Report on active participation in EMBO Conference: Cellular signalling and cancer therapy

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Radoslaw Zagozdzon

EMBO is an organization of more than 1500 leading researchers that promotes excellence in the life sciences. The major goals of the organization are to support talented researchers at all stages of their careers, stimulate the exchange of scientific information, and help build a European research environment where scientists can achieve their best work (www.embo.org).

Meetings organized under auspices of EMBO always pose a valuable opportunity for European and world researchers to exchange their knowledge and to discuss on the most up-to-date information as well as to start up new collaborations between top-class laboratories in their research field. Participation of Dr. Zagozdzon in the EMBO Conference was a great opportunity to present his own research findings and to share scientific ideas with the top researchers studying cellular signaling in cancer.

Title of the poster presentation**: Peroxiredoxin-1 regulates estrogen receptor alpha protein content in breast cancer cells undergoing oxidative stress and is a prognostic biomarker in this disease**

Authors: Radoslaw Zagozdzon (presenting author), Patrick C. O'Leary, Gaj Pawel, Bryan T Hennessy, Gordon B. Mills, Ana M. Gonzalez-Angulo, Han-Dong Sun, Fredrik Pontén, Karin Jirström, William M. Gallagher, et al.

BACKGROUND: Estrogen receptor (ER) alpha is the most fundamental therapeutic target in ER-positive breast cancer and the regulation of its presence/function has been a subject of intensive research activities for more than three decades. Nevertheless, the knowledge in this area is still far from complete. Recently, the role of the oxidative stress as a modulator/regulator of tumorigenicity in ER-positive breast cancer has gained increased attention. Prevention or alleviation of this effect can be of

importance in treatment of ER-positive breast cancer. In our study, we decided to evaluate the role of a prominent antioxidant enzyme, peroxiredoxin-1 (PRDX1), as a modulator of ERalpha presence and activity in ER-positive breast cancer.

METHODS: Using lentivirus-mediated genetic modifications, we have generated a range of breast cancer cell lines with variable expression of PRDX1. Induction of oxidative stress by exogenous agents resulted in a dramatic downregulation of ERalpha protein expression in these cells, which was accompanied by an increased phosphorylation of Ser473 in Akt protein kinase. Overexpression of PRDX1 potently alleviated this effect, while PRDX1 knockdown resulted in a pronounced sensitization of breast cancer cells to ERalpha suppression under oxidative stress conditions. This effect could be also mimicked by treatment of breast cancer cells with a recently described PRDX1/2 inhibitor – adenanthin.

RESULTS: To gain further insight into the potential role of PRDX1 in mammary malignancies, we have studied PRDX1 expression in malignant tissues derived from breast cancer patients. Protein expression was evaluated using two independent breast cancer cohorts: a screening reverse phase protein array (RPPA) (n = 712) and a validation tissue microarray (TMA) (n = 498) cohorts. In the screening cohort, increased levels of PRDX1 protein were associated with improved survival. Interestingly, this trend was seen only in the subgroup of ER-positive tumors, and not in the ER-negative patients. In the validation TMA, high PRDX1 protein expression was again a predictor of improved survival, but only in the ER-positive cases. The discovery of the prognostic importance of PRDX1 expression levels especially in ER-positive subtype of breast cancer, corroborates a mechanistic link between PRDX1 and ER.

CONCLUSION: In conclusion, we have identified PRDX1 as an independent predictor of favorable prognosis in ER-positive breast carcinomas. Based on our accumulated data, we hypothesize that PRDX1 shields the dependence of mammary tumors on estrogen-mediated growth stimulation, which eventually is of benefit for the patient. In this regard, PRDX1 expression may be utilized in the therapeutic decision making process in this disease, especially in light of PRDX1 being recently considered a therapeutic target in cancer.

Please note: Dr. Zagozdzon was also a co-author of a poster presented by Dr. Malgorzata Bajor at the same meeting. This has been described in a separate report.