Brain tumour cells interconnect to a functional and resistant network.

Osswald M1,2, Jung E1,2, Sahm F3,4, Solecki G1,2, Venkataramani V5, Blaes J1,2, Weil S1,2, Horstmann H5, Wiestler B1,2,6, Syed M1,2, Huang L1,2, Ratliff M2,7, Karimian Jazi K1,2, Kurz FT8, Schmenger T1,2, Lemke D1,2, Gömmel M1,2, Pauli M9, Liao Y1,2, Häring P10, Pusch S3,4, Herl V11, Steinhäuser C11, Krunic D12, Jarahian M13, Miletic H14, Berghoff AS15, Griesbeck O16, Kalamakis G17, Garaschuk O18, Preusser M19,20,21, Weiss S19,20,21, Liu H22, Heiland S8, Platten M1,23, Huber PE24,25, Kuner T5, von Deimling A3,4, Wick W1,2, Winkler F1,2.

Abstract

Astrocytic brain tumours, including glioblastomas, are incurable neoplasms characterized by diffusely infiltrative growth. Here we show that many tumour cells in astrocytomas extend ultra-long membrane protrusions, and use these distinct tumour microtubes as routes for brain invasion, proliferation, and to interconnect over long distances. The resulting network allows multicellular communication through microtube-associated gap junctions. When damage to the network occurred, tumour microtubes were used for repair. Moreover, the microtube-connected astrocytoma cells, but not those remaining unconnected throughout tumour progression, were protected from cell death inflicted by radiotherapy. The neuronal growth-associated protein 43 was important for microtube formation and function, and drove microtube-dependent tumour cell invasion, proliferation, interconnection, and radioresistance. Oligodendroglial brain tumours were deficient in this mechanism. In summary, astrocytomas can develop functional multicellular network structures. Disconnection of astrocytomas by targeting their tumour microtubes emerges as a new principle to reduce the treatment resistance of this disease.

Comment in

Neuro-oncology: Astrocytoma cells interconnect to resist radiotherapy. [Nat Rev Neurol. 2015]
Brain cancer: Tumour cells on neighbourhood watch. [Nature. 2015]
Gioma: Tumour cell teamwork. [Nat Rev Cancer. 2016]
CNS cancer: Astrocytoma cells interconnect to resist radiotherapy. [Nat Rev Clin Oncol. 2016]