Antibody–drug conjugates (ADCs) are among the fastest growing drug classes in oncology cancer drug development. ADCs exploit the specificity of a tumor-specific antigen to deliver a potent cytotoxic payload directly to tumor cells while minimizing toxicity to normal tissue. ADCs have been called “magic bullets” and consist of a cytotoxic drug (cytotoxic payload) linked to a monoclonal antibody (mAb) that specifically recognizes a surface antigen unique to tumor cells. When administered to the patient an ADC will seek out tumor cells uniquely expressing the tumor-specific antigen and deliver its toxic payload directly to tumor cells at the tumor site, improving efficacy of chemotherapy while reducing systemic exposure and toxicity (ref1). Since the first ADC, Mylotarg® (gemtuzumab ozogamicin), was approved in 2000 by the US Food and Drug Administration (FDA), 14 have received market approval with over 100 candidates investigated in various clinical stages (ref 2).

A multitude of highly-specific monoclonal Abs to tumor-specific antigens have been developed and are currently in use for ADCs. Currently, most ADCs are constructed with two main families of highly toxic compounds acting either on microtubules or DNA structure. The most widely used drugs for ADC formulation comprise microtubule-inhibiting agents such as taxanes which target the tubulin class of proteins to disrupt microtubule formation. Drugs that target DNA structure such as irinotecan and doxorubicin which target topoisomerase activity to inhibit DNA synthesis are also gaining wide acceptance. The choice of tubulin inhibitors and disruptors of DNA synthesis as payloads is appropriate since rapid cellular proliferation is one of the major discriminating features between cancerous and normal cells.

Based on the formulation of ADCs, it is imperative that expression of both a tumor-specific antigen and cellular protein targets of a chemotoxic payload be demonstrated in the same tumor cells for optimal patient benefit. This requires interrogating protein expression in patient tumor cells, obtained either through surgical means or biopsy, to match the correct ADC to specific combinations of tumor cell protein expression patterns. This “knowledge” approach to determine appropriate ADC treatment strategies prevents cycling through multiple different chemotherapy drugs resulting in unnecessary toxicity to the patient and loss of valuable time searching for the “right” therapy.

mProbe’s OncoOmicsDX platform (Figure 1) provides quantitative protein expression in tumor cells procured directly from cancer patient tumor tissue and is the only CAP-accredited, CLIA-certified clinical proteomics laboratory that analyzes formalin fixed paraffin embedded cancer patient tissue using mass spectrometry (MS) (ref 3). We detect and quantify expression of tumor-specific antigens, chemo-resistant protein markers, chemo-response protein markers, prognostic protein markers, and clinical trial markers. Our technology is covered by 40+ patents and 30+ peer reviewed publications.

Figure 1

Currently, mProbe routinely provides clinical evaluation of 70+ target proteins directly in FFPE patient tissue and can evaluate critically important information on 377+ proteins. This depth of analysis can be used to guide ADC treatment decisions. We measure both the sixteen (16) most common tumor-specific antigens (protein receptors) targeted by ADCs and the two (2) most common ADC payload protein targets (TUBB3, TOPO1, and TOPO2) in patient tumor cells. The mAb and payload target proteins that mProbe measures in its clinical laboratory are listed below (Tables 1,2). Measuring both the ADC-targeted tumor-specific antigen and the payload target proteins provides for advanced clinical evaluation, patient stratification, and informed drug treatment decisions.

 Table 1 Table 2

mProbe currently has demonstrated capability of informing ADC treatment decisions in solid tumor settings for multiple FDA-cleared ADCs. We are also working closely with pharmaceutical companies to develop protein expression profiles to inform ADCs currently in experimental, pre-clinical, and clinical trial stages. Examples of recent FDA-cleared ADCs for which mProbe provides clinical evaluation are: 1) Kadcyla® (Her2 mAb plus microtubule inhibitor emtansine) and 2) Trodelvy® (Trop2 mAb plus Topoisomerase 1 inhibitor [govitecan](https://en.wikipedia.org/wiki/Sacituzumab_govitecan)).

Key mProbe technology advantages:

* Minimal Tissue Required (2x10 micron thick tissue section)
* Over 70 Biomarkers Analyzed
* Wide Dynamic Range Including Identification of “Super-Expressors”
* Supported by Collaborative Publications with Top-Rated Institutions
* Superior Sensitivity and Specificity Compared to Current Clinical Diagnostic Methodologies
* Reproducible Results Regardless of Age of the Tissue Block
* 5 Business Days to Report
* Cost is reimbursed by Medicare

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