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Translational Research on novel Targets and Therapy for Triple Negative Breast Cancer (TNBC)

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In our previous MOHW grant (103-106) we aimed to study triple-negative breast cancer (TNBC) with 4 themes: (1) Interference of mitochondrial stress signaling in TNBC progression. (2) Targeting epithelial-mesenchymal transition in early metastatic TNBC. (3) Identification of biomarkers and therapeutic targets for recurrent TNBC. (4) Development of novel phosphatase-related agents in TNBC therapy. We found cystine deprivation induces necroptosis and ferroptosis by interfering cancer mitochondria. Cancer stem cells initiate tumor and metastasis via PP2A-STAT3 mechanisms. In particular, we found characteristic molecular subtyping in Taiwanese TNBC patients differing from Western population, and molecular characteristics of recurrent TNBC, including novel pathway such as BDNF-TrkB signaling and gene expression profiling. Preclinically, we developed phosphatase-related pathways such as SHP-1/p-STAT3, PP2A/p-Akt as anti-TNBC therapy, and found some “repurposing” agents such as nintedanib, an approved anti-pulmonary fibrotic drug, that induce TNBC cell death by SHP-1/p-STAT3 pathway. In summary we have fruitful results in basic and translational research fund by the MOHW grant (103-106), and published a total of 21 SCI journal articles. A selection of some important contribution was illustrated as figure below: