Extracellular vesicle trafficking in GBM

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Background & objectives

Extracellular vesicles (EVs) are secreted by all cell types, including tumor cells, and are found in increased numbers in the plasma of GBM patients. EVs may contain high-value genetic material that can be useful for tracking tumor development, as well as membrane proteins that affect other cells. This prompted us to investigate how tumor EVs might influence immune cells in glioma, and in primary and secondary lymphoid organs as well as in the circulation.

Methods

We used a syngeneic GBM mouse model and tracked tumor EVs from the brain to the meninges, cervical lymph nodes, plasma, bone marrow and spleen using ImageStream imaging flow cytometry .

Results

We were able to identify tumor EVs mostly in the cervical lymph nodes by ImageStream imaging flow cytometry just 30min after tumor EV injection into the brain. However, when tumor EVs were produced by a large gliomas transfected with dTomato, we found them mainly in plasma, less frequently in bone marrow and never in the spleen. We confirmed these data by extracting DNA from EVs and detecting specific dTomato sequences using digital droplet PCR. In addition, we detected CD11b+ macrophages in the meninges that likely travel through the lymphatics that have taken up tumor EV or tumor material.

Conclusion

We concluded that tumor EV are able to travel fast to the lymph nodes and to the systemic circulation. We confirm that tumor EVs are capable of eliciting an immune response by activating T cells. However, prolonged contact and large number of EVs could also block antigen recognition by T cells and thus contribute to the propagation of an immunosuppressive environment in GBM.