

Guest editorial:

HIGHLIGHT REPORT: INTRATUMORAL METABOLOMIC HETEROGENEITY OF BREAST CANCER

Regina Stoeber

IfADo – Leibniz Research Centre for Working Environment and Human Factors at TU Dortmund, Ardeystr. 67, D-44139 Dortmund, Germany

E-mail: stoeber@ifado.de

<http://dx.doi.org/10.17179/excli2017-1045>

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>).

Recently, Mikheil Gogiashvili and colleagues from TU-Dortmund have published a study about the metabolomics heterogeneity of breast cancer (Gogiashvili et al., 2017). The background of this study is the practically relevant question, whether measurement of a single biopsy is sufficient when analyzing tumors from a cohort of patients. In recent years metabolic profiling by high-resolution magic angle spinning nuclear magnetic resonance spectroscopy has been increasingly used to characterize the metabolome of breast cancer (Sitter et al., 2010; Giskeodegard et al., 2012; Cao et al., 2012; Choi et al., 2012; 2013). However, so far only a single study has addressed the possible influence of metabolic heterogeneity within a single breast tumor (Park et al., 2016). Therefore, the authors performed multi-core sampling of six small specimens from individual tumors and quantified 32 metabolites. Not unexpectedly, the inter-tumoral differences were larger compared to intratumoral differences (Gogiashvili et al., 2017). More importantly, a random forest-classifier trained on a sample set of individual tumors correctly predicted tumor identity of an additional set of independent cores from the same tumors (Gogiashvili et al., 2017). Therefore, the study shows that despite the intratumoral heterogeneity the analysis of only

one or few replicates per tumor can be justified. This is of high relevance, when large cohorts of patients have to be analyzed.

Currently, the majority of prognostic studies with cancer patients has been performed based on mRNA (Grinberg et al., 2017; 2015; Marchan et al., 2017; Cadenas et al., 2014; Ghallab et al., 2015; Lohr et al., 2015; Hellwig et al., 2016; Stock et al., 2015; Hammad et al., 2016) or immunostaining (Heimes et al., 2017; Mattsson et al., 2015; Schmidt et al., 2012; Barone et al., 2016). Studies with metabolic profiling by HR MAS ¹H NMR are still relatively rare in breast cancer. Therefore, the present study of Gogiashvili and colleagues represents an important milestone in this field of research.

REFERENCES

- Barone E, Corrado A, Gemignani F, Landi S. Environmental risk factors for pancreatic cancer: an update. *Arch Toxicol.* 2016;90:2617-42.
- Cadenas C, van de Sandt L, Edlund K, Lohr M, Hellwig B, Marchan R, et al. Loss of circadian clock gene expression is associated with tumor progression in breast cancer. *Cell Cycle.* 2014;13:3282-91.

- Cao MD, Sitter B, Bathen TF, Bofin A, Lønning PE, Lundgren S, et al. Predicting long-term survival and treatment response in breast cancer patients receiving neoadjuvant chemotherapy by MR metabolic profiling. *NMR Biomed.* 2012;25:369-78.
- Choi JS, Baek HM, Kim S, Kim MJ, Youk JH, Moon HJ, et al. HR-MAS MR spectroscopy of breast cancer tissue obtained with core needle biopsy: correlation with prognostic factors. *PLoS One.* 2012;7:e51712.
- Choi JS, Baek HM, Kim S, Kim MJ, Youk JH, Moon HJ, et al. Magnetic resonance metabolic profiling of breast cancer tissue obtained with core needle biopsy for predicting pathologic response to neoadjuvant chemotherapy. *PLoS One.* 2013;8:e83866.
- Ghallab A. Highlight report: Role of the circadian clock system in breast cancer. *EXCLI J.* 2015;14:540-1.
- Giskeødegård GF, Lundgren S, Sitter B, Fjøsne HE, Postma G, Buydens LM, et al. Lactate and glycine-potential MR biomarkers of prognosis in estrogen receptor-positive breast cancers. *NMR Biomed.* 2012;25:1271-9.
- Gogiashvili M, Horsch S, Marchan R, Gianmoena K, Cadenas C, Tanner B, et al. Impact of intratumoral heterogeneity of breast cancer tissue on quantitative metabolomics using high-resolution magic angle spinning ^1H NMR spectroscopy. *NMR Biomed.* 2017. [Epub ahead of print].
- Grinberg M. Highlight report: Erroneous sample annotation in a high fraction of publicly available genome-wide expression datasets. *EXCLI J.* 2015;14:1256-8.
- Grinberg M, Djureinovic D, Brunnström HR, Mattsson JS, Edlund K, Hengstler JG, et al. Reaching the limits of prognostication in non-small cell lung cancer: an optimized biomarker panel fails to outperform clinical parameters. *Mod Pathol.* 2017;30:964-77.
- Hammad S, Osman GS, Ezzeldien M, Ahmed H, Kotb AM. Highlight report: Predicting late metastasis in breast cancer. *EXCLI J.* 2016;15:867-9.
- Heimes AS, Madjar K, Edlund K, Battista MJ, Almstedt K, Gebhard S, et al. Prognostic significance of interferon regulating factor 4 (IRF4) in node-negative breast cancer. *J Cancer Res Clin Oncol.* 2017;143:1123-31.
- Hellwig B, Madjar K, Edlund K, Marchan R, Cadenas C, Heimes AS, et al. Epsin family member 3 and ribosome-related genes are associated with late metastasis in estrogen receptor-positive breast cancer and long-term survival in non-small cell lung cancer using a genome-wide identification and validation strategy. *PLoS One.* 2016;11(12):e0167585.
- Lohr M, Hellwig B, Edlund K, Mattsson JS, Botling J, Schmidt M, et al. Identification of sample annotation errors in gene expression datasets. *Arch Toxicol.* 2015;89:2265-72.
- Marchan R, Büttner B, Lambert J, Edlund K, Glaeser I, Blaszkewicz M, et al. Glycerol-3-phosphate acyltransferase 1 promotes tumor cell migration and poor survival in ovarian carcinoma. *Cancer Res.* 2017;77:4589-601.
- Mattsson JS, Bergman B, Grinberg M, Edlund K, Marincevic M, Jirstrom K, et al. Prognostic impact of COX-2 in non-small cell lung cancer: a comprehensive compartment-specific evaluation of tumor and stromal cell expression. *Cancer Lett.* 2015;356:837-45.
- Park VY, Yoon D, Koo JS, Kim EK, Kim SI, Choi JS, et al. Intratumoral agreement of high-resolution magic angle spinning magnetic resonance spectroscopic profiles in the metabolic characterization of breast cancer. *Medicine (Baltimore).* 2016;95:e3398.
- Schmidt M, Hellwig B, Hammad S, Othman A, Lohr M, Chen Z, et al. A comprehensive analysis of human gene expression profiles identifies stromal immunoglobulin κ C as a compatible prognostic marker in human solid tumors. *Clin Cancer Res.* 2012;18:2695-703.
- Sitter B, Bathen TF, Singstad TE, Fjøsne HE, Lundgren S, Halgunset J, et al. Quantification of metabolites in breast cancer patients with different clinical prognosis using HR MAS MR spectroscopy. *NMR Biomed.* 2010;23:424-31.
- Stock AM, Klee F, Edlund K, Grinberg M, Hammad S, Marchan R, et al. Gelsolin is associated with longer metastasis-free survival and reduced cell migration in estrogen receptor-positive breast cancer. *Anticancer Res.* 2015;35:5277-85.