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## Breast cancer stem cell function: Molecular genetic determinants and the cell fate determination pathway

A subpopulation of cells have been identified within tumors referred to as tumor initiating cells (BTIC) (cancer stem cells). These cells have been hypothesized to contribute to therapy resistance and tumor recurrence. Contributions to the understanding of the molecular genetic drivers of TIC using multigenic tissue specific temporally and spatially inducible transgenic mice have shown endogenous mammary tumor stem cells expansion is maintained by endogenous c-Jun, and NFkB. The cell cycle control protein p21CIP1 restrains, and cyclin D1 promotes, TIC populations respectively and Notch requires cyclin D1 for BTIC expansion.

Recent studies from this laboratory have shown the RDGN (retinal determination gene network) is a dominant regulator of BTIC. In *Drosophila Melanogaster*, the Retinal Determination Gene Network (RDGN) determines organismal cell fate. The RDGN human homologues include *DACH*, *EYA*, *Six*, and *Toy*. We showed the RDGN (*DACH1*, and *Eya*) governs BTIC. The *Drosophila* Eyes Absent Homologue 1 (*EYA1*) is a component of the retinal determination gene network and serves as an H2AX phosphatase. *EYA1* enhanced breast tumor growth in mice in vivo, requiring the phosphatase domain. *EYA1*-dependent induction of breast cancer cell proliferation and mammosphere formation was cyclin D1-dependent. The induction of cellular proliferation and cyclin D1 abundance, but not apoptosis, was dependent upon the *EYA1* phosphatase domain. The relative proportion of cells, with characteristics of breast tumor stem cells were assessed in mice with targeted deletion of *Dach1* in the mammary gland. The function of the RDGN and the interface with the cell cycle control genes in BTIC will be discussed

## Biography

Richard Pestell (MD, PhD, MBA, FRACP, FACP, MBBS) is a leader in the global cancer community. He has galvanized international teams to fight cancer, has >600 published works, and multiple patents in cancer diagnostics and treatment including light-activated gene therapy. He founded companies (ProstaGene, AAAPhoenix) and Institutes, led cancer not-for-profits and directed two US Cancer Centers (Lombardi Comprehensive Cancer Center, and the Sidney Kimmel Cancer Center at Thomas Jefferson University. He was most recently Executive Vice President Thomas Jefferson University in Philadelphia, USA. His work in breast and prostate cancer and the cell cycle is highly cited (>41,500 citations, H index >100).

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