



DRUG TARGETING

Powered by MPI's
Universally applicable Drug Response Predictor

- Speed up drug development
- Save millions on development cost
- Increase drug development success
 - Maximize on-patent sales period

MEDICAL PROGNOSIS INSTITUTE

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Universal Drug Response Predictor based on gene expression

Identifying indications and patients where a new drug is efficient

MPI's proprietary drug response predictor (DRP) is unrivalled in efficiency and universality. Predictors have been developed for 59 out of 65 drugs attempted. That includes small-molecules, RNA antagonists and monoclonal antibodies.

SERVICES

IN VITRO ANALYSIS

This is the first analysis step for a potential drug candidate. It will give a good indication whether in vivo prediction of response will be feasible.

ANIMAL MODELS

MPI can predict the drug response in animals. This can be the final test before going into human subjects.

IN VIVO ANALYSIS

Microarray analysis of samples from patients that are later treated with the drug. This is the final validation.

Near perfect match between prediction and clinic:

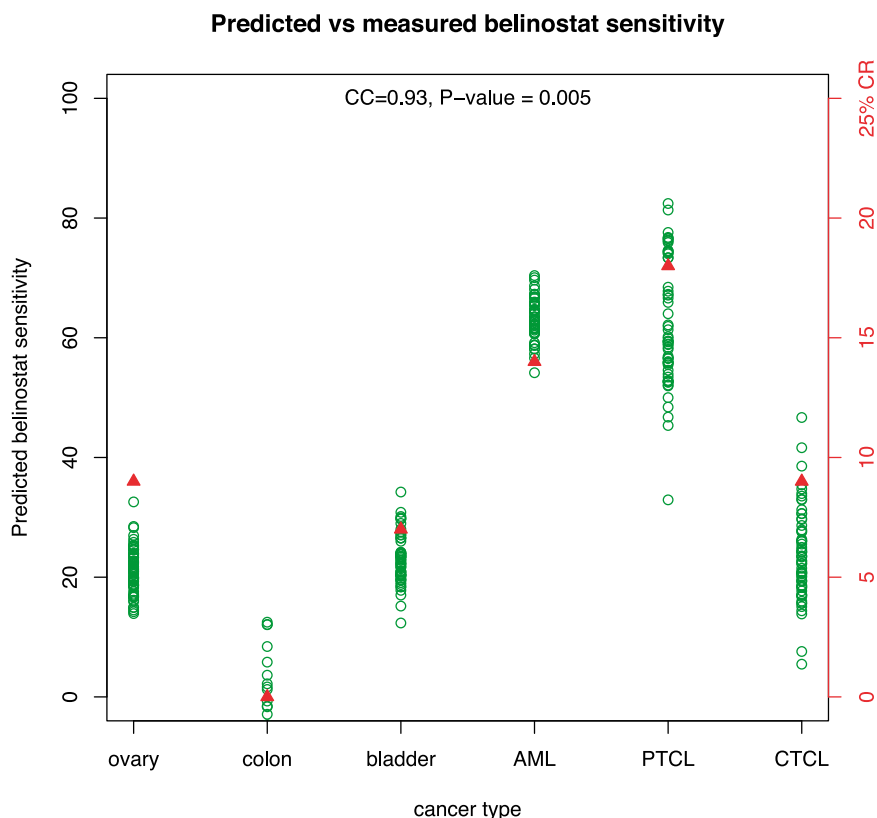


Fig 1. Predicted sensitivity of cancer patients with different cancer types (each patient is one green circle, left scale) compared to measured response rates for the same drug (red triangles, right scale).

Why does it work so well?

MPI has invested years of research and millions of Euros in the development, improvement, patenting and blind clinical

validation of the DRP. The investment has paid off in the most universal and accurate drug response predictor on the market.

Near perfect prediction of clinical result:

