ORIGINAL RESEARCH PAPER

Oral Pathology

ORGANOIDS- A CURRENT APPROACH TO TEST THERAPEUTIC DRUGS WITH EMERGING DISEASES.

KEY WORDS: Drug testing, organs 2D and 3D model.

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ABSTRACT

Till date cell culture is an important and necessary process in testing the potentiality of various drugs in cancer and various ailments to newly emerging viral diseases of SARS-COV-2 with genome variations as in current Covid-19 cases. The potentiality of testing various drug therapies is based on creating cell lines from the diseased individuals and testing the drugs. These cell lines taken from diseased tissues are conditionally programmed and cultured in vitro to analyse the efficacy of testing drugs. But the main problem or obstacle in these 2D type of expanded culture models is that they represent tissues inaccurately, So a new way is to create a 3D model culture (organoids) close to the organ so that it represents a model of a cell in vivo while being cultured in vitro. This review hence focuses on future applications of this model to know the drug's efficacy in various diseases and tumours.

What are Organoids?

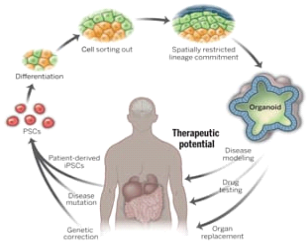
- An *organoid* is a miniaturized and simplified version of an organ produced in vitro in three dimensions that shows realistic microanatomy.
- Like organogenesis in vivo, organoids are derived from primary tissue or embryonic stem cells (ESC) or induced pluripotent stem cells(iPSC) from the desired organ (lung, heart, skin, intestine)and they should be capable of self-regulatory and self-organizing in three-dimensional culture.[1,2]
- Recently developed (since past 5 to 10 yrs.) 3D culture technologies have led to the development of physiological human healthy tissue and cancer models, to test drug toxicity and their efficacy in various ailments affecting the organs including the current situation of novel COVID 19 virus.

In this review, we discuss the use of the3D (organoid) technology over routine 2D cultures in general and also a brief emphasis on studies done in COVID-19 cases which primarily damages the pulmonary system.

Advantages of cell cultures in 3D over 2D:

In 2D cell culture models:	3D cell models:
Lack of cell-cell and cell-matrix interactions.	Closely resemble cell organizations and interactions.
Cells lose their phenotype.	Have more potency for self-renewal and differentiation when compared to 2D cell models and can mimic cellular functions and signally pathways as in vivo condition.3
They can't mimic cellular functions and signalling pathways as in-vivo conditions.	

Model representing organoids



APPLICATIONS OF ORGANOIDS:

Organoids are physiologically relevant in both basic research and translational applications.

As of now, its use is being more in:

- Developmental biology
- Regenerative medicine
- Personalized medicine

ROLE of ORGANOIDS IN INFECTIOUS DISEASES AND CANCER:

Organoids represents all components of organ and are suited to study infectious diseases affecting specialised human cell types.

Like, forebrain organoids derived from human iPSC and were engaged in studying Zika virus infection on neural progenitors, similarly lung organoids derived from iPSC's from healthy child carrying null alleles of interferon regulatory factor-7 gene was employed to study influenza virus replication.[4,5]

Now *Organoids* can help overcome the limitations and can change how scientists understood and could test potential COVID19 therapeutics to capture the complexity of infection.

Current studies going on COVID 19 viruses:

Scientists are beginning to perform more experiments to explore how the SARS-COV-2 viruses are replicate in hosts and are even testing vaccines and drugs against COVID-19.

- *Penninger and his colleagues from the University of British Columbia* said that: "COVID -19 puzzles how the virus lives inside the cells and how can its port of entry be blocked via organoid studies". He also added that 'tracking the virus and preventing it from finding the ACE2 entry gate, especially in lung and heart tissue would probably be the most rationale therapy for replicating viruses(COVID-19).'
- *American Association for the advancement of science:* Organoid model has shown that the virus enters the epithelial cells in the lungs and gut epithelial cells by exploiting an enzyme called ACE2 and hence, allowing the virus to replicate and spread further in patients with the gastrointestinal symptoms.
- *Lasners et al* and colleagues generated 3D structures that display all cell types of human. They suggested that human organoid models will offer a useful resource for researchers studying the basic biology of SARS-COV2.

Therefore, such organoid technology is being applied to study host-pathogen interactions in a range of infective pathogens to make possible to test efficacy and toxicity of drugs against representative targets or organs.6,7

Similarly in tumours affecting different organs, cancer models are being developed using primary cells with immortalized cell lines and thus in future, the collection of organoids will be

representative of the respective cancer group and might in future help patient stratification as well as oncogenic therapeutics.[8]

CONCLUSION:

With ongoing research, the scientists are focussing on reculpitating the organs in vitro by using 3D organoid culture technology systems over routine 2D cell cultures and trying to understand the pathogenesis of infection right from their entry into humans and collateral tissue damage. Similar studies are going on with cancer cells so that emphasis can be given on personalized medicine and also in therapeutic approaches in other medical maladies.

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