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Letter to the Editor – Brief Communication

Letter to the editor re: "Expression of CD56 in patients with adenomyosis and its correlation with dysmenorrhea" from F Wang and colleagues

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Dear Editor,

We read with interest the article by Wang et al.(1) on the role of CD56 in adenomyosis. The authors, using a mouse monoclonal antibody and immunohistochemistry, reported that there was increased expression of CD56 in ectopic adenomyotic tissue in patients suffering dysmenorrhoea when compared to the eutopic tissue and corresponding ectopic adenomyotic tissue from patients without dysmenorrhoea.

The mouse monoclonal antibody (MOC31, AbCam #ab187270, Cambridge Science Park, Cambridge, UK) that the authors employed in their work is raised against human epithelial cell adhesion molecule (EpCAM) protein that is known to be expressed by endometrial epithelial cells according to the AbCam website. The expression pattern of EpCAM in the human endometrium is available in the Human Protein Atlas (http://www.proteinatlas.org/ENSG00000119888-EPCAM/tissue/endometrium) and is similar to the figures presented in Wang et al's manuscript. It is commonly used to isolate endometrial epithelial cells in endometrial studies (2).

CD56, also known as Neural Cell Adhesion Molecule (NCAM), is a well-established marker for uterine Natural Killer (uNK) cells. There is a plethora of papers which describe the immuno-expression pattern of CD56 in the endometrium, and there are validated scoring methods of CD56 expressing uNK cells in the endometrium (3). Figure 1 illustrates CD56 immuno-staining using Novocastra clone 1B6 (Leica Biosystems, Newcastle, UK) in cells within the human eutopic endometrium, and matched ectopic endometriotic lesions and adenomyosis from our group. In accordance with previously published work and the data available on the Human Protein Atlas (http://www.proteinatlas.org/ENSG00000149294-NCAM1/tissue/endometrium) uNK cells were localised within the stroma, while the glandular epithelium remained immuno-negative. We were surprised that there was no mention of uNK cells and the numerous previous publications on endometrial CD56 expression (reviewed in(4)) in the current manuscript. In particular, the absence of reference to previous papers on adenomyosis, for example the 1998 manuscript by a well-known uNK cell research group in the UK was a striking omission (5).

When consulting the Abcam website monoclonal anti-human CD56 antibody clone MOC1 (AbCam, #ab133345) was one of several available antibodies. It seems that the authors could have confused MOC1 with MOC31.

Considering the information presented by the authors on the antibody they used; the known, previously published and well-established expression pattern of EpCAM and CD56 in the human endometrium; and the use of IHC only as a method to confirm the protein of interest by the authors in this manuscript, we conclude that Wang et al.(1) may have misinterpreted the EpCAM protein immuno-localisation for CD56 in their paper. In order to prevent misdirection of scientific readership, we believe that this paper needs to be revised accordingly to confirm whether the conclusions reached by the authors can be supported by the presented data.

