

## Highlights: Follicular lymphoma

### Commentary

# Recent advances of the pathobiology and treatment of follicular lymphoma and challenging to the new therapeutic avenues

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Follicular lymphoma (FL) is the second most common B-cell lymphoma subtype in the world wide. Although around 85–90% of FL harbors t(14;18)/*IGH-BCL2* translocation, this entity is clinically and genetically heterogeneous from *in situ* lesion to advanced stage disease.<sup>1</sup> Also, a part of FL transforms to aggressive lymphomas such as diffuse large B-cell lymphoma and rarely lymphoblastic lymphoma.<sup>2</sup> Histologically, tumor follicles are characterized by containing abundant of tumor microenvironments such as follicular dendritic cells as well as T-follicular helper cell, T-regulatory cell, and vascular stromal cells.

Recent progress of genetic studies using next generation sequencing revealed genetic alterations as represented by *EZH2*, *CREBBP*, and *MLL2* mutations in “common progenitor cells” in addition to *BCL2* translocation.<sup>3,4</sup> Moreover, several single cell studies are elucidating FL characteristics in the point of view of not only tumor cell heterogeneity but also the composition of tumor microenvironment.<sup>5,6</sup>

In this issue, we reviewed the recent advances of FL pathology, biology and therapies. Abe Y. describes “Follicular lymphoma microenvironment: insights provided by single-cell analysis” based on his unique approaches using single cell analysis.<sup>7,8</sup> Carreas J. discusses “The pathobiology of follicular lymphoma” in terms of histopathological and genetic characteristics.<sup>9</sup> Oishi N. explains “Precursory or early lesions of follicular lymphoma: clinical features, pathology, and genetics” especially *in situ* follicular neoplasms.<sup>10,11</sup> Maeshima AM. discusses “Histologic transformation of follicular lymphoma: pathologist’s viewpoint”<sup>12</sup> and Maruyama D. will discuss FL transformation at the point of view of clinical characteristics (in preparation). Finally,

Fukuhara N. will describe the recent progress of FL treatment including epigenetic drugs (in preparation).

I believe this review series will let us understand the pathogenesis and behavior more accurately and handle it, that I hope it will lead to new therapeutic avenues for the patients.

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