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## The quest for biomarkers of earliest signs of invasive breast cancer

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**Background:** A subset of patients with ductal carcinoma in situ (DCIS) will develop invasive breast cancer (IBC). To date, there are no predictive biomarkers for identifying this subset with worse prognosis because progressive cancers in situ (CIS) are essentially indistinguishable histologically from those with favorable outcomes. We hypothesized that the measurable parameters discriminating CIS from CIS with concurrent microinvasion may serve as early diagnostic biomarkers (BM) of cancer progression.

**Methods:** Using a novel imaging-based method, we measured the relative expression levels of proteins implicated in cancer progression- the insulin-like growth factor I receptor (IGF-IR), Ras-related protein 1 (Rap1), and Vav2 oncoprotein. Protein profiles were compared in 42 histologically normal mammary samples, 71 CIS (35 without/36 with invasion either on diagnostic biopsy or final surgical excision), and 98 IBC of known estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) status.

**Results:** The levels of the IGF-IR and Rap1 protein expression were significantly elevated in ER-positive (ER+/PR+/-/HER2-) DCIS relative to normal epithelium (P<0.0001). The IGF-IR protein expression was also significantly up regulated in HER2-positive (ER+/-/PR+/-/HER2+) DCIS relative to normal epithelium (P=0.0002). IGF-IR and Rap1 protein expression levels were similar among DCIS patients without or with concurrent invasion. Vav2 upregulation in DCIS relative to normal group was not associated with steroid hormone receptor and HER2 status, but was associated with the presence of concurrent invasion. DCIS with high Vav2 were more than twice as likely to progress to invasive cancers as DCIS with low Vav2 (odds ratio, 2.42; 95% CI, 1.26-4-65; P=0.008). Furthermore, a receiver operating characteristic curve analysis revealed moderate ability of Vav2 protein expression measurements in DCIS to predict the existence of invasion concurrent with DCIS (area under the curve, 0.71; 95% CI, 0.59-0.84).

**Conclusions:** Our novel findings hold promise for utilizing Vav2 as a predictive BM for differentiating progressive from non-progressive DCIS.

## Biography

Marina A Guvakova completed her PhD in Cell Biology at Russian Academy of Sciences and Post-doctoral training at Columbia and Thomas Jefferson University, USA. She is an Assistant Professor at University of Pennsylvania Perelman School of Medicine and a Senior Research Investigator in Department of Surgery. She is an author of 20+ papers, recipient of New Investigator Award from Endocrine Society, Breast Cancer Research Award from DoD BCRP and Gordon Research Conferences Awards. 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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