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THE HUNT FOR BIOMARKERS OF THE EARLIEST STAGE BREAST CANCER PROGRESSION

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Ductal carcinoma *in situ* (DCIS) of the breast is a non-invasive proliferative tumour. This so-called stage "0" breast cancer has not yet developed or may never develop to advanced cancer. With the use of screening mammography worldwide, DCIS has become a clinical challenge due to its increasing incidence and uncertain prognosis. Presently, an indolent DCIS cannot be distinguished from a progressive tumour, making the appropriate treatment for DCIS patients, a major clinical dilemma. Researchers hope to identify predictive biomarkers (BM) that can forecast the pro-malignant potential of DCIS to guide the treatment. Although a variety of high throughput transcriptomics technologies have been employed for the molecular analysis of DCIS, predictive biomarker (BM) able to determine beforehand which patients might have progressive disease were not determined. The employment of new technologies and alternative approaches are important next steps. We have been developing methodology to delve into tissue's protein BM that in advance of the treatment have determined the likelihood that DCIS becomes invasive, as opposed to remaining indolent tumour. We assumed that DCIS with synchronous microinvasive carcinoma (T1mic) represents the earliest stage 1 breast cancer, because invasion increases the likelihood of metastasis. Using our novel imaging method for archival tissue analysis, we performed quantitative protein profiling on 211 human breast tissues: 42 histologically normal, 71 cancer *in situ* (including 11 T1mic) and 98 invasive carcinomas. In this pilot study, we identified Vav2 oncoprotein as a promising BM of progressive DCIS. We found that DCIS with high Vav2 protein were more than twice as likely to progress to invasive cancer as DCIS with low Vav2 protein (odds ratio, 2.42; *p*=o.008). Furthermore, measurements of Vav2 revealed previously unidentified discriminating power of Vav2 to predict the existence of invasion synchronous with DCIS. Our further studies are underway to characterise additional BM.

Biography

Marina Guvakova has received her PhD in Cell Biology from the Russian Academy of Sciences and Post-doctoral training in Cancer Research from Columbia University and Thomas Jefferson University, USA. She is an Assistant Professor at the University Of Pennsylvania Perelman School of Medicine and a Senior Research Investigator at the Department of Surgery. She is an author of 20+ papers, recipient of the New Investigator Award from the Endocrine Society, Gordon Research Conferences awards, Breast Cancer Research Award from the DoD BCRP. She serves as a Reviewer for several journals, Editorial Board Member of *ISRN Endocrinology*, and a CDMRP peer-review panel member.

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