

Review

Recent Advances in the Genetic of MALT Lymphomas

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Simple Summary: Mucosa-associated lymphoid tissue (MALT) lymphoma is the most common subtype of marginal zone lymphomas. These B-cell neoplasms may arise from many organs and usually have an indolent behavior. Recurrent chromosomal translocations and cytogenetic alterations are well characterized, some of them being associated to specific sites. Through next-generation sequencing technologies, the mutational landscape of MALT lymphomas has been explored and available data to date show that there are considerable variations in the incidence and spectrum of mutations among MALT lymphomas of different sites. Interestingly, most of these mutations affect several common pathways and some of them are potentially targetable. Gene expression profile and epigenetic studies have also added new information, potentially useful for diagnosis and treatment. This article provides a comprehensive review of the genetic landscape in MALT lymphomas.

Abstract: Mucosa-associated lymphoid tissue (MALT) lymphomas are a diverse group of lymphoid neoplasms with B-cell origin, occurring in adult patients and usually having an indolent clinical behavior. These lymphomas may arise in different anatomic locations, sharing many clinicopathological characteristics, but also having substantial variances in the aetiology and genetic alterations. Chromosomal translocations are recurrent in MALT lymphomas with different prevalence among different sites, being the 4 most common: t(11;18)(q21;q21), t(1;14)(p22;q32), t(14;18)(q32;q21), and t(3;14)(p14.1;q32). Several chromosomal numerical abnormalities have also been described, but probably represent secondary genetic events. The mutational landscape of MALT lymphomas is wide, and the most frequent mutations are: *TNFAIP3*, *CREBBP*, *KMT2C*, *TET2*, *SPEN*, *KMT2D*, *LRP1B*, *PROM1*, *EP300*, *TNFRSF14*, *NOTCH1*/*NOTCH2*, and *B2M*, but many other genes may be involved. Similar to chromosomal translocations, certain mutations are enriched in specific lymphoma types. In the same line, variation in immunoglobulin gene usage is recognized among MALT lymphomas of different anatomic locations. In the last decade, several studies have analyzed the role of microRNA, transcriptomics and epigenetic alterations, further improving our knowledge about the pathogenic mechanisms in MALT lymphomas development. All these advances open the possibility of targeted directed treatment and push forward the concept of precision medicine in MALT lymphomas.

Keywords: MALT lymphoma; marginal zone; *Helicobacter pylori*; extranodal lymphoma; gastric lymphoma



Citation: Rodríguez-Sevilla, J.J.; Salar, A. Recent Advances in the Genetic of MALT Lymphomas. *Cancers* **2022**, *14*, 176. <https://doi.org/10.3390/cancers14010176>

Academic Editor: Francesco Bertoni

Received: 28 November 2021

Accepted: 29 December 2021

Published: 30 December 2021

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1. Introduction

Mucosa-associated lymphoid tissue (MALT) lymphoma was first described in 1983 by Isaacson and Wright in the stomach but may arise from other mucosal tissues [1]. According to the WHO classification [2], MALT lymphomas are one of the three recognized subtypes of marginal zone lymphomas (MZL), a group of indolent lymphoid neoplasms which represents 7% of all mature non-Hodgkin lymphomas (NHL) [3]. Based on data from SEER-18 program, MALT lymphomas represent 60.8% of MZLs, followed by nodal MZL (NMZL) (30.3%) and splenic MZL (SMZL) (8.9%) [4]. According to this program, the incidence of

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