Pathology & Oncology Research (2020) 26:1353–1354
https://doi.org/10.1007/s12253-019-00642-z

LETTER TO THE EDITOR

The Potential Role of Organoids in Pathology and Oncology Research

S. Satish Kumar[1] · Sreena Nellimad Sreedharan[2] · Shankargouda Patil[3] · A. Thirumal Raj[4]

Received: 25 January 2019 / Accepted: 13 March 2019 / Published online: 18 March 2019

Organoids represent a 3-dimensional, simplistic representation of an in vivo organ that is replicated in in vitro conditions. An organoid simulates the microanatomy of the organ and even retains some of the functional abilities of the organ. Organoids are generated by inducing pluripotent stem cell populations to differentiate into multiple organ-specific cell types, which in turn are conditioned to form organized tissues that model in vivo organs [1]. Organoid culture systems have been developed to form tissue structures from all three primary cell lineages. Organoids are grown in the presence of 3D cell culture media that is made using the extracellular matrix hydrogel Matrigel, which is a laminin-rich extracellular matrix that contains specific growth factors that mimic in vivo signaling. Organoid cultures have been described for a variety of tissues, including kidney, liver, pancreas, prostate, lung, brain and optic cup [2]. Organoid-based studies allow the exploration of disease pathology in the context of an entire tissue rather than in a few individual cells, as is the case in typical in vitro cell culture studies. Organoids are an ideal tool for examining the etiopathogenesis of a disease entity and for formulating therapeutic strategies [3]. A major problem in current therapeutic research is the inability to successfully translate in vitro cell culture and in vivo animal model-based therapeutic success to the success of human trials. The reason for this failure stems from the limitations of in vitro cell culture, which is unable to closely model the disease microenvironment. Although animal models can replicate the disease microenvironment, the species-specific genetic profile presents a major hurdle to the translation of these data to human trials. Thus, the use of organoids obtained from human stem cells could overcome the limitations of both the animal models and in vitro cell culture. In addition, from an ethical standpoint, in vitro-based organoid systems have greater acceptance than animal models. In the development of cancer therapeutics, apart from assessing the efficacy, optimal dosage, potential cytotoxicity, and drug interactions, the molecular basis of therapeutic resistance can be examined by comparing the mutational profiles of treatment-sensitive and treatment-resistant organoids. Based on the resulting mutational profile differences, specific mutations can be targeted to alter sensitivity towards various treatment modalities.

Despite the numerous advantages of organoid-based research, organoids remain imperfect models that lack the key features of an in vivo microenvironment. Recent studies that used mesenchymal stem cells (MSCs) have shown that MSCs are able to form stromal elements, including fibroblastic, vascular and neural cells [4]. Thus, the introduction of MSCs into organoids and the induction of stromal differential could provide a tissue microenvironment that is capable of closely simulating in vivo conditions. An active in vitro tumor microenvironment would allow the assessment of the host immune response and provide accurate modeling of neural and vascular invasion and metastasis [5]. The final hurdle in therapeutic research is individual genetic and epigenetic variation within the species that causes treatment resistance. Thus, customized organoids from a patient's cancer tissues that are co-cultured with an MSC -derived microenvironment from the patient's normal tissue would provide an ideal model of the in vivo tumor microenvironment. Experiments performed with such customized in vitro organoid-based cancer models would allow the formulation of personalized treatment strategies.

✉ A. Thirumal Raj
thirumalraj666@gmail.com

S. Satish Kumar
sathishpath@hotmail.com

Sreena Nellimad Sreedharan
nsreenas@gmail.com

Shankargouda Patil
dr.ravipatil@gmail.com

[1] Sai Srinivas Dental Care, Sithalapakkam, Chennai, India

[2] Corning Dental Associates, Corning, NY, USA

[3] Department of Maxillofacial Surgery and Diagnostic Sciences, Division of Oral Pathology, College of Dentistry, Jazan University, Jazan, Saudi Arabia

[4] Department of Oral Pathology and Microbiology, Sri Venkateswara Dental College and Hospital, Thalambur, Chennai 600130, India

Compliance with Ethical Standards

Conflict of Interest None to declare.

References

1. Lancaster MA, Knoblich JA (2014) Organogenesis in a dish: modeling development and disease using organoid technologies. Science 345(6194):1247125. https://doi.org/10.1126/science.1247125
2. Huch M, Koo B-K (2015) Modeling mouse and human development using organoid cultures. Development 142(18):3113–3125. https://doi.org/10.1242/dev.118570
3. Duong HQ, Nemazanyy I, Rambow F, Tang SC, Delaunay S, Tharun L, Florin A, Büttner R, Vandaele D, Close P, Marine JC, Shostak K, Chariot A (2018) The endosomal protein CEMIP links Wnt signaling to MEK1-ERK1/2 activation in Selumetinib-resistant intestinal organoids. Cancer Res 78:4533–4548. https://doi.org/10.1158/0008-5472.CAN-17-3149
4. Ullah I, Subbarao RB, Rho GJ (2015) Human mesenchymal stem cells - current trends and future prospective. Biosci Rep 35(2): e00191. https://doi.org/10.1042/BSR20150025
5. Jabs J, Zickgraf FM, Park J, Wagner S, Jiang X, Jechow K, Kleinheinz K, Toprak UH, Schneider MA, Meister M, Spaich S, Sütterlin M, Schlesner M, Trumpp A, Sprick M, Eils R, Conrad C (2017) Screening drug effects in patient-derived cancer cells link organoid responses to genome alterations. Mol Syst Biol 13:955. https://doi.org/10.15252/msb.20177697