A Novel Predictive Classifier of Follicular Lymphoma Patients for Improved Treatment Strategy

Accurate predictive biomarker to guide risk-adapted frontline therapy for follicular lymphoma

Technology

The investigators have identified and characterized transcriptionally distinct subtypes of follicular lymphoma (FL) that are predictive of frontline treatment outcomes and survival. As described in unpublished data, seven distinct transcriptional subtypes were identified using non-negative matrix factorization on 302 FL microarray transcriptomes. These subtypes were further validated in 850 FL samples from 10 independent microarray and bulk RNAseq datasets. Each subtype was found to be associated with unique B-cell states, microenvironment compositions, and responses to frontline immunochemotherapy. The investigators also identified specific tumor microenvironment (TME) features associated with the transcriptional signatures, including distinct immune and stromal cell populations, which were predictive of patient survival. These findings support the use of these transcriptional classifications (grouped into 7 FL subtypes) as an improved method for accurately stratifying FL patients and identifying subtype-specific therapeutic vulnerabilities in order to guide personalized treatment approaches that will improve the rate of durable remissions and increase patient survival.

Background

Follicular lymphoma (FL) is an indolent B-cell lymphoma that is virtually incurable despite advances in chemoimmunotherapy regimens. While most FL patients achieve long-term survival rates similar to the general population, a subset experience early disease progression within 24 months of frontline therapy initiation, often involving histologic transformation, and receive a dismal prognosis (5 year overall survival of 50%). Currently, there are no robust predictive biomarkers to guide risk-adapted front-line therapy. The development of a transcriptional classifier that better accounts for FL biological heterogeneity and includes the features of both malignant B-cells and the tumor microenvironment (such as the one described herein) could dramatically refine current FL risk models and thereby improve selection of patients for appropriate therapies, thereby improving patient outcomes. INTELLECTUAL PROPERTY NYU has filed a U.S. provisional patent application covering methods for classifying patients into distinct FL subtypes and determining the respective treatment regimen using compositions of probes/primers (in kit or array form) and a software tool to read out the results.

Application

Category

Life Sciences/Diagnostics

Authors

Matthew M. Klairmont, MD

Christopher Y. Park, MD, PhD

Learn more

- **Risk stratification:** FL patients can be classified into distinct FL subtypes predictive of response to immunochemotherapy and overall survival rate.
- **Augmentation of well-established clinico-genetic risk models:** This methodology could be combined with m7-FLIPI (and/or other risk stratification models) to improve the prognostication of patient outcomes.
- **Personalized medicine:** FL subtype classification can guide tailored frontline therapy regimens.

Advantages

- **Novel risk stratification methodology:** Identifies transcriptionally distinct FL subtypes predictive of treatment response and survival outcomes.
- **More comprehensive transcriptomic signatures:** Biomarkers more completely capture FL biological heterogeneity by including TME alterations.
- **Differentiated from current clinico-genetic risk models:** The FL subtypes offer predictive value beyond well-established clinico-genetic risk models (e.g., m7-FLIPI).
- **Speed and convenience:** Limited sequencing is required for subtype classification and the method can be conveniently implemented in clinical settings by physicians with access to gene expression profiling modalities, including RNA sequencing

Intellectual Property

NYU has filed a U.S. provisional patent application covering methods for classifying patients into distinct FL subtypes and determining the respective treatment regimen using compositions of probes/primers (in kit or array form) and a software tool to read out the results.