# Development of a new treatment for chemotherapy-resistant triple-negative breast cancer


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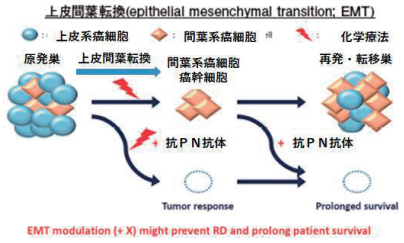
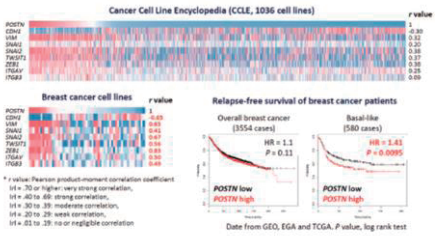
## Project Outline

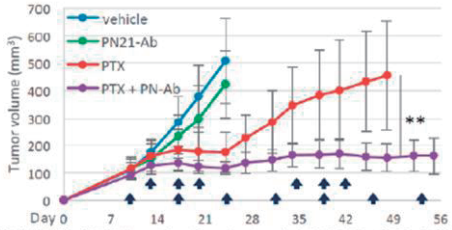
Epithelial -to-mesenchymal transition（EMT）is currently considered to be a major mechanism responsible for chemoresistance. It is thought that mesenchymal cancer cells that are resistant to anticancer drugs later undergo mesenchymal-epithelial transition and become stagnant (figure on the right). Next, in order to search for specific targets, we conducted a joint research with UCSD in US, using tissue samples from more than 1,000 cases of malignant tumors to comprehensively identify the gene of eight mesenchymal markers that have the strongest correlation. As a result, we discovered the periostin gene. In particular, in breast cancer, there was a clearer relationship between periostin gene expression and EMT. Furthermore, it was found that there is a strong correlation with the prognosis of basal type (mainly TNBC). The periostin gene has a splicing variant in which an exon is dropped, so when we investigated which exon's expression was strongly altered in a chemotherapy -resistant model, we found that it was periostin exon 21 (see figure on the right). Therefore, we administered a pathological periostin -neutralizing antibody that uses exon 21 as an antigen to a chemotherapy -resistant model of TNBC, and confirmed that it significantly suppressed recurrence. (Patent already obtained) Furthermore, we have developed a diagnostic agent to measure blood pathological periostin (patent applied for), and plan to study its potential as a companion diagnostic agent. On the other hand, in addition to TNBC, many cases of HER2-negative breast cancer develop into TNBC due to metastasis or recurrence, and the prognosis is similarly poor. Therefore, in 2024, an investigator-initiated clinical trial Phase 1/2a is planned at four institutions led by Osaka University Department of Breast Endocrine Surgery targeting metastatic and recurrent HER2-negative breast cancer. The market size is large as shown in the figure on the right.



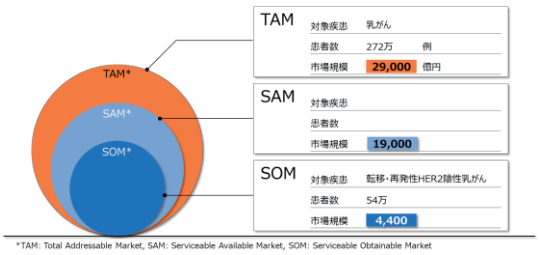

化学療法抵抗性（早期再発）獲得メカニズム




抗がん剤治療後に残存する治療抵抗性乳がん（間葉系転換した癌）ではペリオスチンの発現が亢進しており、予後と逆相関する。




抗がん剤投与後再発はペリオスチンエクソン21中和抗体併用で著明に抑制され、同時にEMTの抑制を伴う。




Target disease: HER2 negative breast cancer
Patent information: PCT applied Technology features: Release existing chemoresistance and safely induce effective results
Marketability and development issues: There is a sufficient market, but Phase I/ IIa development is required for FIH Desired corporate collaboration details: We are looking for a licensing-out corporate collaboration.