



**SU2C–Dutch Cancer Society Translational Research Team:  
“Prospective Use of DNA-Guided Personalized Cancer Treatment”**



*[This abstract was provided by the scientists when their application was accepted.]*

Over the past decade, we have begun to realize that our limited success in the treatment of cancer stems to a large extent from the heterogeneity of tumors at the molecular level. Thus, tumors that appear very similar when evaluated by conventional diagnostics (the microscope) may differ significantly when analyzed at the molecular level. Molecular studies have taught us that specific alterations in the DNA of a tumor (mutations) can be used to predict the response of a patient to cancer drugs. Therefore, the ultimate goal of delivering the right drug to the right patient (personalized medicine) requires a detailed understanding of how alterations in the tumor DNA are linked to responses to cancer drugs.

Here we propose to study how changes in the tumor DNA of patients can be used to predict sensitivity to specific anti-cancer agents. This requires studies in which we analyze in detail the alterations in large numbers of genes in tumors. These alterations will then be studied in relation to the responses of these patients to specific cancer drugs.

By discovering how mutations in tumor DNA are linked to responses to cancer drugs, we will be able to make far more educated choices for the treatment for individual patients, leading to greater therapeutic benefit, while at the same time reducing the toxicity of ineffective cancer drugs.

In this project we will investigate several important aspects of this DNA-guided Personalized Cancer Treatment approach. In the context of 3 clinical studies we will invite patients to undergo biopsies before and 2 months after start of defined treatment regimens.

DNA will be isolated from these biopsies and analyzed for mutations in 2,000 of the most important genes. Genetic changes will be correlated with treatment outcome to generate DNA profiles that will predict whether patients with breast or colorectal cancer will respond to a given treatment. This project also includes a novel aspect of personalized cancer treatment: dynamic tumor assessments.

By repeating the tumor biopsies after 2 months of treatment, we are able to determine genetic changes as a result of treatment and to identify pathways that the tumor uses to become resistant to treatment. This allows us to initiate intelligent combinatorial drug treatments that avoid the development of drug resistance.

The final innovative aspect of this project is that we will incorporate computational biology in our efforts to generate predictive DNA profiles. Computational biology takes into account all available information on interactions of genes within a cancer rather than linking a single mutation to clinical





## Scientific Abstract

outcome. By linking the clinical data to the genetic data of the tumor and utilizing all available information on the biology of that cancer, we can further refine patient selection criteria for a specific treatment through computational methods.

The outcome of this project will have an impact at multiple levels of clinical cancer care: i) it will generate novel DNA analysis tools to better select cancer patients for specific treatments; ii) it will expedite cancer drug development by delivering tools that can match the right patient for the right drug; iii) it will show the value of dynamic tumor assessments by repeated biopsies to understand mechanism of cancer drug resistance; and most importantly iv) it will contribute to increased cancer survival and quality of life by helping to deliver the most effective drug to the patient early on, while reducing toxicity of ineffective drugs.