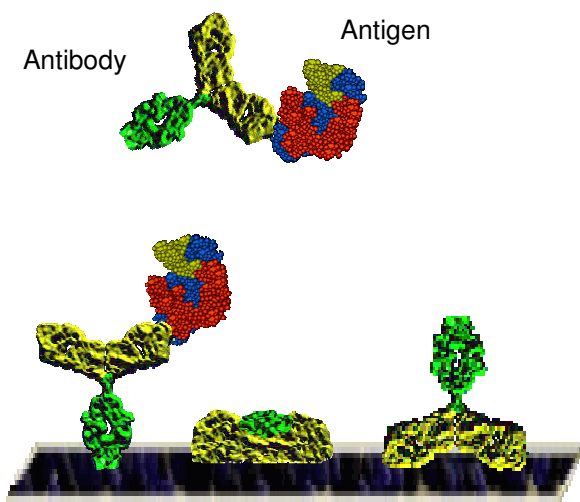


Technology

Technology Limitations in Immunoassays Development:

The simplest and by far, the most dominant test formats in diagnostics are where biological materials are tested on the surface of synthetic surfaces (solid supports). Such solid supported assays simplify automation, miniaturisation, ease of use as well as multiple or parallel testing. There are many different solid support products (plates, slides, beads, membranes, etc) used for diagnostic testing. However, it is relatively common for batch to batch variations to be sufficiently different that assay developers will order very large batch sizes to mitigate risks associated with poor reproducibility between batches. This situation exists simply because biological materials and synthetic materials (solid supports) are usually not compatible, and results in partial to total damage of the structure and function of these biological materials.

For example, the most commonly used reagent to identify the presence or absence of some target molecule (antigen/biomarker) in drug discovery research and diagnostics are antibodies. In solution, a monoclonal antibody (mAb) will have one constant binding affinity to its target antigen. However, when mAb are immobilised on some synthetic/artificial surface, its structure is damaged such that a range of different binding affinities result instead of just one constant binding affinity. Depending on the type of synthetic surface, there is a different distribution of binding, non-binding and partially binding mAbs.



The outcome of this existing situation is that a high affinity mAb to some target biomarker does not mean that it is useful for diagnostic applications. On certain miniaturised formats, 95% failure rates were typical (The Scientist 2003, 17(14) 42). Under these circumstances, multiple mAbs need to be sourced for the same biomarker when assays are being developed. What's worse is that performance of the mAb was so dependent of the surface that a functional mAb on one surface does not mean it will work on another surface.

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The whole process of assay development is empirical and trends to simple, miniaturised or multiplexed formats are making the situation even more difficult. This situation has severe consequences in all solid phase assay development (immunoassays, functional proteomics, etc), such as;

- Lack of suitable antibodies for the many prospective biomarkers identified from the proteomics and genomics revolution.
- Non-uniform binding affinities leading to lower than expected detection sensitivity and poor dynamic range.
- Time consuming process of trial and error in identifying mAb for assay development.

In the past, these issues did not severely affect the practical development and use of these solid phase tests. Even if >90% of antibodies were completely damaged, the remainder was more than sufficient to produce a meaningful result. With increasing miniaturisation and use of smaller and smaller quantities of reagents, this situation is changing. It is becoming critical that all or the greater majority of antibodies maintain their binding activity when immobilised on synthetic surfaces.

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