FUNCTIONAL VALIDATION OF PREDICTIVE BIOMARKERS FOR TARGETET CANCER THERAPIES

Lead partner:
IMC Hochschule für Angewandte Wissenschaften Krems

Scientific management:
Andreas Eger

Research field:
Onkologie, Personalisierte Medizin

Funding tool: Basic research projects

Project-ID: LS09-023

Project start: 01. Juli 2010

Project end: will follow

Runtime: 36 Monate / finished

Funding amount: € 256.000,00

Brief summary:
The genomic revolution has boosted the development of novel cancer therapeutics targeting critical oncogenic signaling molecules. The clinically most effective agents inactivate protein kinases, which affects proliferation and induces cancer cell death. However, the clinical benefit is limited to subpopulations of cancer patients prompting the need to identify the genetic factors that influence drug sensitivity. Intense interdisciplinary research efforts have revealed myriads of genetic changes (biomarkers) that are functionally associated with drug efficacy and safety in tumor patients. Personalized cancer medicine now seeks to combine biomarker research and clinical treatment protocols to tailor patient-specific therapies that ensure a more successful patient outcome and minimal drug toxicity. However, the tremendous information in the biomarker field has to be translated into clinical practice yet.
In the present project we propose to develop standardized diagnostic procedures that allow the detection and quantification of promising biomarkers in tumor specimen. We selected only those marker classes that reliably predicted receptor tyrosine kinase inhibor (RTKI) responsiveness in large retrospective clinical studies (markers with high predicting index). The diagnostic tools will be designed either to detect single markers or recognize multi-gene genetic fingerprints. The clinical relevance and the predictive value of the diagnostic procedures will be validated in clinical studies encompassing large cohorts of cancer patients. Initially we will focus on widespread malignancies of the colon, breast and lung, for which approved RTKI therapies are clinically implemented. Statistical analyses integrating clinical outcome and biomarker status will be performed to assess the predictive power of the novel biomarker assays. In addition, complementary biomarker studies are carried out in our different proprietary organotypic tumor models. The precise characterization of biomarkers in cancer cells combined with high-throughput drug response studies will help to gain insight into the complex relationship between genotype and drug responsiveness.
The present proposal requires an interdisciplinary and multi-institutional collaboration between the clinics in Lower Austria and the University of Applied Science in Krems. The project is likely to significantly stimulate oncological research and personalized cancer medicine in Lower Austria. Considering the financially constrained health care system stakeholders are increasingly demanding straight proof of efficacy, safety, and cost-effectiveness of therapeutic treatments. The proposed project is supposed to target that issue.

Keywords:
personalized medicine, drug efficacy, oncogenes, tyrosine kinases