**Project title: Precision medicine on early-onset luminal type breast cancer**

# Effect of the GATA3 Signaling and its Single Nucleotide Polymorphism on Clinical Outcome of Breast Cancer Patients

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Genome-wide association studies have revealed a multitude of breast cancer-associated SNPs. The majority of these SNPs are located in noncoding regions of the genome. Our breast cancergenome data have been derived fromtumor samples of 72 patients. We analyzed whole-genome sequences ofthose tumor tissuesto identify DNA variations. Our data showed several SNPs including GATA3- Ser237Alafs, pro409Alafs and Glu360Alafs- to be associated with significant risk in spontaneous, non-hereditary breast cancer. GATA3 is a transcription factor regulating luminal cell differentiation and has been implicated in the luminal types of breast carcinoma. Our data showed that GATA3 depletion led to a significantdecrease of migration, invasion and proliferation. Previous study indicated that GATA3 regulated expression of interferon response genes. We found that GATA3 and Interferon-induced protein 44-like (IFI44L)mRNA expression levels were lowerin the in vivo selected highly invasive breast cancer cell lines. Besides, GATA3 knockdown resulted in significantly decreased IFI44L expression. IFI44L is a type I interferon-stimulated gene (ISG) and belongs to the IFI44 family. Our data showed that overexpression of IFI44L decreased chemoresistance towards paclitaxel and knockdown of IFI44L promotes sphere formation. Furthermore, we found that depletion of IFI44Lenhancedmigration, invasion, and proliferation through activating the c-Met/Src signaling pathway.Taken together,our data indicated that targeting a novel GATA3/IFI44L signaling affected cancer stemness, metastasis, and drug resistance via regulating c-Met/Src signaling pathway in breast cancer.GATA3 and IFI44L can potentially be used as useful prognostic markers.