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INTRODUCTION TO INVITED REVIEW ARTICLES

Introduction: Lynch syndrome—its molecular mechanism and current topics

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Lynch syndrome(LS) is one of the most common hereditary cancer syndrome which has specific clinical features such as early onset cancer, multiple colorectal cancer, extra-colonic cancer occurrence in various organs, e.g., endometrium, stomach, small intestine, urinary tract, hepatobiliary tract, ovary, etc.

The history of LS begins from the report in 1913 by one dedicated pathologist, Professor Aldred S. Warthin in The University of Michigan, who had documented 3 families predisposing multiple cancer involvement with suggestive autosomal dominant inheritance [1]. This syndrome was further investigated by Professor Henry T. Lynch in 1966 [2], and the concept of "cancer family syndrome" had been gradually expanded worldwide.

Molecular mechanism underlying in carcinogenesis of this syndrome has been investigated by many researchers and finally genes related to mismatch repair system during DNA replication were found to be the cause of this disease during 1990s.

During above-mentioned stream of research in this field, the nomenclature of this syndrome has been changed. It was once determined as hereditary non-polyposis colorectal cancer (HNPCC), however, this nomenclature has been considered to be not so appropriate because of this syndrome's nature with cancer occurrence in multiple organs other than colorectum, and the term "Lynch syndrome" was defined as the hereditary cancer syndrome with autosomal dominant inheritance due to germline defect in mismatch repair system, and now used in general.

The clinical diagnostic criteria, Amsterdam criteria, then Amsterdam criteria II, have been developed and used for clinical diagnosis of this syndrome. However, these criteria for LS diagnosis have major limitations. It was reported that half of the LS cases would be missed by screening of colorectal cancer patients using the Amsterdam criteria [3].

And now, universal screening, not depending on these history-taking-based criteria, has been proposed and its clinical usefulness has been investigated in various aspects.

Several guidelines for this hereditary disorder had been published so far in the world. Also in Japan, the guideline for hereditary colorectal cancer was published first in 2012, and was revised in 2016 [4]. Importantly, this revised version of the guideline was immediately translated into English and published [5].

On publication of this special issue of *International Journal of Clinical Oncology*, I had considered to try to show clearly the latest understandings of this important clinical entity, "Lynch syndrome", thus invited two experts in this field in Japan [6, 7]. Professor K. Tamura is originally GI surgeon and now one of the most famous basic researchers in the field of familial cancer in Japan. And Dr. K. Tanakaya is a dedicated surgeon and has a lot of experiences to manage patients with LS.

I hope all readers to learn much about the novel knowledge about Lynch syndrome.

Compliance with ethical standards

Conflict of interest The author has no conflict of interest.

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