Cytomegalovirus Reactivation Orchestrates Myeloid Reprogramming to Drive Brain Metastasis Progression

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Background/Introduction

>90% brain metastatic tumors from a variety of cancers display human cytomegalovirus (HCMV) positivity with HCMV confined within tumor lesions[1-3].

Research Methods

Conducted spatial transcriptome analysis and Gene Set Enrichment Analysis of primary tumor as well as brain metastatic lesions in patients, both HCMV positive and negative.

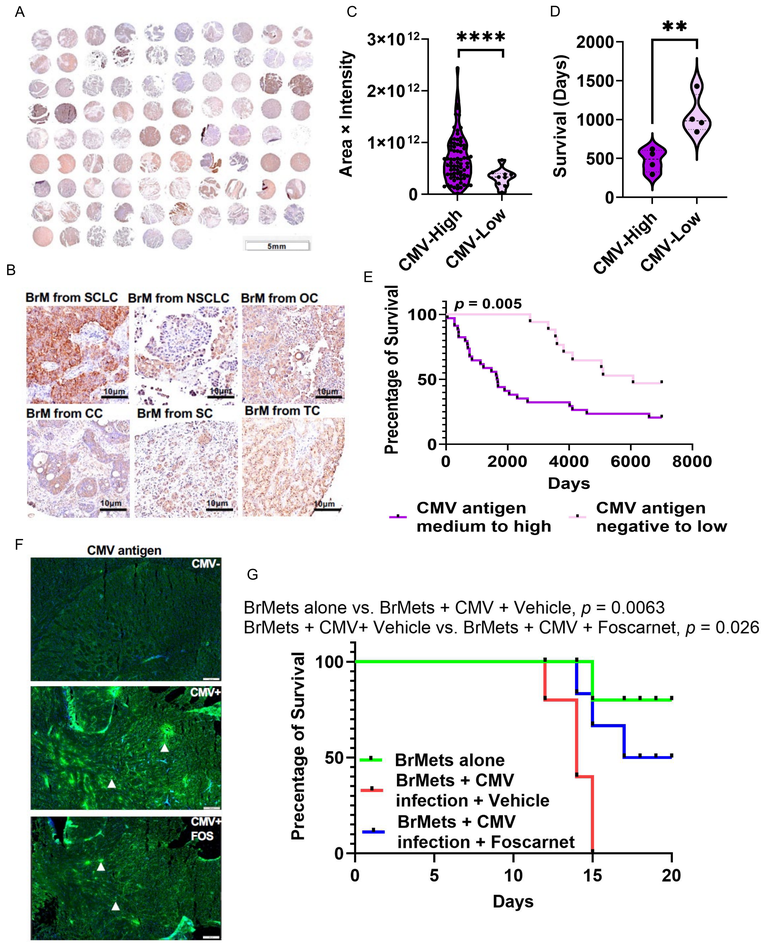
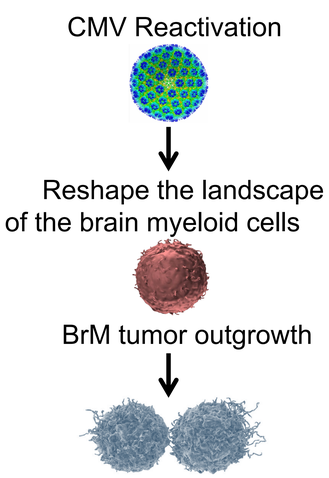


Fig. 1. Human cytomegalovirus (HCMV) reactivation correlates with patient survival; Anti-CMV therapy with foscarnet prolongs survival and reduces tumor burden in a CMV-infected breast cancer brain metastasis mouse model.

Results



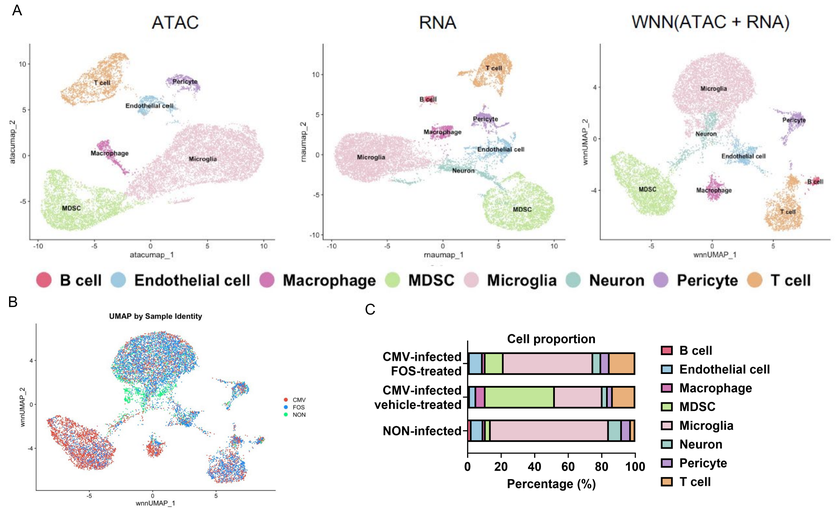


Fig. 2. Single-cell multi-omics landscape of CMV-infected breast cancer brain metastasis progression.

