Novel antigens LMA and KMA are expressed on malignant bone marrow plasma cells from patients at all stages of multiple myeloma

Mary Sartor, BSc PhD,1, David Gottlieb, MBBS MD FRACP FRCPA,2 and Rosanne Dunn, PhD3

1Centre for Cancer Research, Westmead Institute for Medical Research, Sydney, NSW, Australia; 2Department of Haematology and Bone Marrow Transplantation, Westmead Hospital, Sydney, NSW, Australia; 3Haemalogix Ltd, Woolloomooloo, NSW, Australia

Abstract

Lambda myeloma antigen (LMA) and kappa myeloma antigen (KMA) are unique antigens on the surface of malignant plasma cells (PCs) in multiple myeloma and other plasma cell dyscrasias (PCD) bone marrow samples, as well as in human myeloma cell lines. In addition:

- LMA and KMA are also found on occasional mononuclear cells in tonsillar tissue and secondary mucosal lymphoid tissue.
- LMA and KMA are NOT present on normal B cells or other normal immune cells.

Characteristics of the antibodies called KappaMab and LambdaMabs (10B3 and 7F1) that bind to specific conformational epitopes in the constant regions of these surface-bound light chains have been described in clinical trials and in vitro experiments.

Here we present data on a larger series of patients with PCDs, and show the expression of LMA versus BCMA on PCs from patients in whom myeloma evolves from monoclonal gamopathy of unknown significance (MGUS).

We also describe the difference in phenotype between LMA and KMA expressing malignant PCs and the frequent expression of KMA in relapsed refractory myeloma patient (RRMM) samples.

Methods

- Patient bone marrow samples (n=59 and n=35) were analysed using multiparametric FCM immunophenotyping with APC labelled LambdaMab (10B3) and KappaMab Fab'2 fragments, CD38, CD138, CD319 (SLAMF7), CD56, CD36, CD45 monoclonal antibodies.
- PCs were identified as previously described by initial gating using CD38 and CD138.
- LMA and KMA expression was determined and compared with the other plasma cell markers.
- Antigen density was calculated using QuantiBrite beads in PE.

Results

- Mean LMA antigen density was lowest in MGUS, was increased in NDMM (untreated) cases, and was highest in RRMM (treated) cases.
- Conversely, the percent of samples expressing BCMA was highest in MGUS, SMM and NDMM, then decreased in RRMM.
- In the RRMM subset who had bone marrow samples taken post stem cell transplant, KMA was expressed in 4/6 cases.

Discussion and Conclusions

- In an enlarged cohort of patients with myeloma, we have confirmed that KMA and LMA are expressed at all stages of disease.
- Our data examining longitudinal expression in two LMA+ patients suggests that expression of LMA on bone marrow PCs increases from MGUS to MM.
- The majority of patients with RRMM expressed KMA. Further data is required to confirm LMA expression in the RRMM population.
- LMA and KMA densities are enriched, while BCMA densities are reduced or remain the same in RRMM relative to NDMM samples, indicating a possible treatment-resistant clone.
- Co-expression of LMA or KMA with BCMA is not consistent, KMA is more consistently co-expressed with CD56 compared to LMA.

Mean LMA antigen density was lowest in MGUS, was increased in NDMM and was highest in RRMM, while BCMA increased in NDMM relative to MGUS, and decreased in RRMM cases.

Mean KMA antigen density was lowest in MGUS, was increased in NDMM and was highest in RRMM, while BCMA was lowest in MGUS and remained the same in NDMM and RRMM cases.

Author contact: Rosanne Dunn: rosanne@haemalogix.com