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Exploring the biology of cancer of unknown primary: breakthroughs and drawbacks.

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Abstract

BACKGROUND:

Cancer of unknown primary (CUP) ranks among the ten most common malignancies worldwide. Cancer of unknown primary presents as disseminated disease, has a dismal prognosis and remains a diagnosis of exclusion. The natural history and biology of the disease is poorly understood, and efforts are focused on identifying the specific 'CUP signature'.

MATERIALS AND METHODS:

We collected and analysed all published research in the biology of CUP from 1974 till present (Medline, Embase, ASCO and ESMO Congresses).

RESULTS:

Current scientific evidence suggests that aneuploidy and karyotype changes are frequent, while more subtle molecular aberrations, such as epidermal growth factor receptor family proteins, cKit/PDGFR are frequently overexpressed, although without prognostic significance. Loss of function of tumour suppressor genes, active angiogenesis, a hypoxic genetic programme and a mesenchymal transitory phenotype have been reported in CUP and may be indicative of unfavourable prognosis. Molecular pathway analyses have identified various biomolecules impacting on survival (pAKT, pMAPK, c-Met, p21 and pPRS6). Finally, circulating tumour cells have recently been reported as a frequent phenomenon in CUP.

CONCLUSIONS:

Overall, advances in understanding CUP biology have been weak and the application of gene expression profiling failed to identify an as yet elusive 'CUP molecular signature'. MicroRNA, epigenetic and proteomic studies are warranted to better characterize the biological profile of CUP and unravel its mystery.