Introduction

Plasma cell dyscrasias (PCDs), also known as monoclonal gammapathies, are a spectrum of diseases associated with monoclonal proliferation of plasma cells (PCs) in the bone marrow and the excess production of monoclonal proteins (M-proteins) consisting of immunoglobulin (ig) and/or free light chains (FLCs).

In this study we describe two monoclonal antibodies, 10B3 and 7F11, that bind to a cell surface lambda myeloma antigen (LMA). We show the presence of LMA in a human myeloma cell line, PCD bone marrow samples, plasmacytoma tissue and normal secondary lymphoid tissues.

A phase I/II clinical trial is using a novel antibody called KappaMab (formerly MDX-1097) that binds to kappa myeloma antigen (KMA)\(^*\) has recently been completed.

Methods

- Binding of the fully human monoclonal antibodies 10B3 and 7F11 was assessed on human myeloma cell lines representing lambda isotypes 1-3.
- Multiparametric flow cytometry was performed in bone marrow samples from 65 patients with various PCDs. Informed consent was obtained for testing.
- The antigen density of KMA or LMA versus BCMA was assessed.
- Tissue distribution on myeloma and normal snap frozen tissues using whole tissue 10B3-FITC was analyzed.

Results

Co-expression of KMA and BCMA was observed in 17/28 (61%) of cases of either untreated sNDMM or treated sRRMM (Table 1). Of the 10 untreated sNDMM cases, BCMA was expressed on 9 and LMA was expressed on 5; all 5 of these cases co-expressed BCMA and 2 co-expressed CD56. Within the 4 sRRMM cases, all expressed BCMA and 2 also expressed LMA (Table 2). SLAMF7 (CD319) was expressed on all patient bone marrow samples tested.

KMA and LMA expression were enriched in cases of RRMM and LMA expression was enriched in cases of AL Amyloidosis (Tables 1-3). Table 1: Marker Expression for Kappa Positive Plasma Cell Dyscrasia.

<table>
<thead>
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<th>Diagnosis</th>
<th>LMA</th>
<th>KMA</th>
<th>CD269</th>
<th>CD319</th>
<th>CD56</th>
<th>BCMA</th>
<th>CD56</th>
<th>CD138</th>
<th>CD5</th>
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<th>LMA &amp; CD56</th>
<th>CD5 &amp; CD138</th>
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</table>

Figure 1. Binding profiles of the 7F11, 10B3 and KappaMab (KMA) antibodies. Antibody F(ab’)\(^2\), antibody fragments conjugated to APC in lambda- and kappa-positive cell lines. Antibody F(ab’)\(^2\), Fragments were used for flow cytometry to avoid Fc binding to leukocytes. 10B3 (orange lines) bound all 3 lambda cell lines, LP-1 (λ1), RPMI-8226 (λ2) and OPM-2 (λ3). 7F11 (mauve lines) bound to RPMI-8226 (orange lines) bound all 3 lambda cell lines, LP-1 (λ1), RPMI-8226 (λ2) and OPM-2 (λ3). Neither 7F11 nor 10B3 bound to the kappa cell line, JH4. KappaMab (KMA) (grey lines) bound only to the JH4 cell line. The human IgG1 isotype control (grey lines) did not bind to any of the cell lines tested.

Discussion and Conclusions

- The presence of LMA on the surface of clonal PCs in the bone marrow of PCD patients was detected using whole tissue 10B3-FITC was analyzed.
- The antigen density of KMA and LMA is higher than that of BCMA on PCs in cases of RRMM and KMA expression is slightly weaker CD38 expression. Abnormal PCs express KMA (B) and have dim expression for CD138 and are very few plasma cells in this sample.

Reference:

3. Tissue distribution on myeloma and normal snap frozen tissues using whole tissue 10B3-FITC was analyzed.

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