Dear Editor,

A small proportion of patients (~4%) with metastatic cancer are diagnosed with cancer of unknown primary (CUP), for whom microarray gene expression analysis may play an important role. Our experience suggests that clinical management would have been changed in 12 out of 21 CUP cases if a 'site-of-origin' microarray result had been available.¹

A 78-year-old woman underwent lumpectomy of the right breast and a sentinel node procedure for an upper outer quadrant tumour (T2N0Mx). Pathology revealed an atypical papillary largely necrotic lesion with a diameter of 1.8 cm, which was considered to be an intracystic papillary carcinoma with no signs of invasion and with a resection margin of 4 mm. In addition, a 3 mm focus of ductal carcinoma in situ was removed with a resection margin of 3 mm. Immunohistochemical analysis revealed that both the oestrogen receptor (ER) and progesterone receptor (PR) were strongly positive. The sentinel node and six resected lymph nodes were free of tumour.

Postoperatively, local radiotherapy was administered. A productive cough prompted the attending physician to order a chest radiograph. The X-ray was highly suggestive for multiple lung metastases and a computed tomography (CT) scan revealed paratracheal lymphadenopathy, as well. Bronchoscopy, radionuclide bone scan and an ultrasound of the liver revealed no abnormalities. Fine needle aspirate of one of the pulmonary lesions was performed revealing hormone receptor negative adenocarcinoma. These results are unsupportive for the diagnosis of metastatic mammary carcinoma. Furthermore, an invasive component had never been identified in the breast lesion.

To gain further insight into the site of origin of the pulmonary lesions, gene expression analysis using CupPrint™ (licensed by Aviara) was performed. The CupPrint classified this patient’s pulmonary tumour as likely originating in the breast. Following the CupPrint test result, the patient was treated for pulmonary metastases of breast cancer with hormonal therapy using an aromatase inhibitor, anastrazole. This clinical decision would not have been anticipated without the CupPrint test result. A CT scan four months later revealed a partial response to therapy with a >50% reduction in the number and size of lung metastases. Three months later, a follow-up CT revealed a complete remission now lasting for >24 months with continuous hormonal therapy. This case illustrates how a dedicated gene expression array can redirect clinical decision making.

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WHAT WAS KNOWN ON THIS TOPIC?
Profiles have been shown to retain part of their gene expression pattern in the metastatic setting and can thus be used to determine the primary tissue of origin. The use of gene expression in the diagnostic setting is becoming more common.

WHAT DOES THIS ADD?
This letter is very illustrative of how gene expression profiling can change clinical management of a patient to a more tailored approach.
A woman with a swollen neck

Dear Editor,

Van Kuilenburg et al. present an interesting case of Ludwig’s angina. In 1836 Ludwig described five patients with rapidly evolving submandibular infections and these infections are now known as Ludwig’s angina. The medical history of a recent dental extraction and the swelling of the submandibular space points to a diagnosis of Ludwig’s angina.

I would like to emphasise that it is important at diagnosis to define to which space this infection has spread. In this case, the computed tomography scan points to advanced spread of infection beyond the submandibular and parapharyngeal spaces to the retropharyngeal space. The retropharyngeal space lies near the ‘danger space’, which descends directly into the posterior mediastinum to the level of the diaphragm.

Most cases of Ludwig’s angina are caused by Gram-positive organisms, mostly Streptococci and anaerobes and not Gram-negative rods. Furthermore, I would like to point out that the first choice of treatment in different guidelines (Dutch guideline available at www.swab.nl) is high-dose penicillin G in combination with metronidazole or broad-spectrum penicillin with a β-lactamase inhibitor instead of a cephalosporin with metronidazole.

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REFERENCES