

CLINICAL PAPER /

BRAIN METASTASES



The biology of brain metastases-trans- lation to new therapies

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ABSTRACT

Brain metastases are a serious obstacle in the treatment of patients with solid tumors and contribute to the morbidity and mortality of these cancers. It is speculated that the frequency of brain metastasis is increasing for several reasons, including improved systemic therapy and survival, and detection of metastases in asymptomatic patients. The lack of preclinical models that recapitulate the clinical setting and the exclusion of patients with brain metastases from most clinical trials have slowed progress. Molecular factors contributing to brain metastases are being elucidated, such as genes involved in cell adhesion, extravasation, metabolism, and cellular signaling. Furthermore, the role of the unique brain microenvironment is beginning to be explored. Although the presence and function of the blood-brain barrier in metastatic tumors is still poorly understood, it is likely that some tumor cells are protected from therapeutics by the blood-tumor barrier, creating a sanctuary site. This Review discusses what is known about the biology of brain metastases, what preclinical models are available to study the disease, and which novel therapeutic strategies are being studied in patients.