10.0%, p = 0.014) in the primary tumor. Among the cases with positive PD-L1, 36.7% of VEGF positive cases had low TILs in the primary tumor, while none of negative VEGF-A cases had low TILs in the primary tumor.

Conclusion: The present study demonstrated that VEGF-A expression in breast cancer may be reflective of the expression of PD-L1 in the tumor. VEGF-A may act as negative regulator of TILs in the PD-L1 positive BC. In light of our results, VEGF-A may be predictive of immunological features and be a useful biomarker for immuno-targeting therapy among patients with breast cancer.

No conflict of interest.

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Gene expression profiles in premenopausal women with HR+ HER2− early breast cancer

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Background: Early breast cancer (EBC) is not a single disease but consists of several clinically relevant molecular subtypes. Within hormone receptor positive (HR+), HER2 negative (HER2−) disease, different luminal subtypes (A vs. B) impact on outcome and response to endocrine therapy. Gene expression signatures predicting risk of recurrence are already part of clinical management. Gene profiles correlated with important tumor pathways such as metastasis and progression, immune response or proliferation also correlate with clinical outcome and therapy response. Premenopausal patients often have poorer prognosis compared to postmenopausal patients. Even though the principle for treating premenopausal patients is consistent with that for postmenopausal patients, the molecular properties of breast cancer in young patients demand special attention in planning the therapeutic strategy. Nevertheless, most studies on gene expression, in particular for risk estimation, focussed on postmenopausal patients. The purpose of our project is to determine gene expression profiles of tumor samples from premenopausal patients with HR+, HER2− EBC. The gene expression profiles will then be correlated to response to therapy response and patient outcome.

Material and Methods: We comprised a collective of 162 premenopausal EBC patients (77 with and 85 without relapse) treated at the LMU breast center over a ten-year follow-up period. Diagnostic, therapeutic, and recent follow-up data were documented and prepared for statistical analysis. Tissue specimens were prepared for laboratory analysis which include a gene expression profiling using a custom-made pan-cancer code set (n = 745 genes) and the Nanostring nCounter® analysis. Gene expression data will be compared with conventional immunohistochemistry subtyping as well as histopathological factors that can be used as surrogates for certain pathways (pan cancer pathways, pathways for tumor progression and tumor immunology, etc.).

Results: Median patient age was 43.98 years of age (range 29–50). The two patient groups (with/without relapse within 10 years) differed with regard to clinical parameters: grade (2.06 ± 0.07/2.29 ± 0.06, $p = 0.024$), tumor diameter (26.62 mm ± 2.11/21.89 mm ± 2.67, $p = 0.033$), percentage of lymphnode metastasis [0.18 (range 0–1)/0.078 (range 0–0.92), $p = 0.001$] (Table 1).

Table 1 Patients' clinical parameters

	With relapse (n = 77)	Without relapse (n = 85)	*p*-value
Age at diagnosis	43.64 ± 0.58 (30–50)	44.29 ± 0.49 (29–50)	0.510
Grade	2.06 ± 0.07 (1–3)	2.29 ± 0.06 (1–3)	0.024
Tumor size (mm)	26.62 ± 2.11 (1–130)	21.89 ± 2.67 (2–110)	0.033
Nodal status	0.1844 (0.00–1.00)	0.0783 (0.00–0.92)	0.001

Conclusion: The project is ongoing. Updated results will be presented at the conference.

Funding: The first author is funded by China Scholarship Council.

No conflict of interest.

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Circulating tumor associated cells in breast cancers are resistance educated towards prior anthracycline treatments

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Background: Doxorubicin and Epirubicin are two anthracycline agents commonly used in treatment of breast cancers. However, chemoresistance towards these agents and subsequent treatment failures are commonly reported. There are presently no means for real-time monitoring of innate and acquired chemoresistance. Repetitive invasive biopsies to obtain tumor tissue for in-vitro chemoresistance profiling (CRP) or viable tumor are not feasible. We describe a non-invasive approach for CRP using peripheral blood Circulating Tumor Associated Cells (C-TACs).

Materials and Methods: We obtained 15 mL peripheral blood from 1034 known cases of breast cancers, among whom 353 were therapy naïve and 681 were pretreated. Viable C-TACs were enriched and harvested from PBMCs using an epigenetically active media that selectively kills normal cells and simultaneously confers survival benefit on apoptosis-resistant cells of tumorigenic origin. Surviving cells (C-TACs) confirmed by immunostaining (EPCAM+, CK+, CD45±, GCDFP+). Viable C-TACs were seeded into multi-well plates and treated with Doxorubicin or Epirubicin and surviving C-TAC fraction was measured to determine % cell-death and chemoresistance.

Results: Among therapy naïve patients (n = 353), innate resistance towards Doxorubicin and Epirubicin was observed in 44% and 46% of samples respectively (overall innate resistance = 45%). Among pretreated patients (n = 681), acquired resistance towards Doxorubicin and Epirubicin was observed in 81% of samples.

Conclusion: Our study demonstrates the feasibility of CRR profiling of C-TACs in therapy naïve and pretreated patients. Adoption of C-TAC – CRR profiling can non-invasively provide real time oversight towards treatment selection, monitoring of drug resistance and timely therapeutic course correction.

Conflict of interest:
Ownership: Rajan Datar is the Founder of Datar Cancer Genetics Limited.
Other Substantive Relationships: Ajay Srinivasan, Dadasaheb Akolkar, Darshana Patil, Revati Patil, Sanket Patil, Vishakha Mhase, Vineet Datta, Sachin Apurwa and Sushant Pawar are full time employees of Datar Cancer Genetics Limited.

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Real-time non-invasive chemoresistance profiling of circulating tumor associated cells in breast cancers to determine resistance towards mitotic inhibitors

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Background: Paclitaxel, Docetaxel and Vinorelbine exert anti-tumor activity by interfering with microtubule dynamics, leading to mitotic arrest. Though these agents are commonly used in treatment of breast cancers, therapy failures are noted due to innate and acquired chemoresistance. Real-time monitoring of chemoresistance towards such treatment agents is an unmet clinical need since conventional methods for chemoresistance profiling (CRP) necessitate invasive biopsies to obtain viable tumor tissue. We evaluated the utility of peripheral blood Circulating Tumor Associated Cells (C-TACs) for real-time non-invasive CRP in breast cancers.

Materials and Methods: We obtained 15 mL peripheral blood from 1034 known cases of breast cancers, among whom 353 were therapy naïve and 681 were pretreated. Viable C-TACs were enriched and harvested from PBMCs using an epigenetically active media that selectively kills normal cells and simultaneously confers survival benefit on apoptosis-resistant cells of tumorigenic origin. Surviving cells (C-TACs) confirmed by immunostaining (EPCAM+, CK+, CD45±, GCDFP+). Viable C-TACs were seeded into multi-well plates and treated with Paclitaxel, Docetaxel or Vinorelbine. Surviving C-TAC fraction was measured to determine % cell-death and chemoresistance.

Results: Innate resistance towards Docetaxel, Paclitaxel and Vinorelbine was observed in 42%, 59% and 56% of samples respectively in therapy