

**HIGH-THROUGHPUT INTERACTION SCREENING FOR THE
ELUCIDATION OF PROTEIN KINASE NETWORKS AND THE
IDENTIFICATION OF PROTEIN KINASE INHIBITORS**

CLAUDIA KRUSE, SERGEY VASILIEV, SABINE HANKE
and HANJO HENNEMANN

Research Center Caesar, Ludwig-Erhard-Allee 2, D-53175 Bonn, Germany,
Hennemann@caesar.de

The analysis of the human genome sequence has led to the identification of more than 500 protein kinases. The role of most deduced kinases in the functional network of human cells is unknown.

We have developed a high-throughput version of the Ras Recruitment System (RRS). The RRS is an *in vivo* system for the analysis of protein-protein interactions, and uses a novel selection mechanism in the cytoplasm of living cells. The RRS has been proven to be well suited for the analysis of protein kinase networks. The use of the HT-RRS has led to the identification of novel regulators of protein kinase networks, which are novel drug target candidates.

The specific interaction of proteins in protein kinase networks is necessary for their signalling function. Interference of these protein interactions provides a very specific way for the

- validation of protein constituents of kinase networks
- search for drugs.

Interestingly the mode of action of this type of drugs should be different from the widely used inhibition of kinase catalytic centers. Possible points of attack are rather the blocking of access of regulatory factors like upstream activators/inhibitors, modulators like phosphatases, specific substrates or residues used for covalent modification. This approach should open the way for the identification of novel drugs having a more specific way to interfere with disease-related protein kinase functions.