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The quest for biomarkers of earliest stages of invasive breast cancer

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Abstract

With the use of screening mammography, the diagnosis of ductal carcinoma in situ (DCIS) is increasing worldwide. Patients diagnosed with DCIS either have not yet developed or may never develop invasive breast cancer (IBC). Presently, an indolent tumor can not be distinguished from a progressive tumor, making the appropriate treatment of DCIS patients a major clinical dilemma. We are interested in developing in tissue biomarkers (BM) to determine the likelihood that initial breast tumor identified on diagnostic biopsy remains contained *in situ*, as opposed to becoming invasive. Molecular studies predicted that the transition from *in situ* to invasive disease was associated with quantitative rather than qualitative differences in gene and protein expression. We developed imaging-based method to measure protein expression as a continuous variable in fixed tissue. We assumed that DCIS accompanying microinvasive carcinoma (T1mic) represented an early progressive DCIS, because invasion increases the likelihood of metastasis. We theorized that molecular BMs of progressive DCIS are the measurable parameters that distinguish cells in *in situ* component of T1mic from cells in normal/benign epithelium. We performed quantitative protein profiling on 210 archived tissues: 42 histologically normal, 19 benign; 54 cancer *in situ*, and 95 IBC. Our measurements in DCIS revealed previously unidentified quantitative differences in the insulin-like growth factor I receptor, Ras oncogene –like protein 1, and Rho GTPase guanine nucleotide exchange factor Vav2, the proteins implicated in the regulation of invasion in preclinical models. These new findings may open doors to molecular-based predictions of individualized risk for developing invasion in DCIS.

Biography

Marina Guvakova received Ph.D. in cell biology from the Russian Academy of Sciences and post-doctoral training from Columbia 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 Gordon Research Conferences awards, the New Investigator Award from the Endocrine Society, 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.