

# AI Based Personalized Theranostics

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## ABSTRACT

When cancer patients were treated by chemotherapy, usually the response rate is about 25%. The inability to pinpoint optimized regimen, drugs and doses to accommodate genetics related human diversities and patient specific physiological responses results in implicitly suboptimal treatment efficacy, which is the reason for low response rate. Assisted by artificial intelligence (AI) based analysis, we can link the drug-dose inputs to the phenotypic outputs with a smooth phenotypic response surface (PRS). AI-PRS based theranostics platform can customize to a specific patient, which leads to major improvement of response rate.

**KEYWORDS:** Personalized Medicine, Phenotypic Response Surface (PRS), Artificial Intelligence

## INTRODUCTION

The current drug development roadmaps are prohibitively long, on the order of 10-15 years, and cost billions of dollars. The success rate of development from *in vitro* assays to regulatory approval is less than a few percent. The two fundamental challenges that impede drug development are: 1) Conventional approaches cannot pinpoint the best *in vitro* drug composition and dose ratios that simultaneously mediate the highest efficacy and lowest toxicity from a large search space. 2) Once preliminary doses are determined using *in vitro* tests, the translation of these doses to *in vivo* applications is performed by matching the PK or by weight/surface area scaling or by determining the maximum tolerated dose (MTD), which implicitly preclude optimization. These are the primary causes of developmental failures.

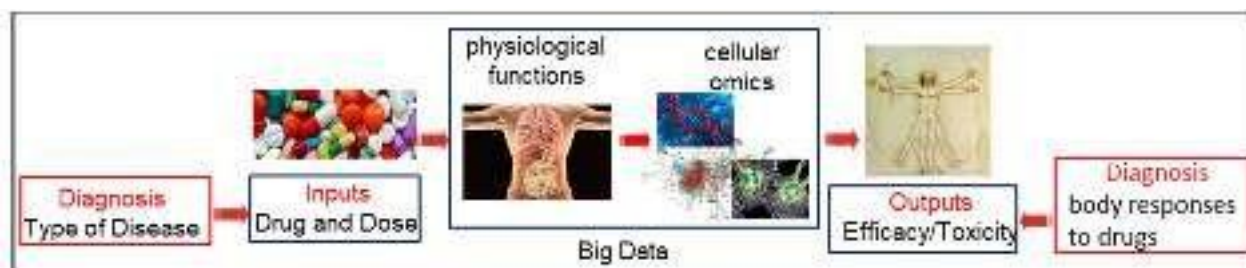


Figure 1: Personalized Diagnosis and Therapeutics

In the clinical setting, clinician has only two actionable parameters, drug and dose, to treat patient after the disease having been identified with marker based diagnosis. Drugs interacting with the physiological system and the diseased molecular mechanisms and eventually lead to the body responses to the drugs, efficacy and/or toxicity. The challenges are: 1) There is no obvious direct relationship between the inputs and outputs. Hence the combinatorial drug is not optimized. 2) It is hard to find definitive molecular markers for determining the type of disease and for quantitative measurements of the efficacy/toxicity.

## PERSONALIZED THERANOSTICS

Through AI analysis, we have found that the treatment outcomes (efficacy/toxicity) could be dynamically correlated with treatment inputs (drugs and doses) through a Phenotypic Response Surface (PRS). This approach defines a new field of artificial intelligence augmented medicine. Deterministically correlating inputs and outputs will immediately converge on actionable, experimentally-optimized treatment outcomes without the need for disease mechanism data. This makes PRS universally applicable towards all indications and to a specific patient or population of patients. The PRS was discovered to be a second order algebraic equation, which is represented by a parabolic shaped surface.

$$E(c, t) = \sum_{i=1}^N x_i(t)c(t)_i + \sum_{i=1}^N y_{ii}(t)c(t)_i^2 + \sum_{i=1}^{N-1} \sum_{j=i+1}^N z_{ij}(t)c(t)_i c(t)_j$$

Where  $c(t)_i$  or  $c(t)_j$  is dose for drug  $i$  or  $j$ .  $t$  is time.  $E(c, t)$  is the efficacy, toxicity or therapeutic window.  $x_i$ ,  $y_{ii}$  or  $z_{ij}$  is the coefficient associated with the first order of dose,  $c(t)_i$ , second order of dose,  $c(t)_j$  or the drug-drug interaction between drug  $i$  and  $j$ . With a few calibration tests to determine the coefficients of the quadratic algebraic equation governing PRS, PRS dictates the composition and the ratio of a globally optimized drug combination.

The number of the calibration tests depends on the number of the drugs in a regimen. For example, 3 drug combination will need to have 10 calibration tests. The 10 dose combinations will follow the experimental design method<sup>1</sup> to strategically decide the values of these combinations. The efficacies/toxicities as the results of the treatments of these 10 dose combinations will be used to solve the coefficients. With the current microfluidic technology, there is no problem to measure any target molecules. However, it is not easy to identify target molecules, which can quantitatively measure the phenotypes (Fig 1), especially for those diseases with no easily definable markers in blood, e. g. solid cancers.

In vitro drug compositions and ratios will not translate into successful preclinical or clinical validation. Since only a very small number of tests are needed in the AI-PRS platform, we can re-optimize drug-dose ratios in animal and clinical tests. Re-optimization has already been successfully demonstrated to converge upon key drugs/combinations of interest. Based on the AI-PRS platform, personalized medicine can realize unprecedented levels of adaptability to identify the optimized drug combination for a specific patient, even if provides dynamically personalized management in a therapeutic window, where has high efficacy and low toxicity. PRS is an indication agnostic and mechanism free platform technology, which has been successfully demonstrated in cancers<sup>2,3,4</sup>, infectious diseases<sup>5,6</sup> and organ transplantations<sup>7</sup> for children and adults.

## CONCLUSIONS

With the discover of the PRS equation, which is the transfer function between the therapeutic inputs and phenotypic outputs, giving the most potent drug-dose combination customized to a specific patient becomes possible. This approach is applicable for cancers, organ transplants and infectious diseases.

## ACKNOWLEDGEMENTS

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