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Title: Deciphering the mechanism of action of SHON gene in breast cancer using CRISPR-Cas9 genomic editing technology

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Endocrine therapies currently remain the most effective form of treatment for ER-positive (ER+) breast cancer. However, not all patients will benefit from these treatments. Up to 50% the patients with ER+ tumours are resistant to the therapies either from onset of therapy or soon after therapy, with devastating consequences. SHON, a novel secreted hominoid-specific oncogene, promotes cell proliferation and tumour growth and has also been shown to be a promising biomarker that can accurately predict the response of patients to endocrine treatment in breast cancer. SHON is an estrogen-regulated gene and the expression of SHON is strongly associated with ER expression in breast cancer. However, the molecular mechanism about how SHON drives breast cancer progression and metastasis and mediates endocrine resistance in breast cancer is still not clear. In this project, we utilized the CRISPR-Cas9 gene editing technology to investigate the mechanism of action. Two ER+ breast cancer cell lines MCF-7 and T47D and two ER- breast cancer cell lines MDA-MB-231 and BT549, were used to generate SHON-knockout (+/-, -/-) cells. For comparison, SHON-overexpressing stable cells were also created from these cell lines. The status of SHON gene in single-cell clones was confirmed by both genomic PCR and DNA sequencing. SHON-overexpressing cell clones were confirmed by RT-PCR at the RNA level and Western Blotting at the protein level. We have obtained monoallelic SHON+/- knockout single-cell clones and SHON-overexpressing MCF-7 cell clones. We are still screening for biallelic SHON-/- knockout cell clones. Once all the cell lines are established, a variety of in vivo and in vitro functional assays to delineate the signaling cascades in these cells.

Biography

Jiawei (Stacey) Li obtained her MD in Clinical Medicine in 2016 and a Master's Degree in 2018 from Jilin University, one of the key universities in China under the Chinese Government's Building World-class University schemes of the "Project 985" and "Project 211". She is now a PhD candidate at the AUT under the supervision of A/Prof Dong-Xu Liu. Her research project is to delineate the mechanism of the SHON breast cancer biomarker using the CRISPR-Cas9 gene editing technique.