EZH2-Mediated Adhesion Dynamics in the Regulation of Leukocyte Migration and Tumorigenesis

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We have previously reported a non-canonical function played by the lysine methyltransferase (KMT), EZH2, in regulating cell adhesion turnover and migration. EZH2 controls leukocyte migration through interaction with the cytoskeleton remodeling effector, VAV, and directly methylates the integrin adaptor, Talin.

Our follow-up study further demonstrates that cytosolic Ezh2 is not only associated with cancer stem cell characteristics and promotes cellular transformation in *vitro*, but also enhances the aggressiveness of murine triple negative breast cancer (TNBC) cells in the 4T1 syngeneic model. As elevated EZH2 expression level and Brca1 mutation are both highly associated with the poor prognosis of breast cancer patients, we employed an mouse model for spontaneous TNBC (*Brca1$^{f/f}$;LGB*-cre;*P53$^{+/-}$;*) with an EYFP reporter to investigate the role of endogenous cytosolic EZH2 in cancer progression.

Using this mouse model, we identified that self-methylated endogenous cytosolic EZH2 was enriched in cancer initiating cells. The molecular mechanisms controlling subcellular localization of methylated EZH2 in TNBC, as well as its contribution to tumorigenesis, will be further investigated.

Our preliminary data also suggest that various circulating immune cells are likely to detect the formation of microscopic neoplasia lesions in the mammary grands before the development of any palpable tumors in mutant female mice, which has the potential to serve as an early diagnostic marker.