ACR Plenary Session

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Salivary Gland FcRL4+ B-Cells Are a Potential Source of Progenitor Cells for MALT Lymphoma in Primary Sjögren’s Syndrome

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Background/Purpose:

Patients with primary Sjögren’s Syndrome (pSS) have an increased risk of non-Hodgkin’s lymphoma, predominantly of the Mucosa Associated Lymphoid Tissue (MALT) type, which commonly occur in the parotid glands. MALT lymphomas in general, express Fc receptor-like 4 (FcRL4/IRTA1/CD307d)1. Normally FcRL4 is expressed on a very small subset of mucosa-associated B-cells. FcRL4+ B-cells might be closely related to the MALT lymphoma cells. Therefore, we assessed whether FcRL4+ B-cells are present in the inflamed salivary gland tissue of pSS patients, and whether these cells are targeted by biological therapy.

Methods:

Forty nine parotid gland MALT lymphomas, 30 parotid gland biopsies, 24 labial gland biopsies and parotid gland biopsies before and after treatment with rituximab...
(18 patients) or abatacept (15 patients), all obtained from pSS patients, were
stained for FcRL4 expression. As control served parotid gland biopsies of 8 non-pSS
sicca patients and 5 non-sicca patients. FcRL4 mRNA was isolated from 8 non-pSS
sicca patients, 9 pSS patients and 11 pSS MALT lymphoma patients.

Results:

Nearly all (96%) parotid
gland MALT lymphomas expressed FcRL4 (Fig. 1). Low numbers of FcRL4+ B-cells
were detectable in parotid glands of most (90%) pSS patients. Intensely stained
FcRL4+ B-cells were in close relation to lymphoepithelial lesions
with some FcRL4+ B-cells within the surrounding infiltrate. Even
lower numbers of FcRL4+ B-cells were discernible in the labial
glands. Levels of FcRL4 were significantly increased in parotis gland tissue of
pSS patients, compared to non-pSS sicca patients. These levels further
increased significantly in pSS patients with MALT lymphomas in the parotid
glands. Treatment with rituximab significantly
reduced the number of FcRL4+ B-cells in the parotid glands, whereas
abatacept treatment did not affect FcRL4+ B-cells in the
glandular tissue (Fig. 2).

Conclusion:

FcRL4+ B-cells
are found in the salivary glands of pSS patients and are likely the cells from
which MALT lymphomas arise. The observation that FcRL4+ B-cells are
enriched in the parotid glands may explain why MALT lymphomas preferentially
develop in these glands. Our treatment studies reveal that FcRL4+ B-cells
can be targeted by anti-CD20 therapy and that these cells are maintained in a CD28-
independent manner.

References

1. Falini B. et al. IRTA1 is
Figure 1. FcRL4+ cells in PSS patients: MALT lymphoma, parotid gland vs labial gland.
(A) FcRL4+ MALT lymphoma in the parotid gland of a PSS patient. The FcRL4+ B-cells cluster in and around the lymphoepithelial lesions and the marginal zone. (B) Corresponding HE stain of MALT lymphoma. (C) FcRL4+ B-cells in the parotid gland of a PSS patient. FcRL4+ B-cells are in close association with the ductal epithelium. Less FcRL4+ B-cells are found in the infiltrate with lower intensity of the FcRL4 stain. (D) Corresponding HE stain of the parotid gland. (E) FcRL4+ B-cells in the labial gland of a PSS patient. Few FcRL4+ B-cells with low intensity are found despite inflammation. (F) Corresponding HE stain of the labial gland.
Figure 2: FcRL4 staining in pSS patient treated with abatacept or Rituximab.
Amount of FcRL4 staining is reduced after Rituximab therapy in pSS patients. The placebo group of the rituximab study remained stable. Abatacept treatment of pSS patients did not effect the amount of FcRL4 staining. All biopsies were taken from the parotid gland. *Wilcoxon Signed Rank p<0.05
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