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Letter to the editor:

PREDICTION OF NEOADJUVANT CHEMOTHERAPY RESPONSE IN BREAST CANCER

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Dear Editor,

Neoadjuvant chemotherapy (NACT) in breast cancer reduces the size of breast carcinomas to improve operability (Burstein et al., 2019; Ditsch et al., 2019). The response to NACT is critical since a pathologic complete response (pCR) is associated with better long-term survival (Spring et al., 2020). Unfortunately, the response rates to currently used NACT with taxanes and anthracyclines are relatively low with pCR between 15 and 40 % (von Minckwitz et al., 2008, 2012; Iwata et al., 2011; Untch et al., 2016; Gianni et al., 2018). Therefore, a classifier that reliably predicts non-response (non-pCR) to taxanes/anthracyclines would be of high relevance, sparing the patients from unnecessary toxicity due to the chemotherapy. Moreover, alternative treatments could be chosen. Unfortunately, currently available expression-based classifiers do not guarantee sufficiently high negative prediction values (NPV) to justify clinical decisions (Chang et al., 2003; Ayers et al., 2004; Hess et al., 2006; Farmer et al., 2009; Hatzis et al., 2011).

Recently, Edlund and colleagues have established an expression-based classifier for prediction of neoadjuvant chemotherapy response that offers some important advantages (Edlund et al., 2021). Initially, the authors realized that it is difficult to establish a classifier that informs each patient whether they will respond to NACT, which is in agreement with previous studies. Therefore, they constructed a classifier that allows very reliable statements but only for a subset of the patients. In the present publication, Edlund et al., present a 20-gene classifier that identifies non-responders with an unusually high NPV of 0.960 considering all four intrinsic subtypes of breast cancer. In patients with the luminal A subtype, NPV was even as high as 0.986 (Edlund et al., 2021). This classifier was trained in a new prospective multicenter trial with 114 patients and validated in a cohort of 619 independent patients with taxane/anthracycline-based NACT. Prediction of the prognosis of breast cancer based on gene expression has been studied since decades (Schmidt et al.,, 2008). Prognostic and predictive genes comprise marker genes of immune cells (Schmidt et al., 2012, 2018; Godoy et al., 2014; Heimes et al., 2017a, b; Edlund et al., 2019), proliferation associated genes (Siggelkow et al., 2012), oxidative stress response (Cadenas et al., 2010), metabolism (Stewart et al., 2012; Cadenas et al., 2014, 2019; Marchan et al., 2017), and ribosome-related genes (Hellwig et al., 2016).

The present study of Edlund and colleagues represents an important progress in research on NACT with the limitation that a reliable recommendation of not to treat can only be made for a subgroup of the patients. The novel 20-gene classifier will become clinically relevant as soon

as alternative treatments to taxane/anthracycline-based NACT such as inhibitors of PARP, cyclin-dependent kinases 4/6 or immune checkpoints will be introduced into clinical routine. In this case, patients that will not respond to the conventional taxane/anthracycline-based therapy will be reliably identified by the present classifier and hence can be treated with a more efficient alternative.

Conflict of interest

The author declares no conflict of interest.

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