In the news

FROM THE EAA CONFERENCE ON THE TME

In March 2020, the European, American and Portuguese Associations for Cancer Research (EACR, AACR and ASPIC, respectively) held a basic and translational research conference on the tumour microenvironment (TME) that brought together more than 600 participants in Lisbon (Portugal). The inability of some speakers to travel owing to precautions relating to COVID-19 was not an obstacle: several excellent talks were delivered remotely.

Interrogating the analysis of the complex interactions between diverse cell types in the TME requires sensitive and reproducible methods, hence many talks focused on various modalities of single-cell analysis as well as multiplex and intravital imaging. The improved performance of these techniques over the past few years has not only enabled the separation of cell subpopulations on the basis of their molecular features, but also their dynamic monitoring during tumour progression and/or in response to therapy.

The role of tissue-resident and recruited tumour-promoting myeloid cells in tumour progression was a common theme. Both subtypes are present within tumours and are associated with distinct gene signatures. Ongoing studies are addressing how these differences affect various stages of tumour progression and, importantly, whether they can be exploited therapeutically.

The role of tumour-associated macrophages (TAMs) has been well characterized in recent years, with several groups showing that they are required for an efficient antitumour T cell response in mice. Aspects discussed in this conference included characterization of the signalling mechanisms involved in TAM recruitment to tumours, the dual role of TAMs as promoters and suppressors of metastasis, and the potential prognostic value of TAMs in patients receiving immune-checkpoint inhibitors.

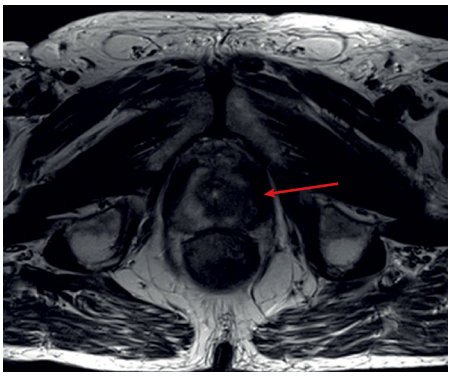
The programme included discussions of other TME components, such as cancer-associated fibroblasts, neutrophils, natural killer cells and endothelial cells. Advances in experimental models have enabled the study of physiological states relevant to tumour progression, such as ageing, tumour dormancy and hypoxia.

In summary, an extensive degree of heterogeneity exists even within cells of the same cell subtypes present in the TME, and efforts are aimed at characterizing cell state transitions in response to tumour progression and/or therapy. Alberto Mantovani drew a comparison with pointillism and said that we can miss the big picture if we focus too much on certain details. Patient outcomes ultimately depend on the net result of a balance between complex tumour-promoting and tumour-suppressive signals within the TME. Whether these signals can be modulated therapeutically remains an active area of research. We hope to hear the results of those studies in future events.

Diana Romero

PROSTATE CANCER

MRI, TRUS or both?



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The majority of men with suspected prostate cancer undergo 12-core biopsy sampling guided by transrectal ultrasonography (TRUS); however, this procedure often leads to false-negative diagnoses, often resulting in under-treatment and/or the need for further clinical monitoring. Now, prospective data from a large cohort of men requiring diagnostic investigations for suspected prostate cancer demonstrates the potential of MRI-targeted prostate biopsy, either alone, or in combination with TRUS-guided sampling, to overcome these limitations.

A total of 2,180 men with an elevated serum prostate-specific antigen level or an abnormal digital rectal examination, with MRI-visible lesions, underwent combined biopsy sampling, involving both TRUS-guided and MRI-guided approaches. Among the 2,103 patients whose data were eligible for analysis, 408 underwent radical prostatectomy (RP).

Both methods resulted in a diagnosis of prostate cancer in approximately half of all men (52.5% with TRUS-guided sampling and 51.5% with MRI-guided sampling). However, MRI-guided procedures resulted in significantly fewer diagnoses of low-grade disease (Gleason grade group 1; $P = 0.01$) and significantly more diagnoses with high-grade disease (Gleason grade groups 3, 4 and 5; $P = 0.004$, $P < 0.001$, and $P = 0.003$, respectively) relative to the TRUS-guided approach.

Addition of data from MRI-guided sampling to that obtained with TRUS resulted in a diagnosis of prostate cancer in an additional 208 men (9.9%), of whom 59 were diagnosed with clinically significant disease (defined as Gleason grade group ≥3). This combination also resulted in 74 new diagnoses of clinically insignificant prostate cancer (Gleason grade group 1) and 134 men with grade group 1 disease being reclassified as having grade group ≥2 disease.

A total of 404 men subsequently underwent RP, of whom 58 (14.4%) had their grade group upgraded on examination of the surgical specimen, including upgrading to clinically significant disease in 3.5%. When classified using only a single diagnostic procedure, 41.6% and 16.8% of patients with prostate cancer diagnosed using only TRUS-guided biopsy required upgrading and upgrading to clinically significant disease, respectively, compared with 30.9% and 8.7% for MRI-targeted sampling ($P \leq 0.002$ for all comparisons). Fewer than 4% of patients diagnosed using any modality required downstaging following RP.

These findings support the use of combined biopsy sampling, which provides the lowest level of diagnostic uncertainty. When only one diagnostic procedure is possible, MRI-targeted biopsy seems to be superior to the TRUS-guided approach. Nonetheless, a subset of clinically significant cancers will continue to go undetected using MRI-targeted biopsy alone.

Peter Sidaway

ORIGINAL ARTICLE Ahdoot, M. et al. MRI-targeted, systematic, and combined biopsy for prostate cancer diagnosis. *N. Engl. J. Med.* **382**, 917–928 (2020)
RELATED ARTICLE Lomas, D. J. & Ahmed, H. U. All change in the prostate cancer diagnostic pathway. *Nat. Rev. Clin. Oncol.* https://doi.org/10.1038/s41571-020-0332-z (2020)