



CXC chemokine receptor type 4 in systemic lupus

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Dear editor

There is increasing interest in the complex links between the immune system and cancer risk. Early data indicated decreased breast cancer risk for women with human immunodeficiency virus (HIV) infection compared to the general population [1]. A case-control study further showed that lower breast cancer risk in women with HIV was significantly and independently linked to infection with HIV strains that bind to CXC chemokine receptor type 4 (CXCR-4) [2]. In most normal tissues, CXCR4 is not generally expressed (or is expressed at very low levels), but is found on some types of cancer cells, including breast cancer. CXCR4 is also expressed on abnormal precancerous breast cells. The authors of the case-control study thus hypothesized that, in women with HIV, involution of the abnormal precancerous cells is mediated by binding of CXCR4.

Systemic lupus erythematosus (SLE) is an autoimmune rheumatic disease which is associated with a strikingly decreased risk of certain malignancies including breast cancers [3]. Given the data suggesting that the decreased risk of breast cancer in women with HIV infection is mediated by interactions with CXCR4, we hypothesized that the sera of women with SLE actively binds to CXCR4 antigen, which might invoke a pathway through which the lower breast cancer risk in SLE is mediated.

Methods

We performed preliminary analyses using banked sera, drawn from women with SLE who are annually followed at the McGill University Health Centre (MUHC) lupus clinic, which currently numbers over 650. We randomly selected 19 of these patients with SLE, to assess whether SLE sera demonstrated active binding to CXCR4 antigen, in an enzyme-linked immunosorbent assay (ELISA) test. Human recombinant CXCR4 was purchased from Abnova (catalog # H00007852-P01). The secondary antibody was alkaline phosphatase-conjugated IgG F(ab')₂ fragment of donkey anti-human-IgG and was purchased from Jackson ImmunoResearch (catalog # 709-056-098). Phosphatase substrate was purchased from Sigma-Aldrich (Catalog # S0942)

and colorimetric detection was at 405 nm. We also compared results of the ELISA test in these SLE patients, to that of banked serum from 23 healthy controls.

Results

In the assay for CXCR4 antigen binding, at 20 minutes, both the mean and median optical density of sera diluted 1:40 was slightly but non-significantly higher, in SLE patients versus controls. For the entire sample, mean value in SLE was 0.461, 95% confidence interval, CI 0.116, 0.638 (while the average for controls was 0.435, 95% CI 0.101, 0.605) and the median value in SLE was 0.493 (0.356 in controls). Limited to Caucasians only, the mean value in SLE was 0.543 (while the average for controls was 0.459) and the median value in SLE was 0.566 (0.423 in controls).

Discussion

We present a novel hypothesis of how the lower risk of breast cancer risk in SLE may be mediated by CXCR4 binding on precancerous cells. Our data suggest that SLE patients have measurable levels of antibodies against CXCR4. Although our preliminary data only suggest a slight trend towards higher mean and median titers in lupus patients than in controls, it would be of interest to determine whether SLE patients have higher levels of functional anti-CXCR4 antibodies that either activate or block signalling through this receptor.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	EN	JR	JJG	CAP	SB
Research concept and design	✓	✓	✓	✓	✓
Collection and/or assembly of data	✓	✓	--	✓	✓
Data analysis and interpretation	✓	✓	✓	✓	✓
Writing the article	✓	✓	✓	✓	✓
Critical revision of the article	✓	✓	✓	✓	✓
Final approval of article	✓	✓	✓	✓	✓

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