Follicular dendritic cell sarcoma (FDCS) is a rare neoplasm of hematopoietic derivation. Until now, little has been known about the genetic changes of FDCS. Few cases have been evaluated by conventional cytogenetics or other genetic techniques. We evaluated 14 cases of FDCS using a molecular inversion probe (MIP)-based assay, which is optimized to evaluate genomic alterations in archived formalin fixed, paraffin-embodied (FFPE) tissues.

A total of 14 deidentified patient samples were recruited from several institutions. Genomic DNA was isolated from FFPE tissues and analyzed by MIP array to assess for copy number (CN) alterations and loss-of-heterozygosity (LOH) in the samples. Genomic alterations were observed in 11 of 14 FDCS cases analyzed. Most cases showed complex genomic profiles with a high number of CN/LOH calls observed. Comparison of abnormalities across samples showed a predominance of losses and LOH, with several recurrent regions observed in 45% (5 cases) or more. Some recurrent regions/gene have known associations with other hematopoietic disorders and sarcomas, including RB1, TP53, CDKN2A, and BIRC3.

We report detailed genetic analysis in the largest series of FDCS to date. Importantly, we identified many areas of recurrent abnormalities in our series of cases. In addition to providing novel genomic profiling, which will aid in genetic diagnosis, this effort may lead to identification of genes contributing to development and/or differentiation of FDCS and potentially actionable target genes, which may suggest new therapies for these rare disorders in the future.

**Background**

Follicular dendritic cell sarcoma (FDCS) is a rare neoplasm of follicular dendritic cells (Fig. 1). Normal follicular dendritic cells are possibly a specialized form of myofibroblasts and are likely derived from non-bone marrow origins, in contrast to most other accessory/dendritic cells. Normal follicular dendritic cells represent the most other accessory/dendritic cells. Normal follicular dendritic cells are fixed against presenting dendritic cells of follicles. FDCS occurs in all ages and without a sex predilection. Patients typically present with a slow growing mass, without any systemic symptoms. At present, treatment consists of surgical excision, with or without adjuvant therapy or local radiotherapy. Local recurrences occur in about 50% of patients, with distant metastases eventually occurring in about 25% of patients. Little has been known about the genetic changes of FDCS. We analyzed 14 patient samples by MIP array to characterize the genomic profile of FDCS.

**Results**

- 11/14 FDCS cases showed genetic abnormalities (Fig. 2).
- Complex genomic profiles, with a high number of calls per case were common (n=8/11 cases with ≥20 calls, range 26–69).
- Losses and LOH calls were predominant.
- 16 genomic regions were recurrently affected by losses/LOH, observed in 45% (n=5) cases or greater (Fig. 2, asterisks; Table 1).
- Alterations of 3p, 13q and 14q were observed in 91% (10/11) cases.
- No recurrent gains were observed.
- Some recurrent regions genes have known associations to other hematopoietic disorders and/or sarcomas: RB1, TP53, CDKN2A and BIRC3.

**Conclusions**

We report detailed genetic analysis in the largest series of FDCS to date. Importantly, we identified many areas of recurrent abnormalities in our series of cases. In addition to providing novel genomic profiling, which will aid in genetic diagnosis, this effort may lead to identification of genes contributing to development and/or differentiation of FDCS and potentially actionable target genes, which may suggest new therapies for these rare disorders in the future.

**Table 1. Summary of Recurrent Losses/LOH Regions in Follicular Dendritic Cell Sarcoma**

<table>
<thead>
<tr>
<th>Genomic region</th>
<th>1p proximal</th>
<th>2p distal</th>
<th>3p proximal</th>
<th>3q distal</th>
<th>6q prox</th>
<th>6q mid</th>
<th>7q mid</th>
<th>8p distal</th>
<th>9p (CDKN2A) region</th>
<th>11q (BIRC3) region</th>
<th>13q prox</th>
<th>14q prox</th>
<th>15q mid</th>
<th>17p</th>
<th>18q mid</th>
<th>22q distal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cyto band</strong></td>
<td>1p21.1-1p13.2</td>
<td>2p23.3-2p23.1</td>
<td>3p14.1-3p12.2</td>
<td>3q26.31-3q28</td>
<td>6q14.3-6q15</td>
<td>6q21-6q23.2</td>
<td>7q31.1-7q31.33</td>
<td>8p23.1-8p22</td>
<td>9p21.3</td>
<td>11q22.2</td>
<td>14q31.3</td>
<td>14q12-14q21.1</td>
<td>15q14-15q15.3</td>
<td>17p13.3-17p11.2</td>
<td>18q12.3-18q21.2</td>
<td>22q12.3-22q13.3</td>
</tr>
<tr>
<td><strong>Approx. Size</strong></td>
<td>7.1 Mb</td>
<td>7.4 Mb</td>
<td>14.0 Mb</td>
<td>18.9 Mb</td>
<td>4.1 Mb</td>
<td>25.3 Mb</td>
<td>17.3 Mb</td>
<td>2.1 Mb</td>
<td>52.9 kb</td>
<td>130 kb</td>
<td>22.1 Mb</td>
<td>16.3 Mb</td>
<td>8.9 Mb</td>
<td>18.5 Mb</td>
<td>10.0 Mb</td>
<td>15.8 Mb</td>
</tr>
<tr>
<td><strong>% Abnl cases (n=11)</strong></td>
<td>55</td>
<td>55</td>
<td>91</td>
<td>45</td>
<td>45</td>
<td>55</td>
<td>72</td>
<td>45</td>
<td>64</td>
<td>55</td>
<td>91</td>
<td>91</td>
<td>64</td>
<td>55</td>
<td>55</td>
<td>55</td>
</tr>
<tr>
<td><strong>Cancer genes list</strong></td>
<td>RBM15</td>
<td>NCOA1, DNMT3A, ALK</td>
<td>MITF, FOXP1</td>
<td>PIK3CA, SOX2, ETVS, EIF4A2, BCL6, LPP</td>
<td>none</td>
<td>PRDM1, ROS, GOPC, STL</td>
<td>MET</td>
<td>none</td>
<td>CDKN2A</td>
<td>BIRC3</td>
<td>BRCA2, LHPF, LCP1, RB1</td>
<td>NIKX2-1</td>
<td>BUB1B</td>
<td>YWHAE, USP6, TP53, PERI, GAS7, MAP2K4</td>
<td>none</td>
<td></td>
</tr>
</tbody>
</table>

**Genetic Array Analysis of Follicular Dendritic Cell Sarcoma**


Clariant Pathology Services, Aliso Viejo, CA

**Abstract**

We report detailed genetic analysis in the largest series of FDCS to date. Importantly, we identified many areas of recurrent abnormalities in our series of cases. In addition to providing novel genomic profiling, which will aid in genetic diagnosis, this effort may lead to identification of genes contributing to development and/or differentiation of FDCS and potentially actionable target genes, which may suggest new therapies for these rare disorders in the future.