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Epithelial Tumours and Melanoma

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Chapter summary

Epithelial malignant tumours and melanoma are prevalent cancers in the general population involving a combination of complex molecular pathways and alterations. By identifying the molecular mechanisms of these diseases advances in appropriate therapeutic intervention are being made. In this context, key considerations for each cancer covered in this chapter are:

- *Colorectal cancer*: The contribution of the Cancer Genomics Atlas and the International molecular consortium has identified different molecular subtypes in CRC associated with different prognosis and survival: molecular subtypes CMS1 (MSI-immune) and CMS4 (mesenchymal) have different prognosis and will benefit from different treatments. On the other hand, CMS2 (canonical) and CMS3 (metabolic) show similar disease-free survival and overall survival, and do not have specific treatments for them.
- *Gastro-oesophageal cancer*: As in colorectal cancer, the international molecular consensus is replacing current classification of these type of tumours (intestinal versus diffuse type), which potentially could lead to improvement of patient selection for targeted therapy. EBV subtype appears to be associated with the best prognosis, while the gnomically stable subtype is probably associated with the worst prognosis.
- *Lung cancer*: Despite being one of the leading cause of cancer death, the introduction of targeted therapies has led to an unparalleled improvement in overall survival. Predictive biomarkers (EGFR mutation status, ALK rearrangements, PD-L1 expression) are now routinely performed in referral/high-volume cancer centres. The application of new technologies, such as liquid biopsy, has the potential to early identify resistance to cancer therapy and monitor minimal residual disease after initial treatment.
- *Melanoma*: Advances in understanding the molecular pathogenesis of malignant melanomas have help to manage more effectively this aggressive neoplasm, particularly in the metastatic setting. The high prevalence of $BRAF^{V600E}$ mutation in melanoma patients has proved to be a very efficient target for anti-melanoma therapy. In addition, novel immune checkpoint inhibitors, single, or in combination (anti-CTLA4 and anti-PD1) is revolutionizing melanoma treatment, even becoming a first line of treatment, preferable to chemotherapy and radiotherapy with long-term response and less severe side effects.
- The very recent introduction of *PD-1 and PD-L1 immune checkpoint inhibitors* is opening the way to the treatment of several cancers such as lung, head and neck, urothelial, and melanoma, where these molecules are expressed on tumour cells or in the tumour associated lymphocytes. The introduction and approval of these new treatments in cancer is seeing an unprecedented durable response in a variety of cancers.