

## Integrative microarray strategy for screening and evaluation of compounds modulating ErbB receptor activity in cancer cells

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### *Abstract*

The ErbB receptor tyrosine kinases govern major signaling pathways and their deregulation results in aggressive tumour growth. Developing efficient small agents towards these attractive targets located both in cytoplasm and nuclear membranes is difficult task because of the complexity of molecular interactions. Peptide ligand binding to the extracellular region triggers receptor's auto-phosphorylation and downstream signal transduction *via* the kinase domain involved in interactions with cytoplasm and nuclear proteins. ErbBs participate also in lateral transactivation of different receptor tyrosine kinases.

To search for molecules recognizing protein-protein interaction interface in ErbBs we used advantages of their domain organization to construct shortened protein probes. Consecutive application of microarrays permitted to select covalent and non-covalent binders, and to define protein signatures in signaling pathways. First, new method of small molecule microarrays was developed for screening compound libraries that allowed us to detect molecules bound to the extracellular or cytoplasm region of ErbBs. Second, antibody and reverse phase protein arrays were employed to assess expression and protein phosphorylation in cancer cells. Allosteric agonist-like and antagonist-like molecules have been discovered, which offer a promising paradigm to investigate new aspects of ErbB protein-protein interaction circuits in cytoplasm and nucleus. The proposed microarray strategy is cost-effective and covers large range in anti-cancer drug discovery, from library screening to lead validation.

### *Biography*

Vehary Sakanyan is a Professor in Nantes University. Under his leadership, several microbial strains overproducing amino acids and biocatalytic enzymes were constructed and applied at industrial scale in ex-USSR. In 1992 he was invited to transfer to Nantes University, where he performed basic research and managed industrial projects with Rhone-Poulenc and Ajinomoto. Since 2000 his research teams have been involved in developing protein and antibody microarrays and their biomedical applications (Snapyan et al., 2003; Arnaud et al., 2004; Gaudin et al., 2008; Dupuy et al., 2009). Antibody arrays developed in collaboration with ProtNeteomix have been used for evaluation of protein expression in breast cancer cells (Yeretssian et al., 2005). Small molecule arrays have been used to assess binding of new cationic porphyrins to plasma proteins for photodynamic therapy of tumor (Gyulkhandanyan et al., 2012). V. Sakanyan is the author of 120 scientific publications and patents, and has presented his research at various international meetings. He is a founder and CSO of ProtNeteomix. His current drug discovery research is focused on protein-protein interactions in diseased cells.