Somatic mosaicism and cancer

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Abstract

Recent studies have documented frequent evolution of clones carrying common cancer mutations in apparently normal tissues, which are implicated in cancer development. However, our knowledge is still missing regarding what additional driver events take place in what order, before one or more of these clones in normal tissues ultimately evolve to cancer. In this symposium, after briefly discussion of somatic mosaicism in various normal tissues, unique evolutionary histories of breast cancers as revealed by phylogenetic analyses of multiple microdissected samples from both cancer and non-cancer lesions harbouring der(1;16), a common driver alteration found in approximately 20% of breast cancers. The approximate timing of early evolutionary events was estimated from the mutation rate measured in normal epithelial cells. In der(1;16)(+) cancers, the derivative chromosome was acquired from early puberty to late adolescence, followed by the emergence of a common ancestor by the patient's early 30s, from which both cancer and non-cancer clones evolved. Replacing the pre-existing mammary epithelium in the following years, these clones occupied a large area within the premenopausal breast tissues by the time of cancer diagnosis. Unexpectedly, evolution of multiple independent cancer founders from the non-cancer ancestors was common, contributing to intratumour heterogeneity. Our findings provide new insight into the evolution of breast cancer.

Biography

Seishi Ogawa, MD, PhD is a Professor at Kyoto University, since 2013. He has been the head of the department of Pathology and Tumor Biology since 2013 developing work on genome analysis of human cancers. His scientific contribution has been central to understand the pathogenesis of myelodysplastic syndromes, clear cell renal carcinoma, neuroblastoma and other cancers through identification of key genetic alterations and mutations. His recent studies are related to the clonal origin of cancer, which he is intensively studying using micro-scale sampling and high-throughput sequencing and single-cell sequencing to reveal age-related remodeling of esophageal epithelium and inflamed colorectal epithelium. This time he will speak about his more recent study on the life history of breast cancer.