Tracking morphological complexities of organ development in culture

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Abstract

Organogenesis is one of the most striking process during development. During this period, organ primordia pass throughout several stages in which the level of organisation increases in complexity to achieve the final organ architecture. Organ culture, a method in which an isolated organ is explanted and maintained ex-vivo, is an excellent tool for following the morphological dynamics during development. While most of the work has been made in early stages of development, culturing organs in mid-late stages is needed to understand the achievement of the final organ anatomy in the new-born. Here, we investigated the possibility of following morphological changes of the mice heart, lung, kidney and intestine using a filter-grid culture method for 7 days starting at E14.5. We observed that the anatomy, histology and survival of the cultured organs were indicative of a continuity of the developmental processes: they survived and morphodifferentiated during 5-7 days in culture. The exception was the heart, which started to die after 4 days. Using a second approach, we demonstrated that heart tissue can be easily cultured in body slices, together with other tissues such as the lung, with a healthier differentiation and longer survival. The culture method used here, permits a high-resolution imaging to identify the dynamic of organ architecture ex-vivo using morphovideos. We also confirmed the suitability of this system to perform lineage tracing using a vital dye in branching organs. In summary, this work tested the feasibility of monitoring and recording the anatomical changes that establish the final organ structure of the heart, lung, kidney and intestine. Additionally, this strategy allows the morphological study of organ development including fate maps with a relative long-term survival up to the onset of differentiation. This work contributes to elucidating how organs are formed, promoting the understanding of congenital malformations and to design organ replacement therapies.

KEYWORDS

Ex-vivo organ culture; Heart development; Intestine development; Kidney development; Lung development; Organogenesis