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CNSC-09. CHI3L1 IS A MOLECULAR MARKER FOR GLIOBLASTOMA NETWORK CONNECTIVITY AND FUNCTIONALLY ORCHESTRATES TUMOR MICROTUBE FORMATION

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Chitinase 3-like 1 (CHI3L1) is a secreted glycoprotein and its RNA expression elevated in glioblastoma (GB) compared to other tumor types and related normal tissues. Furthermore, transcript levels in GB dictate aggressiveness through modulating stemness, proliferation and tumor microenvironment. This ultimately influences patient survival. We here provide evidence that the pathogenic relevance of CHI3L1 expression is associated with the extent of tumor microtubes (TMs) - ultralong membrane tubes that connect GB cells (GBCs) to a network with considerable relevance for tumor progression and therapy resistance. Single cell RNA profiling of xenografted GBCs with different degrees of morphological and functional TMs identified CHI3L1 as a prognostic marker for TM network extent. We demonstrate that both RNA and protein expression levels are suitable markers in preclinical *in vitro* systems modeling TM connectivity as well as in clinical specimens. Genetic perturbation of CHI3L1 influenced GBC network integration, caused a shift of the dominant cell state and altered the phosphorylation status of the TM-driver GAP43. Pharmacological blocking of CHI3L1 with an antibody reduced TM networks, thus providing a handle for future clinical translation. Together, these data identify a functional and upstream role of CHI3L1 in governing tumor cell connectivity, CHI3L1 RNA and protein expression as a novel way to determine overall GBC connectivity for future trials, and finally a new therapeutic target for tumor network-disrupting strategies.