Clinical trial in a dish; A rewarding step towards translation & perspectives on its limitations

The cost of developing a new pharmaceutical drug has been estimated to cross US $ 2 billion, of which 20% is spent during the discovery and preclinical development phases and balance in clinical development. Further, about 10% of the total sum is spent on compounds which finally see the light of the day and get approved, while approximately 90% of the total investment—i.e., spent on candidate drugs that failed along the way, especially in the clinical phase. Thus, there is a dire need to bring down the risk of failures during clinical trial phase\(^1\) to save cost for which ‘Clinical trials in a dish’ is evolving as a potential tool.

‘Clinical trials in a dish’ earlier reported\(^1\) is based on testing drugs on human induced pluripotent stem cells (hiPSCs) which not only represent the response of human tissues when studied against a specific drug in vitro, but also can recapitulate the drug response of their specific donors. Evaluating the sensitivity of chemotherapeutic agents on cancer tissues obtained from the patient in vitro could be considered the forerunner of ‘clinical trials in a dish’ phenomena; however, the former being specific only to that particular cancer, with the hiPSC based ‘clinical trials in a dish’, any cell type of the patient can be grown in the lab. hiPSC-derived Cardiomyocytes (CMs) have already been demonstrated for their ability to function as clinical trial in a dish in several studies wherein there was interindividual susceptibility in the moxifloxacin (MOX)-induced prolongation of the QT interval on the cardiac electrocardiogram in one of the studies, patient-specific clinical susceptibility to doxorubicin (DOX) being revealed in another study\(^1\).

In the current issue of JSRM, Kimura et al\(^2\) have reported that usage of BMP4 is efficient for promoting mesoderm differentiation for deriving cardiomyocytes from hiPSCs for ‘clinical trials in a dish’, while they also point that protocol used by other studies vary, we should therefore, expect that the results too may vary between studies using different protocols. While this mission of clinical trial in a dish is expected to yield a better platform closer to clinical side,

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**Figure 1:** A schematic illustration of overview for bench to bedside in which ‘clinical trials in a dish’ is positioned between animal studies and human clinical trials.
which is logically superior to the study in an in vivo animal model, the following limitations cannot be ignored:

1. The cells alone are tested in the lab and not their environment, which is a major limitation to what is in vivo, where influence of the other systems of the body would be in force.
2. The bio-availability of the tested drug in the lab vs that in vivo is a parameter that may differ between the two.
3. Protocols of deriving cells from iPSCs for creating ‘clinical trials in a dish’ have to be the same or standardized with reproducibility before these ‘clinical trials in a dish’ are considered gold standard.

Apart from serving as an advanced step from animal studies closer to an in vivo clinical study, the results of clinical trials in a dish when compared to the outcome of actual human clinical trial, may throw further insights into understand how closer of how far the hiPSC clinical trials in a dish are to the clinical environment, which may help us further improvise the hiPSC technology as well.

References

1. Fermini B, Coyne ST, Coyne KP. Clinical Trials in a Dish: A Perspective on the Coming Revolution in Drug Development. SLAS Discov. 2018;23(8):765-776.