Our study suggests that there are age and gender specific genomic alterations in FL. We plan to follow up with validation studies in a larger cohort.

We identified BCR as a potentially novel prognostic marker for high grade/transformed follicular lymphomas 

REFERENCES:


BACKGROUND

Follicular lymphoma (FL) is the second most common B-cell non-Hodgkin lymphoma that is defined by unique somatic mutations and gene expression profiles. In FL, age and sex have not been well characterized.

METHODS

We analyzed data from 135 patients with FL who underwent next generation sequencing (NGS) and RNA expression analysis using the Genomic Testing Cooperative Hematologic Malignancies platform. The DNA and RNA panels assessed 179 genes and 1408 genes, respectively. Our analysis was based on two cohorts, monthly basis, from January 2015 to December 2019. The first cohort included patients aged 65+ years, n=197 (M) and n=197 (F). Data and datasets were analyzed with StringDB (version 1). Infranomic and Broad Institute Gene Set Enrichment Analysis (GSEA).

RESULTS

- MEX2 and BIM mutations are clinically enriched in men and women, respectively with prognostic implications.
- BCR, CREBBP, STAT3, and TET3 mutations were enriched in the elderly population.
- EP300 mutations were enriched in the young population.
- No difference in expression of large cell lymphoma genes is seen between elderly and young populations.
- BCR mutations are associated with more aggressive follicular phenotypes.
- BCR mutations are enriched in DLBCL, GCB type.
- BCR mutations are clustered at the N terminus of the protein affecting homodimerization and may affect the balance of downstream GSI and GAP activity.

CONCLUSIONS

- Follicular lymphoma is underrepresented in genomic studies. We report age and sex-related genomic alterations and RNA expression.
- BCR gene has not been previously identified as a prognostic marker for high grade/transformed follicular lymphomas.

BCR (BREAKPOINT CLUSTER REGION GENE)

Table 1: Genomic profiles of BCR mutants in follicular lymphoma

Figure 1: Top 5 altered genes in Follicular Lymphoma

Figure 2: Significant sex related alterations. a. Clinically enriched somatic mutations b. RNA expression gene set enrichment analysis

Figure 3: Significant age related alterations. a. Clinically enriched somatic mutations b. RNA expression gene set enrichment analysis

Figure 4: BCR gene lollipop plot in follicular lymphomas

Figure 5: BCR gene protein interactome

Figure 6: BCR mutated vs unmutated RNA expression gene set enrichment analysis

Figure 7: BCR prevalence in lymphoma