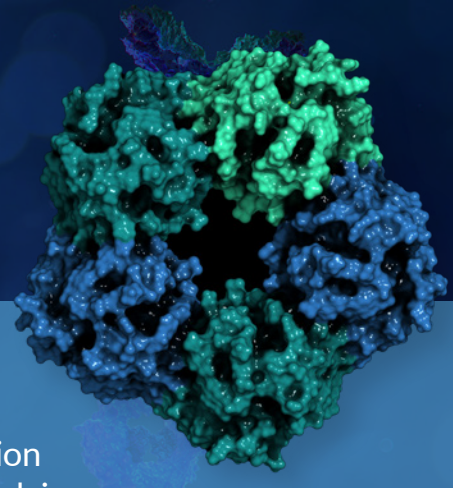
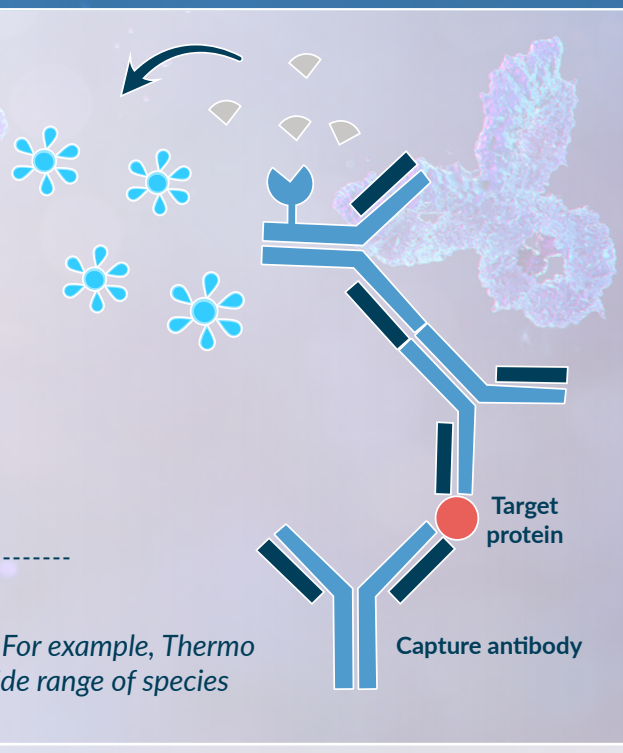
# Comparison of Protein Biomarker Detection Methods



There are myriad protein biomarkers—useful in clinical research as well as basic applications—and numerous means of detecting them. Each approach has benefits and drawbacks; careful consideration is necessary to select what is best for your needs. This infographic explains the underlying premise of selected techniques, presents a main advantage and disadvantage, and lists common applications as well as representative platforms.

## Sandwich ELISA[1]

The protein biomarker is bound between two primary antibodies, and biomarker detection is by reaction of an enzyme-conjugated secondary antibody.




**Advantages**

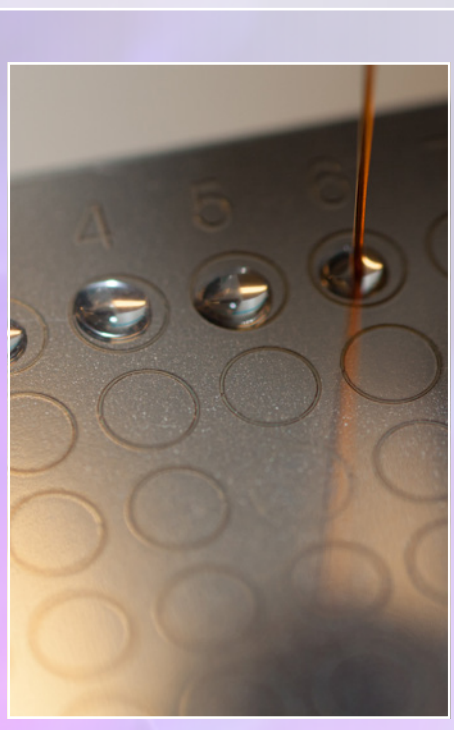
Flexibility of detection method for the same capture antibody

**Disadvantages**

Limited multiplexing capability

***Applications and Platforms***

*Long-standing in medicine, food safety, and drug discovery. For example, Thermo Fisher Scientific provides many kits that are specific for a wide range of species*



## Mass Spectrometry[2]

The protein biomarker—commonly enzymatically digested beforehand—is ionized in the gas phase before analysis.

**Advantages**

Readily compatible with proteome-scale and multi-omics analysis

**Disadvantages**

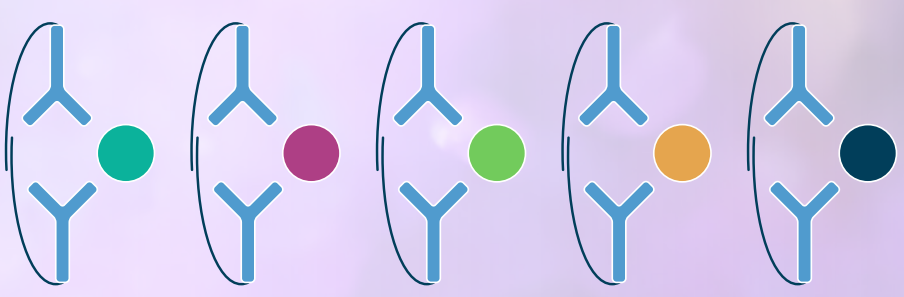
Expensive equipment that requires extensive training to operate and interpret

***Applications and Platforms***

*A complement to next-generation DNA sequencing. For example, Biognosys uses Hyper Reaction Monitoring technology to simultaneously detect thousands of proteins*

## Proximity Extension Assay[3]

The protein biomarker is tagged with DNA-linked antibodies that hybridize—and thus can be extended and amplified—only when they are in close proximity.



