Aim: Triple negative breast cancer (TNBC) is defined by the lack of estrogen and progesterone receptors expression and the absence of human epidermal growth factor receptor 2 amplification. TNBC has specific clinical/pathological features and molecular biology. The absence of effective targeted therapies requires new biomarkers to develop therapeutic strategies. FASN, the sole mammalian enzyme capable of de novo fatty acid synthesis, is highly expressed in several carcinomas. FASN is associated with poor prognosis and its inhibition is selectively cytotoxic to breast cancer cells. Therefore, lipogenesis mediated by FASN represents a potential target. The aim of our study was to evaluate the clinical and histopathologic features of a large population of TNBC patients and to analyze FASN expression in vitro and in vivo.

Methods: We retrospectively evaluated 91 cases of primary TNBC diagnosed between 1990 and 2012 in our institution. We collected clinical/pathological features: age, histology, grade, stage, surgery and chemotherapy. FASN expression was preliminarily evaluated in 30 core-biopsy of TNBC patients by immunohistochemistry (IHC). FASN expression was graded from 0 to 3+ (0-1+ normal, 2+ moderate and 3+ high). Concurrently, we evaluated the cytotoxic effect of FASN inhibitors (cerulenin, C75 and EGCG), alone or in combination, in subtypes of TNBC cell lines (MDA-MB-231, BT549, MDA-MB-468, HCC1806).

Results: Mean age was 54 years. Most of the tumors were grade 3 (85.2%) and ductal (85.9%). Mean ki 67 index was 64.5%. The type of surgery was 49.4% mastectomies and 43.5% lumpectomies (7.1% not operated). 22% of the patients had stage I, 43% II, 31.4% III and 3.6% stage IV. 90.6% patients received chemotherapy. The most common regimen was a combination of antraciclines and taxanes. The preliminary results showed that 20 patients had a high FASN expression (FASN 3+) and 10 had a moderate expression (FASN 2+). In vitro, FASN inhibitors displayed strong cytotoxicity in MDA-MB-468 and HCC1806 cells and moderate in MDA-MB-231 and BT549 cells. The combination of EGCG with cetuximab or doxorubicin in TNBC cells improved the results of the monotherapy.

Conclusions: FASN is highly expressed in TNBC tumors. The absence of effective target therapies for this subtype and its poor prognosis, led to exploring the role of FASN as a potential target for TNBC therapy.

Disclosure: All authors have declared no conflicts of interest.