
Abstract

Cancer cell invasion into healthy tissues develops preferentially along preexisting tracks of least resistance, followed by secondary tissue remodelling and destruction. The tissue scaffolds supporting or preventing guidance of invasion vary in structure and molecular composition between organs. In brain, the guidance is provided by myelinated axons, astrocyte processes and blood vessels which are used as invasion routes by glioma cells. In the human breast, containing interstitial collagen-rich connective tissue, disseminating breast cancer cells preferentially invade along bundled collagen fibrils and the surface of adipocytes. In both invasion types, physical guidance prompted by interfaces and space is complemented by molecular guidance. Generic mechanisms shared by most, if not all, tissues include (i) guidance by integrins towards fibrillar interstitial collagen and/or laminins and type IV collagen in basement membranes decorating vessels and adipocytes, and, likely, CD44 engaging with hyaluronan; (ii) haptotactic guidance by chemokines and growth factors; (iii) and likely physical pushing mechanisms. Tissue-specific, restricted guidance cues include ECM proteins with restricted expression (tenascins, lecticans), cell-cell interfaces, and newly secreted matrix molecules decorating ECM fibers (laminin-332, thrombospondin-1, osteopontin, periostin). We here review physical and molecular guidance mechanisms in interstitial tissue and brain parenchyma and explore shared principles and organ-specific differences, and their implications for experimental model design and therapeutic targeting of tumor cell invasion. Copyright © 2011 Pathological Society of Great Britain and Ireland. Published by John Wiley & Sons, Ltd.

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