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Oestrogen receptor determination in breast and gynaecological tissue. What is the best approach to reproducible measurement?☆

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The biochemical determination of oestrogen receptor (ER) content has been the subject of many studies. All of these have concluded that External Quality Assurance (EQA) is essential to any agreed programme. This is because simple, well established procedures, such as the determination of the total protein content of a sample, can still be subject to significant variation, even in the best laboratories [1], demonstrating the need to check the quality of every step of each process, including initial tissue handling and storage, through to sample preparation and subsequent data analysis. As laboratories switch increasingly to immunohistochemical methods, it is critical [2] to ensure adequate, prompt fixation so that there is even penetration of the whole sample, use of a fully established antibody, a controlled and proven antigen retrieval system and a sensitive immunohistochemical detection method. Positive and negative controls [3,4] must be included in each batch of staining. Where semi-quantitative analysis of immunohistochemical staining is required, Quality Assurance (QA) of interpretation is just as important as the methodology [5].

Oestrogen and progesterone receptors

It is well established that the length of response of advanced breast cancer to endocrine therapy is proportional to the quantity of ER contained in the tumour [6]. The overview of early breast cancer treatment has, more recently [7], shown that the amount of benefit from adjuvant endocrine therapy is also proportional to the ER content. Finally, when tamoxifen is used for chemoprevention (or delaying onset?) of breast cancer, a dramatic reduction is seen in the ER+ group (treated versus controls), whereas there is no difference between treated and control among the ER− tumours [8]. For all these reasons, there is a strong case for ER to be determined in all primary breast cancers. There is now good evidence [9] that immunohistochemical determination of ER is at least as powerful in predicting response to adjuvant therapy as is biochemical measurement. An appropriate methodology has been published in Ref. [10] which makes the recommendation that EQA be mandatory and identifies schemes such as those run by UK National External Quality Assurance Scheme (NEQAS) (contact: rmkdhcr@ucl.ac.uk). A simple scoring system is found to be the most effective [9,10]. This awards up to five points for % nuclei staining 0 = no nuclear staining; 1 = < 1% nuclei staining; 2 = 1–10% nuclei staining; 3 = 11–33% staining; 4 = 34–66% staining; 5 = 67–100% staining) and up to three marks for intensity of stain (0 = no staining; 1 = weak staining; 2 = moderate staining; 3 = strong staining). If a tumour scores zero for ER using this system, the progesterone receptor (PR) content should be determined. Patients whose tumours are zero for both ER and PR will not respond to endocrine therapy and should receive alternate therapies, as appropriate. As the score for ER increases, so the chance of response to endocrine therapy increases.

The detection of a second ER, now known as ERβ, makes matters a little more complex [11]. Other presentations at this meeting will comment on the relative amounts of the two types of receptor in breast cancer, and on the way that the ratio of the two might influence the response to endocrine therapy.

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