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CDCP1 cleavage is necessary for homodimerization-induced migration of triple-negative breast cancer

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Triple negative breast cancer (TNBC) is a highly aggressive and metastatic form of breast cancer that lacks the estrogen, progesterone, and HER2 receptors and is resistant to targeted and hormone therapies. TNBCs express high levels of the trans-membrane glycoprotein, CUB-domain containing protein 1 (CDCP1), which has been correlated with the aggressiveness and poor prognosis of multiple carcinomas. Full-length CDCP1 (fCDCP1) can be proteolytically cleaved, resulting in a cleaved membrane-bound isoform (cCDCP1). CDCP1 is phosphorylated by Src family kinases in its full-length and cleaved states, which is important for its pro-metastatic signaling. We observed that cCDCP1, compared to fCDCP1, induced a dramatic increase in phosphorylation of the migration-associated proteins: PKC δ , ERK1/2, and p38 MAPK in HEK 293T. In addition, only cCDCP1 induced migration of HEK 293T cells and rescued migration of the TNBC cell line, MDA-MB-231, expressing shRNA against CDCP1. Importantly, we found that only cCDCP1 is capable of dimerization, which can be blocked by expression of the extracellular portion of cCDCP1 (ECC), indicating that dimerization occurs through CDCP1's ectodomain. We found that ECC inhibited phosphorylation of PKC δ and migration of TNBC cells in 2D culture. Furthermore, ECC decreased cell invasiveness, inhibited proliferation and stimulated apoptosis of TNBC cells in 3D culture, indicating that the cCDCP1 dimer is an important contributor to TNBC aggressiveness. These studies have important implications for development of a therapeutic to block CDCP1 activity and TNBC metastasis.

Implant-based breast reconstruction with abdominal dermal graft

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Purpose: Implant-based breast reconstruction is an appropriate procedure for post-mastectomy breast cancer patients and other breast diseases. This technique combined with abdominal dermal graft enhances the aesthetic result and decreases the implant complications.

Methods: 4 patients (4 breasts) including one prophylactic mastectomy, two phyllodes and one breast cancer patient underwent mastectomy and implant-based breast reconstruction with abdominal dermal graft. Dermal flap was harvested through a curvilinear lower abdominal ellipse. The epidermis was de-epithelialized with the scalpel and full thickness skin was harvested. The upper border of the flap was sutured into the lower border of the pectoral major muscle and the lower border was sutured into the IMF to cover the inferior part of the implant.

Results: Age of the patients is 39, 32, 48 and 45. Implant sizes are 320g, 253g, 290g and 230g. Follow-up are 14 months, 9 months, 4 months and 1 month. There were no implant losses. One case has skin dehiscence; one case has partial areolar-nipple necrosis. No case with seroma or infection.

Conclusions: Implant-based breast reconstruction combined with autologous dermal graft has the advantages of the bioprosthetic mesh without the associated cost. The technique also has low complication rate and could be a good choice for patients in developing countries.