



innovations from nature



acib Project Proposal

Predicting drug resistance mutations in receptor tyrosine kinases

Drug resistance mutations are the major limitation of kinase inhibitors in cancer therapy. We are developing a novel in vitro method for predicting drug resistance mutations in tumors, thereby allowing cost-efficient optimization of new inhibitors and inhibitor combinations for reduced resistance potential.

Background

Receptor tyrosine kinases are frequently mutated and activated in cancer. Within the last two decades a number of highly promising receptor tyrosine kinase inhibitors entered the clinic. Despite strong initial responses in many patients, **in virtually all cases the tumor eventually develops drug resistance**, in many cases by obtaining additional mutations in the targeted kinase domain. Currently, there are two types of strategies for studying the emergence of resistance mechanisms in tumor cells. The first method is the analysis of tumor tissue derived from **biopsies** after the emergence of resistance in patients. While this approach will always be the gold standard, performing clinical trials and analyzing biopsies is **extremely expensive** (millions of dollars) and **time-consuming** (several years). An alternative approach is the prolonged cultivation of cancer cell lines in the presence of the inhibitor until resistance evolves. Although this method is much cheaper and faster, it still takes several months until resistant clones emerge. Moreover, experimental data strongly suggest that **not all possible resistance mutations can be sampled using cancer cell lines**.

acib-Technology

We are currently developing a **novel in vitro method for rapidly predicting all possible drug resistance mutations** in receptor tyrosine kinases upon treatment with kinase inhibitors and have already obtained very **promising data**. Importantly, predicting drug resistance mutations for a given receptor tyrosine kinase will be **inexpensive** (estimation approx. EUR 5,000 – 10,000, once the method has been fully established), **fast** (about 4 – 6 weeks) and it will **cover virtually all possible mutations in a single experiment**. Moreover, it will be straight forward to test **several different inhibitors in parallel**, which is impossible in clinical trials.

acib-Offer

Our approach offers a number of competitive advantages for an industrial partner: (i) one can **screen several lead compounds** for potential drug resistance mutations **before entering the clinic**. A compound that is less likely to yield resistance mutations will be **more competitive on the market**; (ii) one can screen several compounds and **choose drug combinations that are unlikely to yield common resistance mutations**; (iii) once an inhibitor enters the clinic, **new resistance mutations can be rapidly anticipated**, enabling the development of a new generation of inhibitors before the resistance mutations are known from the clinic, ultimately obtaining a **head start over competing companies**.

Please contact us, if you want to co-develop this highly interesting new technology.

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