References

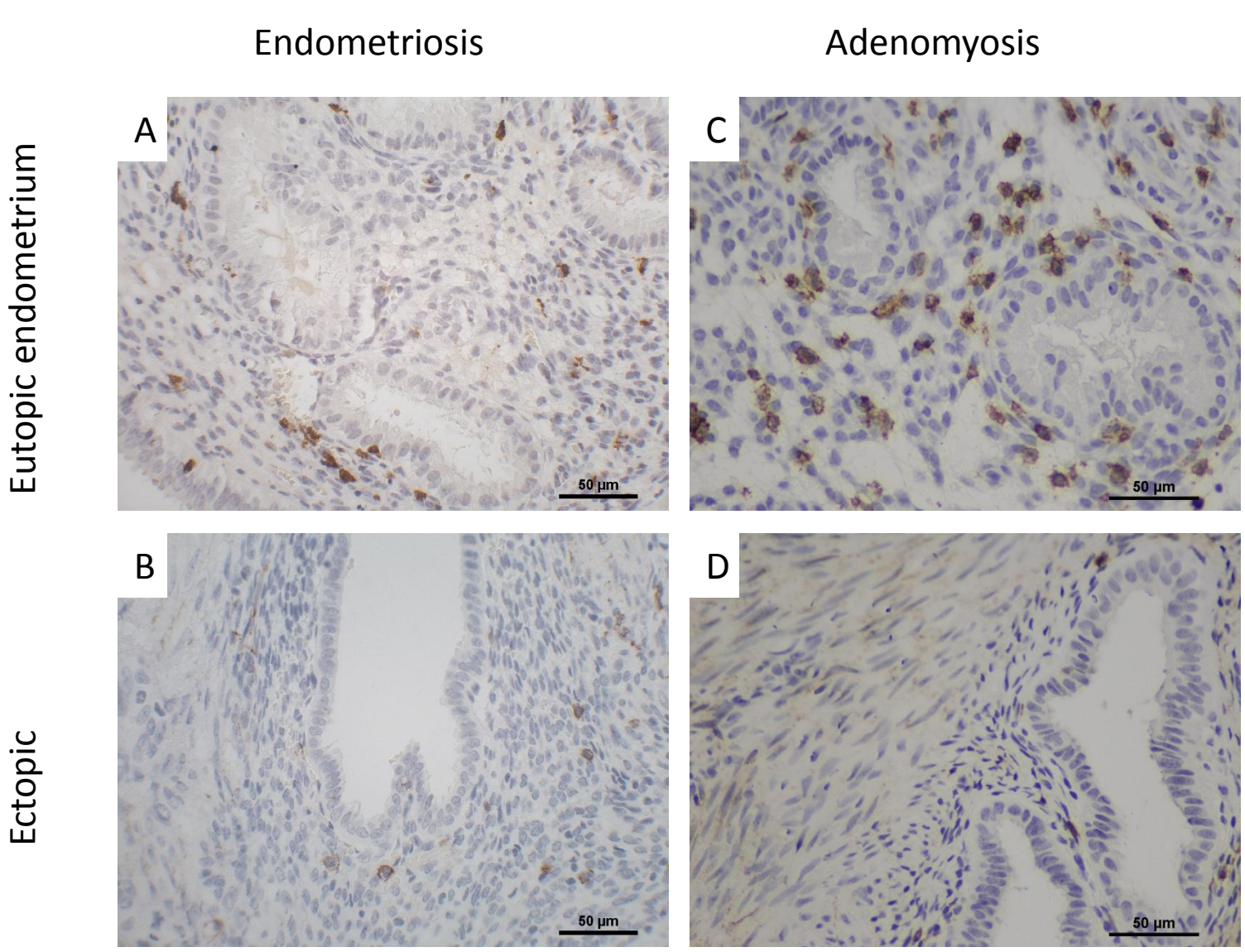
1. Wang F, Shi X, Qin X, Wen Z, Zhao X, Li C. Expression of CD56 in patients with adenomyosis and its correlation with dysmenorrhea. Eur J Obstet Gynecol Reprod Biol. 2015;194:101-5.
2. Valentijn AJ, Palial K, Al-Lamee H et al. SSEA-1 isolates human endometrial basal glandular epithelial cells: phenotypic and functional characterization and implications in the pathogenesis of endometriosis. Hum Reprod. 2013 Oct;28(10):2695-708.

3. Drury JA, Tang AW, Turner MA, Quenby S. A rapid, reliable method for uNK cell density estimation. J Reprod Immunol. 2013;97(2):183-5.

4. Bulmer JN, Lash GE. The Role of Uterine NK Cells in Normal Reproduction and Reproductive Disorders. Adv Exp Med Biol. 2015;868:95-126.
5. Bulmer JN, Jones RK, Searle RF. Intraepithelial leukocytes in endometriosis and adenomyosis: comparison of eutopic and ectopic endometrium with normal endometrium. Hum Reprod. 1998;13(1O):2910-5.

Figure legend

Figure 1 Representative micrographs showing CD56 (Novocastra clone 1B6, Leica Biosystems, Newcastle, UK) immunohistochemical staining of human secretory phase eutopic endometrium, endometriosis and adenomyosis lesions. Brown DAB staining shows localisation of CD56 positive uterine Natural Killer cells with blue nuclear haematoxylin counterstain. In all micrographs, CD56 immunostaining is localised to the stromal compartment, while the glandular epithelium remains negative. A; secretory phase eutopic endometrium from a patient with endometriosis. B; Matched peritoneal ectopic endometriotic lesion. C; secretory phase eutopic endometrium from a patient with adenomyosis. D; matched adenomyotic lesion. Magnification x400.


Endometriosis
Adenomyosis
Eutopic endometrium
Ectopic
A
B
C
D
50 µm
50 µm
50 µm
50 µm