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Molecular pathways involved in prolactin-dependent JAK2/PAK1 action: Implication in breast cancer cell motility and invasion

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Despite efforts to discover the cellular pathways regulating breast cancer metastasis, little is known as to how prolactin cooperates with extracellular environment and cytoskeletal proteins to regulate breast cancer cell motility and invasion. We have shown that serine-threonine kinase PAK1 is a novel target for prolactin-activated JAK2. JAK2 tyrosyl phosphorylates PAK1 in response to prolactin and increases both PAK1 kinase activity and scaffolding properties of PAK1. Tyrosyl phosphorylated PAK1 facilitates prolactin-dependent cell motility via two mechanisms: Formation of complexes with paxillin and GIT1/ β PIX proteins resulting in increased adhesion turnover and phosphorylation of filamin A, an actin cross-linker. Increased adhesion turnover is the basis for cell migration and phosphorylated filamin A stimulates the kinase activity of PAK1 and has increased actin-regulating activity to facilitate cell motility. Tyrosyl phosphorylated PAK1 also stimulates invasion of breast cancer cells in response to prolactin and three-dimensional collagen IV via transcription and secretion of MMP-1 and MMP-3 in a MAPK-dependent manner. These data illustrate the complex interaction between prolactin and the cell microenvironment in breast cancer cells and suggest a pivotal role for prolactin/PAK1 signaling in breast cancer metastasis.

Biography

Maria Diakonova has completed her PhD at the age of 30 years from the Institute of Cytology Russian Academy of Science and Postdoctoral studies from the European Molecular Biology Laboratory (EMBL, Heidelberg, Germany). She is the Associate Professor in the Department of Biological Sciences at the University of Toledo, OH, where she directs research focusing on a role of prolactin in breast cancer progression. She has published more than 27 papers in reputed journals and has been serving as a lead editor of "Recent Advances in Prolactin Research" book (*Advances in Experimental Medicine and Biology series*, Springer).

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