AU1: New immunocytochemical marker for detecting epithelial cells in body cavity fluids

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Abstract
Further to detailed genetic and biochemical characterisation of AU1 as a surface glycoprotein present on epithelial cells, the antibody against AU1 was used as an immunocytochemical marker of epithelial cells in body cavity fluids in an attempt to improve the diagnosis made on routine staining. AU1 was initially tested in 144 morphologically clear cut effusions. It was positive in 46 of 52 (88%) carcinomas and negative in 82 of 84 (98%) benign effusions, including technically inadequate or poorly cellular preparations. There were no false positive results. AU1 was subsequently used more selectively—that is, in 42 of 175 (24%) of morphologically difficult fluids. AU1 provided essential diagnostic information in 15 of 42 (36%) and confirmed diagnosis in 17 of 42 (40%), thus enabling accurate diagnosis in a further 32 of 42 (76%) of the difficult cases. The total diagnostic accuracy was therefore 94.3%.

AU1 is a reliable immunocytochemical marker for detecting epithelial cells in body fluids. Its use improves diagnostic accuracy of morphological assessment in difficult cases.

AU1 is a human cell surface antigen defined by the monoclonal antibody AU1. It was raised conventionally by Arkle (1981) by immunising BALB/c mice with the colonic adenocarcinoma cell line LoVo. The genetic locus for this antigen has been assigned to chromosome 2. The product of the gene MIC18 is a single 35 kilodalton protein expressed by a limited set of normal epithelial cells and a wide variety of epithelial tumours.1 Further to the successful application of this antibody as an immunohistochemical marker to histological sections of various epithelia,12 we were interested to establish whether AU1 could be used as an aid in the detection of epithelial cells in body cavity fluids. Particularly encouraging was the fact that, unlike the antibodies to low molecular weight keratins, such as CAM 5-2, AU1 does not stain normal mesothelium.

Methods
Initially we used AU1 (Unipath Ltd) as an immunocytochemical marker in addition to routine staining of 144 morphologically diagnosed effusions (80 pleural and 64 peritoneal). Slides for immunocytochemistry were kept unfixed (air dried), stored at 20°C and were stained according to the alkaline phosphatase-antialkaline phosphatase (APAAP) method modified for cytological preparations. More recently, we have used AU1 more selectively—in 42 of 175 (24%) of fluids where morphological diagnosis was difficult and was confirmed by either poor clinical outcome or by tissue biopsy.

Results
Comparison of the morphological assessment with AU1 staining in 144 of the morphologically clear cut cases showed that AU1 was positive in 46 of 52 (88%) of the malignant effusions and negative in 82 of 84 (98%) of benign effusions, including those which were technically inadequate or poorly cellular. The two positively stained benign effusions

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Accepted for publication 14 August 1991

Pleural effusion containing cells from a metastatic breast carcinoma. (A) Malignant cells; mesothelial cells are indicated with arrows (May-Grunwald-Giemsa, oil immersion); (B) AU1 staining with APAAP highlights the malignant cells. Mesothelial cell is negative (arrow) (oil immersion).
**AUAI: New immunocytochemical marker for detecting epithelial cells in body cavity fluids**

A panel of antibodies on our effusions are using only AUAI instead. Caution should be exercised in the interpretation of positive AUAI staining of benign epithelial cells in peritoneal washings and effusions. These can originate from epithelia of the fallopian tube or from foci of pelvic endometriosis. We have found positively stained epithelial cells originating from ovarian adenofibroma. Particularly useful is the absence of staining in malignant mesothelioma. Although there are only two cases in this series, we are encouraged by the experience described with histological material from this department.

In conclusion, AUAI is the most sensitive of the currently available immunocytochemical markers for detection of epithelial cells in body fluids, and for the distinction between benign and malignant mesothelial cells. Combined with morphological assessment it can improve diagnostic accuracy.

**Discussion**

Conventional cytological diagnosis of malignant cells in effusions has its limitations, ranging from 15%–27% false negative reports. Various techniques, including conventional histochemistry, morphometry, electron microscopy and immunocytochemistry, are all used in an attempt to discriminate between benign and malignant cells and also between mesothelioma and peripheral pulmonary adenocarcinoma. Wick et al found that, although specific, periodic acid Schiff-diastase stained only 63% of the peripheral adenocarcinomas while hyaluronidase sensitive colloidal iron positivity, although restricted to mesothelium, stained only 41% of cases. The most commonly used immunocytochemical markers in effusions are cytokeratins, epithelial membrane antigen (EMA), carcinoembryonic antigen (CEA), and oncofetal protein B72-3. Cytokeratins and EMA stain both mesothelium and epithelium with varying intensity. CEA shows high specificity but variable sensitivity, ranging from 68%–96% for malignant effusions. B72-3 positivity for malignant epithelial cells ranges between 84% and 90%. Among markers, B72-3 positivity has been successfully characterised on histological material and, like AUAI, seems to be highly specific for epithelial cells although, in our preliminary experience, less sensitive.

In the light of our own experience and that of the others, we have recently stopped using a panel of antibodies on our effusions and are using only AUAI instead.

AUA1: new immunocytochemical marker for detecting epithelial cells in body cavity fluids.

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doi: 10.1136/jcp.45.4.358

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