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Increasing R&D productivity in drug development:

The power of label free technology

One of the important issues currently being raised in the pharmaceutical industry is the increasing cost of drug development. Depending on the source the current average cost for the launch of one new drug on the market ranges from $2.6 billion to $4.2 billion [1][2]. Not only does this put an enormous strain on the industry but it also leads to ever increasing drug prices for the patient.

The main reason for this increase in cost is an ongoing decrease of R&D productivity, due to compound failure for both technical and non-technical reasons. On the non-technical side this is caused both by ever more strenuous testing being required by the governing bodies. On the technical side the culprit can be found in the high attrition rate of candidate drugs in the final stages of the drug development process. This is mainly caused by unexpected toxicity effects [3]. All of this means the development of new truly innovative drugs has stagnated as can be seen from Fig. 1 which shows the number of new molecular entities that make it to market compared to the amount of R&D spending.

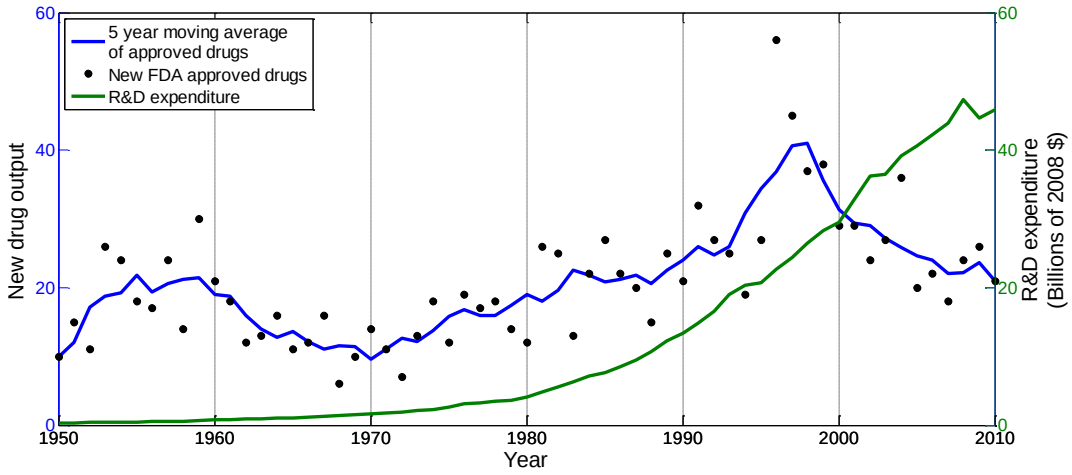

Fig. 1 : Evolution of the number of New Molecular Entities (NME) per year vs the Total R&D spend per year in the pharmaceutical industry [4].

An opportunity to alleviate this problem lies in the usage of label free technology during the early stages of drug discovery. Label free technology facilitates an R&D strategy that withholds unsuccessful candidate drugs during the early stages of drug discovery while delivering as much information as possible on the candidates with true potential.
To see how this can be achieved, we describe the potential effect on R&D productivity using the following relationship [5]:

$$P \alpha \frac{WIP \times p(TS) \times V}{CT \times C}$$

In which the productivity P is described as proportional to the elements in the numerator: the amount of research being performed at once (WIP, work in progress), the probability of technical success (p (TS)) and the value (V) divided by the elements in the denominator: cycle time (CT) and cost (C).
Although this can be applied to many different characteristics of a candidate drug the initial focus in this paper will lie on detecting failure due to toxic behavior of the candidate, this being the most severe need of the market at the moment [3].

WIP

At the early stage of drug discovery, during the preclinical phase the capacity of simultaneous research that can be performed is greatly determined by the amount of tests that can be performed in parallel. Due to their non-specific nature, label free techniques can deliver a broad spectrum of information on the working mechanism of a candidate drug. Thus reducing the amount of separate tests / time needed to obtain a certain amount of information on the drug candidate.
Toxicology: label free technology makes it possible to determine the specific type of toxic behavior a compound provokes using one test where otherwise this would require a batch of several more time consuming tests.

p (TS)

To increase the technical success rate the offering of label free technology is to decrease the attrition rate of candidate compounds by providing detailed information on the compounds activities at an early stage, reducing the chances of failure later on. This is again made possible by the wide variety of information one measurement can deliver. In this way missing any unwanted behavior is avoided, which with label dependent techniques is still possible.
Toxicology: when testing the toxic behavior of a candidate drug label free techniques can simultaneously detect the presence of any of the different types of toxic behavior. Meaning that even if an unexpected type of behavior is present it will be noticed, while with label dependent techniques this behavior could be missed resulting in the failure of the candidate after large investments in its development.

V

The value of a drug can be seen as the ratio between the benefits it provides and the risks that come with using it. Since the type of testing has no effect on the drug target, the way label free techniques improve the value of a drug candidate is by reducing its risks. This again is done by exposing off target effects that might be missed by label dependent techniques.
Toxicology: A good example of this is the current case of cardiac toxicity related to domperidone (Motilium) [6]. Here a long used pharmaceutical compound provokes an unexpected toxic behavior in cardiac tissue. While a certain amount cell types were undoubtedly screened for this behavior this type of behavior in cardiac tissue was apparently not tested / detected.

However with label free this possibility does not exist since any type of toxic behavior will be detected anyway.

CT

Cycling time is the time needed for each phase of the drug development process. Reductions in CT can lead to large reductions in cost of the process as well as lead to a shorter time to market. Although the reduced amount of tests needed when using label free techniques does result in shorter cycling times for the preclinical phase is does not directly affect the later phases, where major time gains can be made. However by reducing the amount of potentially failing drug candidates that make it to these phases it avoids any waste of time from the start.

Toxicology: Although the early phases of drug discovery are not those where mayor time gains can be made, label free technology can still offer an advantage by replacing several tests needed to assess different types off toxicity.

C

Cost comprises of all operating expenses required to bring a drug candidate to market. Again label free technology can help reduce this factor on different levels. On one side it reduces pure operational costs by reducing the amount of tests needed in the preclinical phase and replacing them by a single test that is often even less time and resource consuming than one of the currently used tests. On the other side it offers a huge reduction in cost in later phases by avoiding unnecessary investment in candidate drug that might otherwise have failed in the expensive phase 2 & 3 trials anyway by providing the necessary information for their elimination early on.

Toxicology: By testing for all different types of toxic behavior at once instead of having to perform a series of tests which are both more time consuming and expensive than label free techniques the cost of testing during the preclinical phase is significantly reduced. Indirect label free technology also offers advantages towards toxicity in later stages since penetration of possibly toxic compounds into stage 2 / 3 or even the market and the losses in investment that are related to this can be avoided.

Conclusions

Label free technology can deliver advantages that will affect nearly every aspect that determines R&D productivity. This mainly due to their broad applicability, making it possible to study several types of behavior in one test and to reduce the chances of missing of target phenomena.

To find out more about how your research can gain the benefits from label free assays, visit **www.CellSine.com**.

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