into the components of ADCs becoming increasingly sophisticated, offering:

- Cytotoxic payloads with diverse mechanism of action
- Refined linkers
- More complex antibodies

…Advancements Adding Complexity

Development and manufacturing of ADCs is becoming increasingly challenging. For each product, unique hurdles to ADCs must be carefully considered and overcome, and must ensure:

- Antibody specificity only to target cells to avoid healthy cell destruction
- Maintained antibody affinity to target epitopes following conjugation
- Avoidance of immune activation and/or neutralization by native patient antibodies
- Improper release of the cytotoxic payload
- Highly potent anti-tumor activity regardless of only a fraction of the dose being delivered.

Discover How Abzena Could Help Support Your Next ADC Project

Contact us today

ABZENA
Moving medicine forward.