blood commentary

LYMPHOID NEOPLASIA

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Distinct miRNA profile in prognosis of early CTCL

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In this issue of *Blood*, Lindahl et al report that expression of 3 microRNAs (miRNAs) (miR-106b-5p, miR-148a-3p, and miR-338-3p) in tissues of the mycosis fungoides (MF) subtype of cutaneous T-cell lymphoma (CTCL) is highly predictive of disease progression.[1]

This set of 3 miRNAs was more powerful in predicting MF progression than the clinical prognostic factors currently in use.[2] The Lindahl et al study is comprehensive and takes advantage of a large and very-well-characterized cohort of MF patients with long clinical follow-up. To a great extent, it is unique and well positioned to address an important diagnostic need for early identification of MF patients poised to experience disease progression.[3] The results of the study may have an impact on the care of patients in the future by introducing miRNA pattern evaluation into routine diagnostic workup of MF biopsy specimens.

However, before this happens, a number of factors need to be considered. First, the results reflect findings in a genetically rather homogeneous Danish population; thus, validation of the prognostic ability of the 3-miRNA classifier needs to be performed in a more ethnically diverse group of patients. Second, the expression fold-difference of these miRNAs as progression predictors is rather small for 2 of the 3 markers (miR-106b-5p and miR-148a-3p), which makes it potentially quite difficult to apply the analysis as a routine diagnostic test. Of note, the identified set of 3 miRNAs has been found to be predictive of progression but is not diagnostic for MF, because the set can also be expressed in inflammatory skin diseases such as psoriasis. This observation may not be unexpected, given the dominant inflammatory component at the early stage of MF,[4] but it raises the question of which type of cells (reactive vs neoplastic) express the identified miRNA triad. This lack of specificity for MF limits the potential clinical utility of the miRNA triad to some degree. Finally, the mechanisms controlling expression of these miRNAs need to be elucidated, once their cellular source is established. Mechanistic evaluation of this kind may include exploring potential links, direct or indirect, to genetic alternations of the neoplastic cells. This important task may prove particularly challenging, given the vast mutational diversity reported in MF and Sézary syndrome, a type of CTCL closely related to MF.[5-10]

In summary, identification of the predictive set of 3 miRNAs holds promise of early stratification of MF patients into groups with high and low risk of progression. However, a number of questions need to be answered before the true significance of this novel classifier and its potential impact on clinical care of MF patients can be fully determined.

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