NEW INHIBITORS OF CANCER RELEVANT PROTEIN KINASES

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4SC AG and ProQinase GmbH collaborate to identify a new generation of protein kinase inhibitors as the basis for the development of new anticancer drugs.

Protein kinases play a pivotal role in the regulation of cellular functions. These include processes like cell growth and division, cell differentiation and cell death, but also many other cellular activities. Several oncogenes are pathologically modified genes which in their proto-oncogenic form encode for protein kinases involved in normal, physiological regulation of cell growth and division. Tumor progression involves (1) cell proliferation/cell cycle control, (2) regulation of programmed cell death (apoptosis) and cell survival, (3) tumor angiogenesis, and (4) tumor metastasis. In each of these processes, certain protein kinases play a key role.

The intention of the project is the identification of monospecific protein kinase inhibitors, which preferentially inhibit one protein kinase causatively involved in tumor progression, but also so-called multi-target protein kinase inhibitors, which inhibit at least two different protein kinases playing a role in two or more different molecular mechanisms of tumor progression.

ProQinase provides disease relevant protein kinase targets using its integrated technology platform, including cell based assays and in vivo models.

New hit structures were identified using 4SC's proprietary virtual High Throughput Screening technology, 4SCan®: Out of a virtual library of 5 Mio compounds, ATP competitive ligands of the desired protein kinases were selected, resulting in a hit rate of 16 % in the enzyme assay. Modification of selected hit compounds by Medicinal Chemistry led to the identification of new classes of selective inhibitors of cancer relevant protein kinases with low nanomolar activity, e.g. on Aurora and VEGF-R2 kinases. Compounds showing this selectivity profile are expected to inhibit cell proliferation and tumor angiogenesis at the same time.