**Advantages**

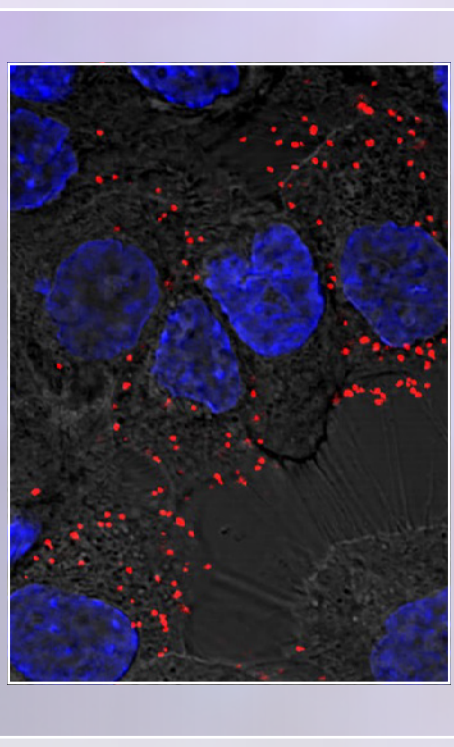
High multiplexing capability and a 9-log dynamic range

**Disadvantages**

Clinical validation can be contentious

**Applications and Platforms**

Spatial biology and other multi-omics work. For example, Olink Proteomics provides panels for dozens of protein biomarkers in most types of biological samples



## Proximity Ligation Assay[4]

Similar to the proximity extension assay, except that instead of extension, the DNA strands are ligated into circular DNA.

**Advantages**

Useful for analyzing single proteins or protein–protein interactions

**Disadvantages**

Nonspecific ligation can lead to a high background signal

***Applications and Platforms***

*Analyzing binding interactions such as those of different epitopes. For example, Abcam provides kits that are compatible with cell lines and fixed tissues*

## DNA Aptamers[5]

Binding is only to protein biomarkers in their native tertiary structure, and the product is detected by standard DNA quantitation.

**Advantages**

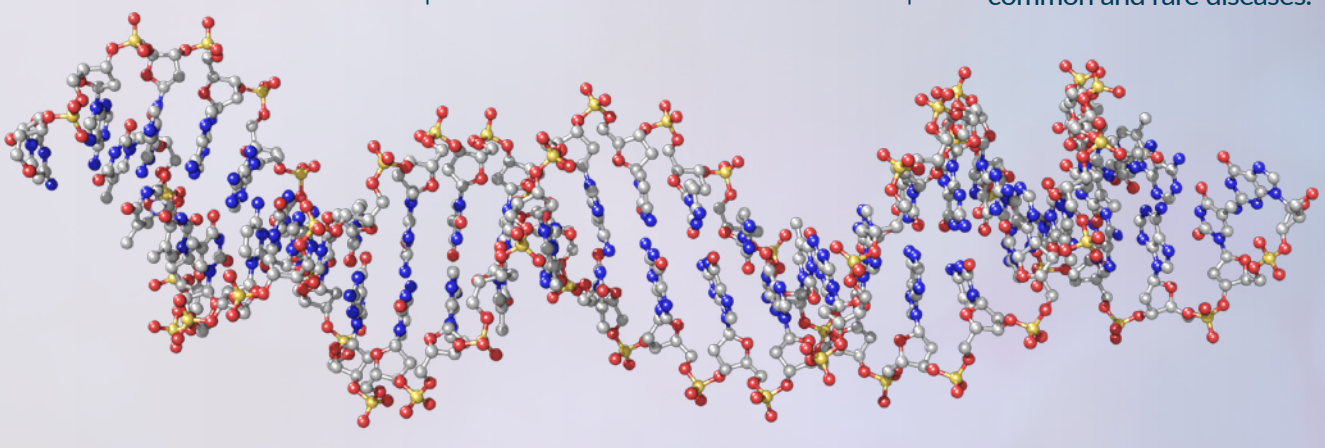
10-log dynamic range for up to 7000 proteins, facilitated by kinetics-limited cross-reactivity

**Disadvantages**

Cross-reactivity, especially in complex matrices such as plasma

**Applications and Platforms**

Separate detection of high- and low-abundance proteins. For example, SomaLogic provides panels for common and rare diseases.



The high dynamic range (>10 orders of magnitude) of protein biomarker concentrations in plasma and serum are especially challenging clinical issues. Ongoing efforts at validation in large datasets will be critical to reliably interpreting the output of modern protein biomarker analysis tools.

## References


1 Kato K, et al. (1977). **Use of rabbit antibody IgG bound onto plain and aminoalkylsilyl glass surface for the enzyme-linked sandwich immunoassay.** J. Biochem. 82(1):261–266.

2 Karas M, et al. (1987). **Matrix-assisted ultraviolet laser desorption of non-volatile compounds.** Int. J. Mass Spectrom. Ion Process. 78:53–68.

3 Lundberg M, et al. (2011). **Homogeneous antibody-based proximity extension assays provide sensitive and specific detection of low-abundant proteins in human blood.** Nucleic Acids Res. 39(15):e102.

4 Fredriksson S, et al. (2002). **Protein detection using proximity-dependent DNA ligation assays.** Nat. Biotechnol. 20(5):473–477.

5 Gold L, et al. (2010). **Aptamer-based multiplexed proteomic technology for biomarker discovery.** PLoS ONE 5(12):e15004.



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