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Revolutionising Drug Development with focus on label-free technologies amid US FDA legislation

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Drug testing on human tissue is a rapidly evolving field with the new legislation taking technology innovations tothe next level. This article will discuss what this means for the drug discovery process as it will assess the benefits of label-free technologies.

The new FDA Modernization Act 2.0 has recently been signed by US president Biden, resulting in the revocation of the long-standing requirement of testing the safety and efficiency of drugs on animals. Researchers will be moving away from the animal preclinical models which have mainly focused on using animals that are as highly homologous to humans as possible. However, with 90% of clinical drug development failing because they are considered too dangerous or ineffective one can look forward to exciting developments in the drug discovery field.

The benefits of human tissue range from in-depth insight into disease pathophysiology to target validation, hit-to-lead identification and biomarker discovery. Overall, more accuracy can be expected in terms of the prediction of the drug's reaction in the human body. As one can rely on the changes in physical or chemical properties of molecules to detect their interactions in human tissue with much greater chances than in animal models, a decrease in failure rates can be expected. Additionally, the chances of identifying individual differences increase and this is especially important for precision medicine as its therapies can be tailored to the individual response.

New models for drug testing have already been developed, with the following article discussing the benefits of one of the experimental techniques: Label-free technologies. Using label-free technologies such as NPOT® & PIMS® offers a reliable technique that allows for a sensitive method under physiological conditions to secure the analysis of membrane proteins,

such as G protein coupled receptors, channels and low-abundance proteins.

Why turn to label-free technologies

Label-free technologies offer a new avenue in the drug target identification process. Previously widely used labeled technologies would fabricate new compound with the target identification mainly treating the modified compound and not the original one.

At a micro-level, the synergy between different molecules is analysed in order to determine the physical and chemical properties of the molecule. However, this is done without altering its properties. The test compound is able to maintain its original structure while also keeping the exact same molecular structure that would be used in therapy.

One is no longer dependent on labels or markers to identify the compound, minimizing the risk of perturbation of the system. Analysing the effects of the compound in its natural environment provides greater physiological relevance and since the compound is likely to reflect the original structure, it also improves the patient's safety and the drug's efficacy.

An unbiased approach: Nematic Protein Organisation Technique

One promising technique that has been developed is the Nematic Protein Organisation Technique, also known as NPOT®, which enables the direct isolation and identification of specific macromolecular proteins from tissue or cells, coming from either normal or diseased tissue. It has three functions including the identification of the drug targets, elucidation of the mode of action, and the identification of pharmacodynamic biomarkers.

It is a favourable approach as it permits the identification of drug-targeted membrane proteins including GPCR, and the premises of the mode of action. Additionally, since optimization steps are fast and robust, these result in an efficient identification of compound concentration and system pH range which are required for the drug’s efficacy and stability. Meeting these parameters is critical to match regulations and secure its approval. Applied to any patient cohort or any pharmacological model, the technology enables the collection of pivotal information such as primary target candidates, a functional signaling pathway, and the compound’s MOA from the biopsy.

Securing the development of a compound requires personalised monitoring

While NPOT® identifies the mechanism of action and response at the molecular level, the physiological intermolecular modulation spectroscopy (PIMS) technology complements it as it is based on the dynamic molecular resonance of proteins and macromolecules. Deciphering responder from non-responder, one can distinguish between patients in their response to the drug.

Identifying different subpopulations within a group and their response to a specific treatment quickly is key. Moreover, capturing the different effects that a molecule has on a cell’s function can reflect the patient's molecular capacity to respond to the drug, revealing the drug’s effectiveness. The result is a response to therapy tailored to the individual's needs. NPOT® and PIMS® allow for sensitive and efficient target identification which is crucial in the drug development process.

What does this mean for target identification?

Label-free technology proves itself to be a promising tool in the drug development process. The ability to directly detect molecule interactions, without the need for additional labeling or modification of the target molecule enables researchers not only to analyse the function but also the behavior of proteins in their natural habitat in real-time. By validating and identifying a potential drug target and associating it with a disease one can offer the patient a therapeutic strategy.

The new FDA legislation does not just free the drug development process from animal testing but it also pushes innovation in research thereby making human tissue the new norm.

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