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Wnt signaling and green tea: A tale of brain and breast

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We seek to understand the mechanisms of triple negative breast cancer (TNBC) progression and to advance new diagnostic and therapeutic strategies at the pre-clinical level. A difficult aspect of TNBC and breast cancer in general is that metastatic disease accounts for 90% of the deaths. With advances, the metastatic patients have extended survival with an acceptable quality of life, but often succumb to fatal brain metastases. Current therapies do not efficiently cross the blood brain barrier (BBB). Thus, effective treatment of brain metastases would be an important step to markedly improving breast cancer patient outcome. Towards this goal, we have previously shown that reductions or mutations of the HBP1 gene are associated with a decreased relapse-free survival and in the context of Wnt and associated metabolic signaling networks and have optimized pre-clinical TNBC model to approach the difficulty problem of brain metastases. We have now discovered that a combination of the green tea compound epigallocatechin gallate (EGCG) and chemotherapeutic agent Decitabine (EGCG/DAC) is exceptionally effective in a pre-clinical model of TNBC with brain and other metastases. The combination was effective in reducing brain and other metastases in an animal model and is known to cross the BBB from other studies. Using RNA-Seq, we are investigating the complete mechanism of action for the EGCG/DAC combination, especially in the context of immunotherapy. At the minimum in the primary xenograft tumors, treatment by EGCG/DAC reduces Wnt signaling, which is linked to onset of brain metastases in humans. Both compounds are in clinical use; Decitabine is FDA-approved for hematological malignancies with well-defined and manageable side effects. Current studies are directed towards refining the pre-clinical data for applications in a future phase 1 trial for TNBC and brain metastases.

Biography

Amy S Yee received her AB and PhD degrees in Biochemistry from University of California at Berkeley and at Davis and was an American Cancer Society Postdoctoral Scholar at the Rockefeller University in New York. She joined the Dept. of Biochemistry at Tufts University School of Medicine in Boston as an Assistant Professor and is now a tenured full Professor of Developmental, Molecular and Chemical Biology. Recently, her work has applied molecular approaches to clinical questions in the areas of breast cancer, epilepsy, and recently to colitis and colon cancer. The work has been supported by the NIH, DOD, Komen, and AICR and by other grants over the years. She has received Junior Faculty awards from the American Cancer Society, Established Investigator award from the American Heart Association and a Zucker award in recognition of research excellence at Tufts. She has served on numerous NIH and DOD review panels and has proudly mentored numerous students at all levels to future success in science and medicine.

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