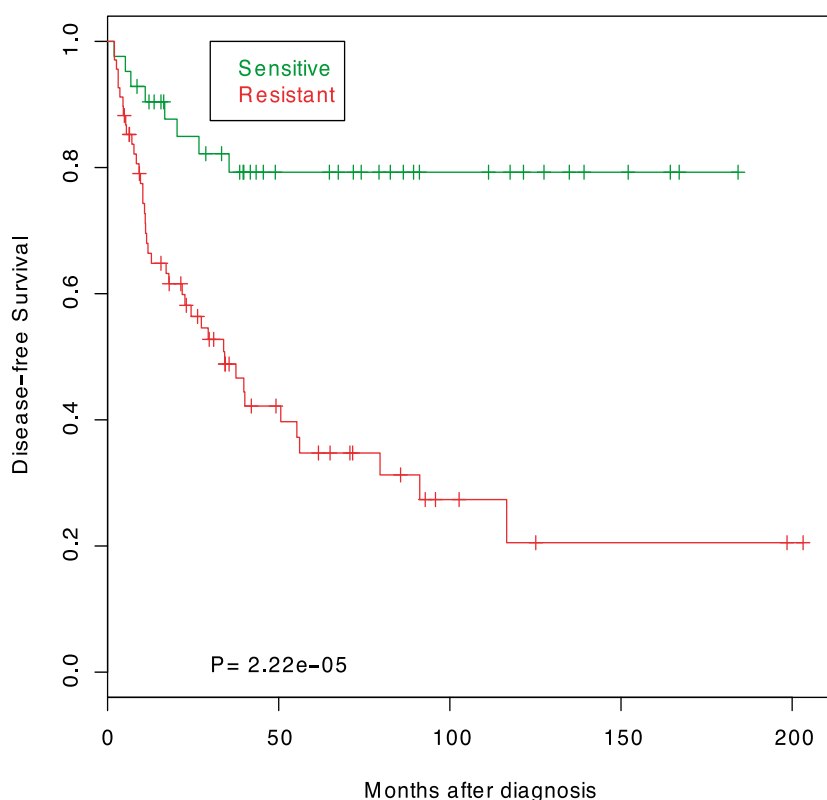


Fig 2. Survival of cancer patients predicted sensitive (green) or resistant (red) to drug they are later treated with.

Based on *in vitro* data

The efficiency is obtained by basing the DRP on *in vitro* data from cell lines treated with the drug.

Selection of cancer type

The DRP is unrivalled in its ability to select a cancer type that will respond to a drug (Figure 1). This can save costs for clinical trials as well as reduce wasted patent time. The cost/benefit ratio in this application is simply outstanding.

Selection of responding patients

Once the best cancer type has been selected, the responding patients with that cancer type can be identified. Figure 2 shows the survival of patients predicted sensitive and patients predicted resistant.

Multiple forms of collaboration

A collaboration to develop a DRP for a drug can take many forms: it can be performed as a fee for service or MPI can take part in the financial risk. The cost involved depend on the circumstances, but one case could look like this: (1) development of predictor 15.000€, including prediction of xenograft response and cancer types; (2) test of clinical samples 1000€ per sample (3) milestone payment or royalty agreement upon transfer of IP or confirmation in clinical trial.

Why not use a SNP or protein?

Because they cannot capture as much clinical variation as our detailed models, often including 100 genes or more. MPI is prepared to guarantee that our model works better than a SNP or protein marker. Thus, there simply is no reason not to have MPI develop a DRP for your drug.

Accuracy and PPV

The accuracy of response prediction observed in retrospective validations of MPI's new technology so far has been between 76% and 92% and positive predictive values have been between 72% and 90%. Such a predictor could improve the response rate from 5% to 86% or more!

Applications

MPI's drug response predictor can be applied to drugs in preclinical, Phase I, II, or III. In those stages it will act as an insurance against failure of the drug due to lack of effect or inability to reach a designed endpoint. It can also dramatically reduce the number of patients required to obtain a given power (Stat Med. 2005, 24(3):329-39). MPI's drug response predictor can also be applied to drugs that have already failed in Phase I, II, or III due to lack of effect. These drugs can be rescued by identifying a subgroup of patients that will respond to treatment with the drug. MPI's predictor needs a sample of the target tissue. Therefore, cancer drugs where a pre-treatment blood sample, biopsy or surgery sample will be available are easiest to work with.

Regulatory Issues

MPI can help you submit the DRP to the FDA. The political trend is toward mandated drug-test companions that ensure highly efficient drugs. In the future, payers may not want to reimburse ineffective drugs.

Maximizing Revenue Potential of your Drug Development Program

Limiting the drug to a subgroup will reduce its market size, but economic models show that this loss is offset by money saved from otherwise unsuccessful Phase III trials (Nature 444:532-533; 2006). Besides, you save

highly valuable patent time (extending the peak sales period), and a higher response rate will lead to a higher price and market penetration (Nature Reviews, Drug Discovery 6:287-293; 2007). In total, the economic rewards of using MPI's Drug Response Predictor are unquestionable!



For more information on DRP's for your specific needs please contact:

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