Understanding of GI cancer initiation and progression using organoids

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Abstract

In homeostatic adult tissues, niche factors play a crucial role in governing the long-term self-renewal and diverse differentiation potential of tissue stem cells. By recapitulating these niche factors in an in vitro environment, tissue stem cells have demonstrated the capacity to assemble into stereotypic organoid structures, sustaining long-term self-renewal. Notably, a spectrum of tissue-specific niche factors has been identified by our team and others, facilitating the successful propagation of organoids derived from various adult tissues. Human tissue-derived organoids have exhibited the remarkable ability to retain the genetic and epigenetic alterations inherent in the original tissues. Moreover, these organoids have shown disease-relevant biological characteristics both in vitro and in vivo.

Our comprehensive phenotypic analysis of patient-derived organoids has unveiled intricate molecular mechanisms governing genotype-phenotype correlations in human digestive tissue cancers. In parallel, the insights gleaned from genotype-phenotype correlations are harnessed in reverse through genome editing technology. The strategic introduction of genetic mutations into normal organoids has enabled the faithful recapitulation of tumor phenotypes. In this symposium, we will present our recent research showcasing genotype-phenotype associations in patient-derived organoids and engineered counterparts.

Biography

1991-1997	MD Keio University School of Medicine
1997-1999	Internship, Keio University Hospital
1999-2003	Internal Medicine, Graduate school, School of Medicine, Keio University
2004	PhD
2004-2005	COE Postdoctoral Researcher, Keio University School of Medicine (Supervisor: Hideyuki Okano)
2005-2006	Resident, TEPCO Hospital
2006-2007	Postdoctoral Researcher, Stowers Institute, Kansas City (Supervisor: Linheng Li)
2007-2011	Postdoctoral Researcher, Hubrecht Institute, Utrecht, the Netherlands (Supervisor: Hans Clevers)
2011-2013	Assistant Professor, Department of Gastroenterology, Keio University School of Medicine
2013-2018	Associate Professor, Department of Gastroenterology, Keio University School of Medicine
2018-2023	Professor, Department of Organoid Medicine, Keio University School of Medicine
2023-Present	Professor, Department of Integrated Medicine and Biochemistry, Keio University School of Medicine