

Do the guardians of the brain need to leave some ammunition behind to fight more efficiently against tumor intruders?

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The brain contains a type of cells that act as guardians against anything that tries to alter the physiological conditions. These protectors are called microglia and their role is to remove toxic compounds, dead cells and perform immune responses. Microglia are scanning throughout the brain for intruders that cause unpleasant conditions. Identification of “foreigners” activates microglia to release several factors in order to eliminate the intruders. Among the released factors there are some that recruit more microglia and others that open the way to the place where the battle is happening.

Cells in the brain and other tissues are positioned in certain places. They are hanging in their places owing to a net that is spread around them. Imagine this like a “spider silk”-like net produced by the cells themselves. This net is offering structural support to the cells and is involved in their communication. This “spider silk”-like net binds messenger molecules released from the cells, thereby altering the cellular behavior. Cells are able to remodel this net depending on their needs.

Glioblastoma tumor cells are the toughest opponent of microglia. These cells arise from a wide variety of cells and possess mechanisms to manipulate the guardians of the brain for their development. During tumor growth and progression, microglia sense the disturbances in normal physiology of the brain. The tumor releases its own factors to grow and compresses the healthy brain tissue, which is subsequently sending signals asking for help. Microglia are sensing this and become activated. Release of molecules to remodel the net and open the way so they can reach their destination faster are observed. Unfortunately, after battling with glioblastoma cells, the tumor takes advantage of microglia and their net-remodeling machinery to open the way for the expanding tumor mass.

Maybe microglia have specific ammunition that the tumor is using and in their absence the tumor becomes more vulnerable. One of this ammunition is able to break down specific components in the “spider silk”-like net. This ammo is called heparanase and chops off parts of a component of the net. In the presence of heparanase several messenger molecules that are trapped on this component of the net are released and promote tumor growth and progression, while in the absence of heparanase the tumor is significantly reduced and the number of the microglia around the tumor is substantially increased.

In this study, a glioblastoma model cell was grown together with glia cells that either had heparanase in their machinery or not. The effect of heparanase in tumor motility was evaluated. Furthermore, microglia were separated from glia cells and the ability of the tumor cells to attract microglia close to the tumor was also performed. This set of experiments was able to explain some aspects of previously observed data. Certainly more efforts are required to elucidate the role of heparanase in the activation of the brain guardians against the tumor.

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