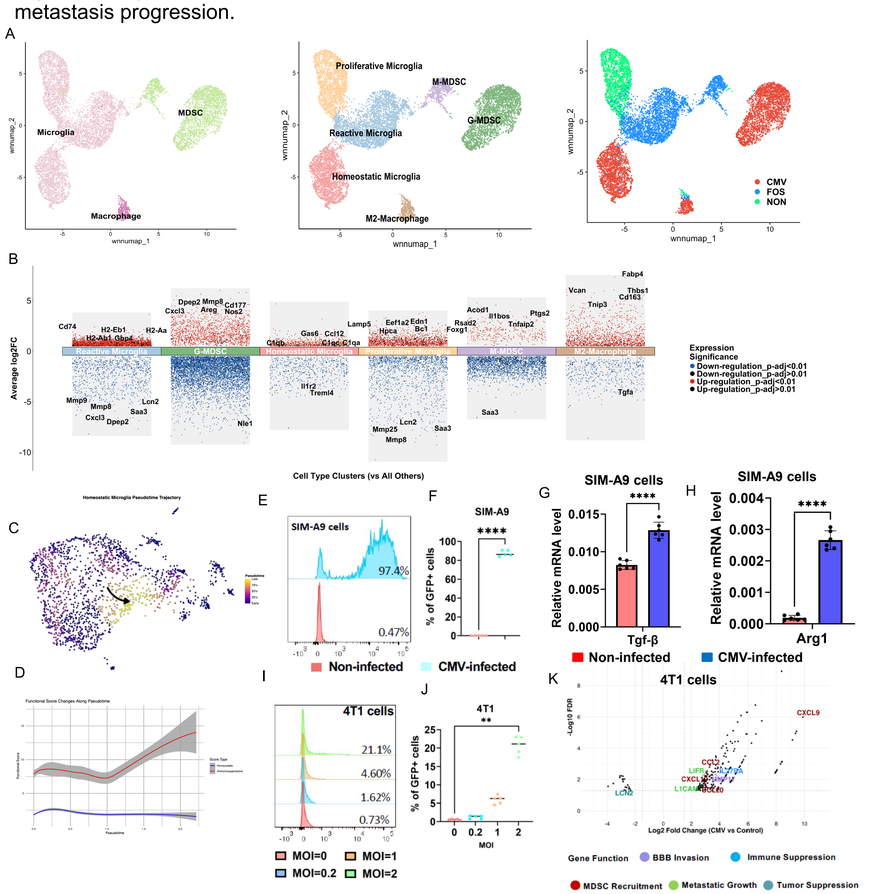
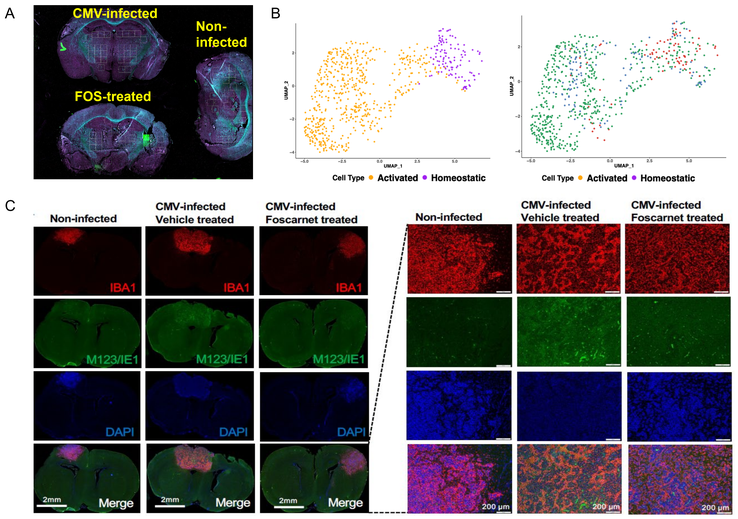


Fig. 3. Characterization of brain myeloid population heterogeneity in CMV-infected breast cancer brain metastasis and landscape reshaping.



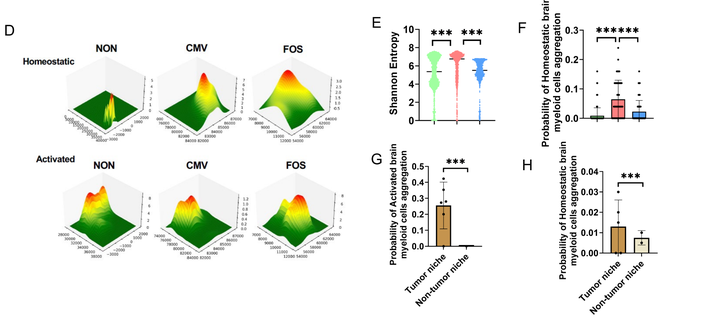


Fig. 4. Single-cell spatial transcriptomic analysis reveals CMV-induced myeloid cell reprogramming and spatial reorganization in brain tumor microenvironment.

Conclusions

- Single-cell multi-omics and spatial transcriptomics map the immune landscape of CMV-driven brain metastasis reprogramming.
- CMV orchestrates brain metastasis progression through systematic myeloid reprogramming and compositional remodeling.
- CMV reprograms homeostatic microglia into immunosuppressive phenotypes via stepwise transcriptional changes.
- Foscarnet inhibition of CMV restores anti-tumor immunity and enhances chemotherapy efficacy in brain metastases.

Acknowledgements

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