CIBIO EXTERNAL seminar

18 SEPTEMBER AT 3.30 P.M.
ROOM A 104 | POVO 1

LEVERAGING SINGLE CELL SEQUENCING AND MOUSE MODELS TO ELUCIDATE MECHANISMS OF IMMUNE EVASION IN BRAIN CANCER

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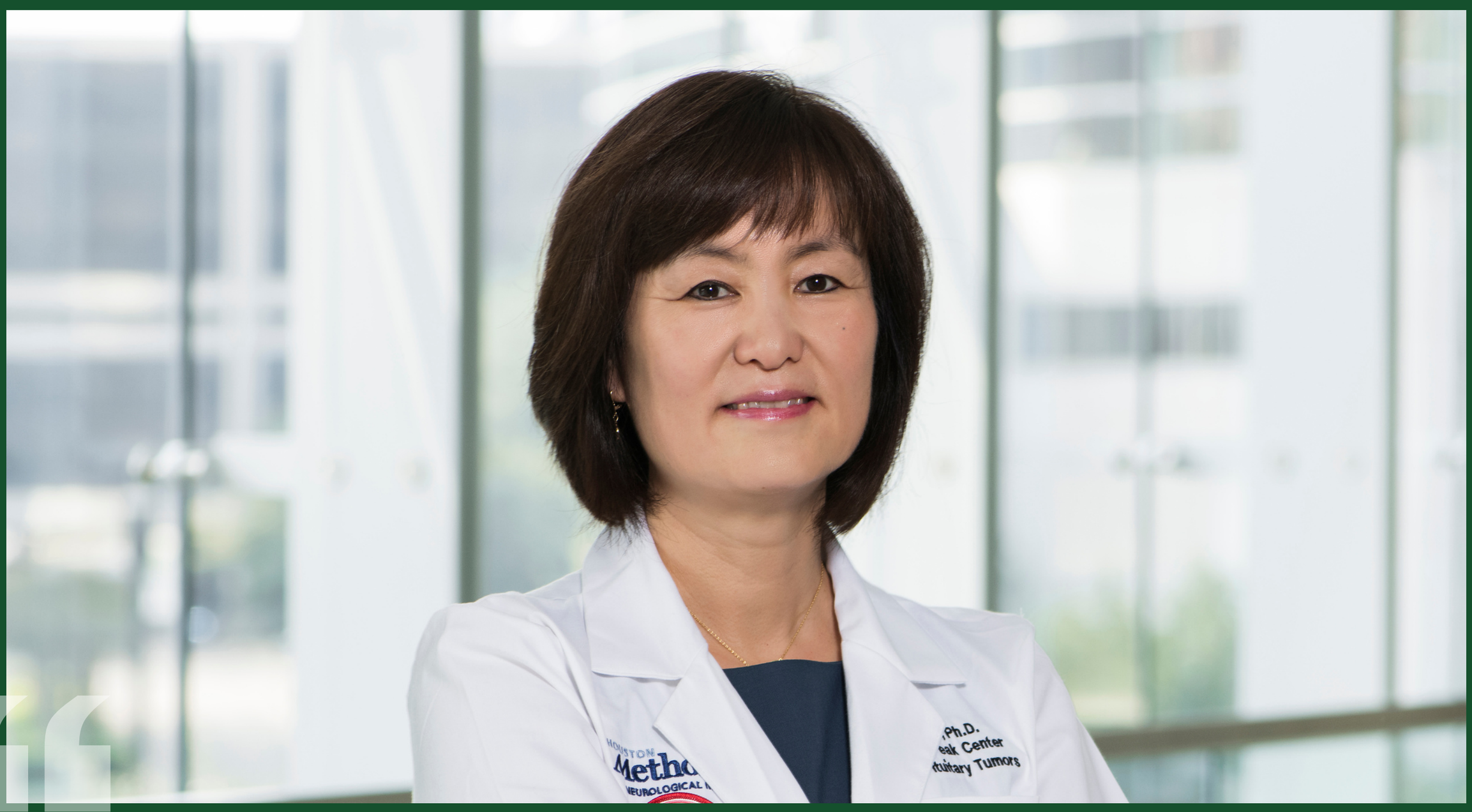

While immunotherapies have provided tremendous benefit to some cancer patients, most human cancers are resistant to immunotherapies. Among the many bottlenecks that hinder the development of more effective immunotherapies are: 1) incomplete understanding of the cellular and molecular heterogeneity of cancer and immune/stromal cells in human cancer, and 2) the paucity of faithful experimental models that recapitulate critical aspects of the human disease.
My laboratory began to address these limitations in brain cancer by first performing a comprehensive single cell RNA-sequencing analyses of human glioblastoma. We isolated and analyzed >210,000 cells, both cancer and immune, and defined molecular subtypes of tumor-promoting vs. suppressing immune cell subtypes in GBM. To experimentally validate our findings and to address the second unmet need in the field, we developed and deeply characterized five new syngeneic mouse models of glioblastoma and identified cross-species similarities and differences in cancer and immune cell phenotypes in GBM at the single cell resolution. By exploiting our human and mouse single cell datasets, we nominate a new promising immunotherapy target for GBM. Finally, we report that cancer:immune interactions occur in sex-specific manners and that biological sex is a critical underlying variable that modulates the Yap1 gene function and sexually dimorphic immune evasion mechanisms in medulloblastoma. Together these studies identify new immune modulators for brain cancers and illustrate the importance of considering the biological sex as a critical variable in cancer studies.

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