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EDITORIAL

HOW STEM CELLS ARE SHAPING OUR DRUG DISCOVERY TECHNIQUES?

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Stem cell biology is a fast-developing field of research that has made significant contributions to a wide range of scientific specialties, from developmental biology to regenerative medicine. One of the most promising implications of stem cell biology in recent years has been drug development. Stem cells are rapidly being employed in novel ways to enhance the drug development processes with applications ranging from academia to biotech start-ups to big pharmaceutical businesses.[1]

Applications of Stem Cell Technologies

1. Disease Modeling

Accurate models of human disease are required for drug development. Traditionally, disease modeling was limited to laboratory animals, simple single cellular organisms such as yeast, and immortalized human cancer cell lines. Animal models have significantly contributed to our understanding towards numerous illnesses, but they do not entirely resemble human physiology, and animal studies cannot be appropriately designed for large-scale comprehensive phenotypic testing. Immortalized cell lines, on the other hand, may be scaled up, but they are occasionally unsatisfactory models for human illness due to significant karyotypic aberrations. For instance, HeLa cells, are reported to have up to 80 chromosomes. Additionally, immortalized cell lines make it difficult to get some cell types, such as terminally developed neuronal subtypes.[1,2]

Shinya Yamanaka's seminal work in 2006 helped to solve these problems by demonstrating that genetic reprogramming might transform terminally differentiated adult cells back into embryonic-condition. These induced pluripotent stem cells (iPSCs) share several properties with embryonic stem cells (ESCs), including pluripotency.[3]

Because cells in the human body cannot reside in isolation, 2-D in vitro disease models can only go so far in replicating genuine disorders. Furthermore, in a 2D tissue culture setting, maturation of iPSCs into functionally mature adult cell types are frequently proven difficult.

2. Compound Screening

Translating complicated stem cell-derived in vitro models into large-scale, repeatable phenotypic assays capable of screening hundreds of chemicals is a critical and difficult step in stem cell-based drug development.[4]

3. Target Identification

The process of discovering a molecular target that has the potential to be altered by a therapeutic drug is known as target identification. Novel drug targets can be discovered utilizing stem cells in a variety of ways. Stem cell-based disease models provide many academic groups with a faster, cheaper, and frequently more accurate approach to research novel disease processes, leading to a better knowledge of illness's molecular foundation.[1,3]

Based on this, a handful of big academic alliances have been established in order to collect a plethora of biological data from iPSCs. The Human Induced Pluripotent Stem Cell Initiative, which collected genomic, transcriptomic, proteomic, and phenotypic data from hundreds of healthy and disease-associated iPSC lines, is a prime example of this. This open-source platform's goal is to offer researchers with a global resource for identifying novel disease-specific molecular targets.

Finally, as previously stated, stem cell-derived

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phenotypic screens provide a comprehensive and empirical tool for discovering new drugs that reverse disease-related phenotypes. It is therefore feasible to uncover novel molecular targets for these disorders using downstream deconvolution methods. This method is very beneficial for identifying novel targets for illnesses where the mechanistic landscape is not entirely known.[4]

4. Toxicity Screening

While stem cell-based models are extremely valuable in early-stage disease-specific phenotypic screening, they may also be an extremely useful tool for finding off-target adverse effects of medications that are currently in development. Detecting such effects early in the drug development pipeline can be significantly cost-effective than detecting them later in animal research – or, in certain situations, during clinical trials. Indeed, some stem cell-derived toxicity screens are demonstrated to be effective in discovering harmful side effects of currently accessible medications. These include cardiac toxicity and hepatic toxicity testing. It is envisaged that screening of toxicity prior to the drugs development process will allow re-designing molecules to lower toxicity.[5]

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CONFLICT OF INTEREST
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