

TRANSLATIONAL BIOMARKERS: IDENTIFICATION OF BIOMARKERS RELATED TO CAPECITABINE RESPONSE IN SOLID TUMORS BY NUCLEIC ACIDS PROGRAMMABLE PROTEIN MICROARRAYS (NAPPA), ANTIBODY ARRAYS, IFISH AND SNPS APPROACHES

M. González-González⁽¹⁾, *J. Sayagues*⁽¹⁾, *R. Bartolomé*⁽¹⁾, *J. Alcázar*⁽²⁾, *J. Garcia*⁽²⁾, *J. Labaer*⁽³⁾, *A. Orfao*⁽¹⁾, *M. Fuentes*⁽¹⁾.

⁽¹⁾ Centro de Investigación del Cáncer. Universidad de Salamanca-CSIC, ⁽²⁾ Hospital Clínico Universitario de Salamanca, ⁽³⁾ Biodesign Institute. Arizona State University.

Biomarkers, particularly those with strong positive and negative predictive value, have many potential uses in the diagnosis and treatment of cancer, including monitoring treatment success, indicating disease progression and detecting early disease. One potentially powerful approach to finding biomarkers is to exploit patients' own immune systems, which produce humoral responses to cancer antigens released by their tumors due to alterations in protein expression, mutation, etc.... Antibodies to tumor antigens have been detected as early as several years before the clinical appearance of cancer. Although the specificity for these responses is high, typically only <20% of patients demonstrate a response to any given antigen, which has limited the usefulness of single antigen responses as biomarkers. The recent development of protein microarrays may offer an ideal tool for screening for immune response to tumor antigens. These arrays offer the advantage that hundreds to thousands of different proteins can be printed and screened simultaneously and only require a few microliters of serum per assay.

Prof. LaBaer's group (Harvard Institute Proteomics) has developed a novel method for producing protein microarrays called nucleic acid programmable protein arrays (NAPPA). Here, we propose adapting the NAPPA protein microarray technology for use in the rapid and efficient screening of sera from cancer patients for antibodies to 6000 known and potential tumor antigens in a multiplex format in order to better characterize and identify new biomarkers related to drug treatment. For this purpose, patient's samples pre- and post- chemotherapy have been included. A set of novel biomarkers suggest that approximately 30% of the patients show resistance against chemotherapy pre- surgery, as it has been reported previously. For the validation of the possible biomarkers found in 20 different patients (pre- & post-chemotherapy), currently we are using *i*FISH and SNPs approaches with the main goal to correlate genomics and functional proteomics.