

Editorial

The Basis of Tumor Marker Determinations - Recommendations of the EGTM

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Scientists from different European countries, from both hospital and university laboratories and from companies involved in the development of tumor marker tests, have been working together for several years in an informal group. In 1997, the European Group on Tumor Markers (EGTM) was formally established. A management structure for the group was agreed upon and a Board elected. The Executive Board of EGTM currently includes Prof. Dr. R. Lamerz (Klinikum Grosshadern, Munich, Germany) as chairman, Dr. P. Bialk (Roche Diagnostics, Mannheim, Germany) as secretary, Prof. Dr. A. van Dalen (Institute of Tumor Marker Oncology, Gouda, The Netherlands) as treasurer and Dr. C. Sturgeon (Royal Infirmary of Edinburgh, United Kingdom) and Dr. A-Ch. Aronsson (Sangtec Medical, Bromma, Sweden) as members.

The aims of the EGTM are:

- to inform clinicians and laboratories about the beneficial use of tumor marker determination
- to give scientific advice in the study of tumor markers and in new marker assessment
- to publish guidelines for clinicians and laboratories
- to support the organization of tumor marker symposia
- to set up a European Quality Control Assessment Scheme and to support national schemes
- to network with regulatory bodies and national QC scheme organizers throughout Europe^[1].

In 1999, the Publication Committee of EGTM published their Consensus Recommendations^[2]. In Kuwait, these recommendations may serve as the basis of tumor marker determinations and could be a valuable tool to extend these determinations in the Gulf States.

The term "tumor markers" embraces a spectrum of molecules of widely divergent characteristics, but sharing an association with malignancy in the

clinical detection (diagnosis, screening) and management (monitoring, prognosis) of cancer patients. Tumor markers are generally not diagnostic, although they can provide information that may contribute to the diagnostic process, particularly in selected patients, e.g. those referred to specialist units. For pre-treatment tumor marker measurements in patients with suspected malignancy, clinical presentation will usually suggest which marker would be most helpful. The diagnostic value of a tumor marker will depend on the prevalence of the disease in the population group being considered and on the sensitivity and specificity of the tumor marker.

Tumor markers may be helpful in differential diagnosis, e.g. in germ cell cancers where there may be different cell types. This may be especially true when there are metastatic deposits but the primary site is unknown, e.g. NSE in lung cancer and CA15-3 in breast cancer. It is important to mention that no tumor marker is specific for malignancy (elevation may be due to benign disease) and that a "normal" tumor marker results does not necessarily exclude malignancy or recurrence. It is well-documented that post-therapy serial monitoring of serum tumor marker concentrations may provide an early indication of recurrence, sometimes months before this is clinically evident. Unless alternative therapy is available and can be instituted based on marker results, such lead-time may not benefit the patient.

Many tumor marker tests were formerly performed in specialized laboratories. With the development of automated immunoassays, however, they are now often available in routine laboratories. Results are consequently more readily available to non-specialized clinicians who may be less familiar with their interpretation. This, coupled with increasing pressure on laboratories in Europe to reduce costs and on clinicians to practice evidence-based medicine, encourages critical appraisal of how to achieve the best use of these

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Table 1.
Characteristics of tumor markers

Tumor marker	Biochemical properties	Molecular weight	Primary clinical applications
Alpha-fetoprotein (AFP)	Glycoprotein; 4% carbohydrate; considerable homology with albumin	70 kD	Diagnosis and monitoring of primary hepatocellular carcinoma and germ cell tumours. Prognosis of germ cell tumours
Cancer antigen 125 (CA125)	Mucin identified by monoclonal antibodies	200 kD	Monitoring ovarian carcinoma. Prognosis after chemotherapy
Cancer antigen 15.3 (CA15.3, BR 27.29)	Mucin identified by monoclonal antibodies	>250 kD	Monitoring breast cancer
Cancer antigen 72.4 (CA72.4)	Glycoprotein identified by monoclonal antibodies	48 kD	Monitoring gastric carcinoma
Cancer antigen 19.9 (CA19.9)	Glycolipid carrying the Lewis a blood group determinant	1,000 kD	Monitoring pancreatic cancer
Carcinoembryonic antigen	Family of glycoproteins, 45-60% carbohydrate	180 kD	Monitoring gastrointestinal and other adenocarcinoma
CYFRA21-1	Fragments of cytokeratin 19	30 kD	Monitoring bladder and lung cancer
Estrogen receptor	Nuclear transcription factor	65 kD	Predicting response to endocrine therapy in breast cancer
Human chorionic gonadotrophin (hCG)	Glycoprotein hormone consisting of two non-covalently bound subunits (alpha and beta)	36 kD	Diagnosis and monitoring non-seminomatous germ cell tumours, choriocarcinomas, hydatiform moles, seminomas. Prognosis of germ cell tumours
Neuron specific enolase (NSE)	Dimer of the enzyme enolase	87 kD	Monitoring small cell lung carcinoma, neuroblastoma, apudoma
Placental alkaline phosphatase (PLAP)	Heat-stable isoenzyme of alkaline phosphatase	86 kD	Monitoring of germ cell tumours (seminomas)
Progesterone receptor	Nuclear transcription factor	A form: 94 kD B form: 120 kD	Predicting response to endocrine therapy in breast cancer
Prostate specific antigen (PSA)	Glycoprotein serine protease	36 kD	Diagnosis, screening and monitoring prostate cancer
Squamous cell carcinoma antigen (SCC)	Glycoprotein sub-fraction of tumour antigen T4	48 kD	Monitoring squamous cell carcinomas
Tissue polypeptide antigen (TPA)	Fragments of cytokeratin 8, 18 and 19	22 kD	Monitoring bladder and lung carcinoma
Tissue polypeptide specific antigen (TPS)	Fragment of cytokeratin 18	22 kD	Monitoring metastatic breast carcinoma

tests. In Table 1^[2], the biochemical properties and the primary clinical application of a number of tumor markers is summarized. This table may serve as the basis for the evaluation of tumor markers in germ cell cancer, prostate cancer, breast cancer, gynecological cancer, gastrointestinal cancer and lung cancer.

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