Modeling and Simulation (M&S) in drug development has also grown in the last two decades, but mostly has been limited to analysis of single studies or to analysis of pooled data from several studies. Such application traditionally has been used either to support a new drug application or to make Go/No Go decisions about a given development program. However, rarely M&S has been integrated as a tool in portfolio management based on a quantitative evaluation of all the data in hand (e.g., translational medicine data). In other words, many organizations utilize M&S still as a tool aiding study data analysis or at best a tool to guide a given development program, but not use M&S in portfolio management systematically (the large dashed box shown in the Fig. 1). Therefore, M&S scientists are mostly labeled purely as technical experts rather than strategic leaders who could provide an evidence based portfolio management. This presentation provides short examples of traditional application of M&S at study and program levels, but also presents examples of application of M&S in portfolio management based on Translational Medicine information.

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## DNA-methylation and autoantibodies based cancer diagnosis from body fluids

Christa Noehammer, Matthias Wielscher, Johana Fuchs-Luna, Istvan Gyurjan, Manuela Hofner, Ulrike Kegler, Linda Stoeger, Christian Singer, Friedrich Längle, Johann Hofbauer, Andrea Gsur, Rolf Ziesche, Klemens Vierlinger, Andreas Weinhaeusel

*AIT Austrian Institute of Technology, Vienna, Austria*

### Abstract

Special focus and aim of our research activities at AIT, the Austrian Institute of Technology, is to define reliable biomarkers suitable for early and non-invasive disease diagnosis from body fluids such as serum/plasma and saliva. Along a selection of research projects, which are described in more detail underneath, we will present and introduce the broad portfolio of high throughput technologies we successfully apply for diagnostic biomarker discovery and validation. As a first show case of successful non-invasive disease biomarker discovery we will present a study where we investigated and compared the genome wide methylation levels of lung cancer patients, patients suffering from lung fibrosis, patients with COPD (chronic obstructive pulmonary disease), and DNA samples derived from healthy lungs. Along this study we could identify specific methylation patterns for each of these lung diseases. After quantitative PCR validation of 240 disease specific methylation markers in the discovery sample set, the 90 top markers were picked and applied for serum testing (n=204). When we applied gradient boosting classification for differential diagnosis of tested lung diseases and healthy controls an AUC value of 0.95 was reached here to separate cancer from all other non-cancer samples whereas in differential diagnosis of healthy-, COPD and fibrosis patients AUC values of 0.71 and 0.49 were obtained for fibrosis, respectively COPD. Thus in case of COPD the presented method may be used to monitor cancer risk within COPD patients. Our second show case comprises a study where we screened cancer patients' sera for tumor-specific antibody profiles using an in-house developed 16k protein-microarray. This methodology, which will be described in detail, enabled us to define different tumor-associated antigen (TAA) classifier panels for the big 4 cancer entities (breast, colon, prostate and lung cancer) which all showed very promising classification successes in distinction of patients versus controls. We will further present preliminary data obtained when comparing serum and saliva auto-antibody profiles of breast-cancer patients and healthy controls.

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## Mass spectrometry-based quantification of malignant biliary stenosis biomarkers in human bile

Annarita Farina, Annie Adrait, Jean-Marc Dumonceau, Myriam Delhaye, Jean-Louis Frossard, Yohann Couté

*University of Geneva, Geneva, Switzerland*

### Abstract

The differential diagnosis of biliary stenosis is a critical problem for gastroenterologists. An early identification of malignant lesions would enable the rapid resort to surgical resection which currently represents the only potentially curative option. Unfortunately, the diagnostic value of all available methods (e.g. imaging technics, standard serum biomarkers) is limited by relatively poor accuracy and negative predictive value. Recently, our group and others highlighted new potential cancer biomarkers in bile by using comparative proteomic analysis. Nevertheless, to date, only a few candidates have been verified for their diagnostic performances in discriminating between malignant and non-malignant stenoses. In addition, no data have yet been collected on the simultaneous measurement of these proteins with the intent of evaluating the diagnostic interest of a panel of biomarkers. To overcome the limitation of classical verification tools and give a new impetus to the translation of bile biomarkers into clinical diagnostics, mass spectrometry-based quantification could represent a rapid and cost-effective opportunity thanks to its capacity for multiplexed, high-throughput analysis, combined with its

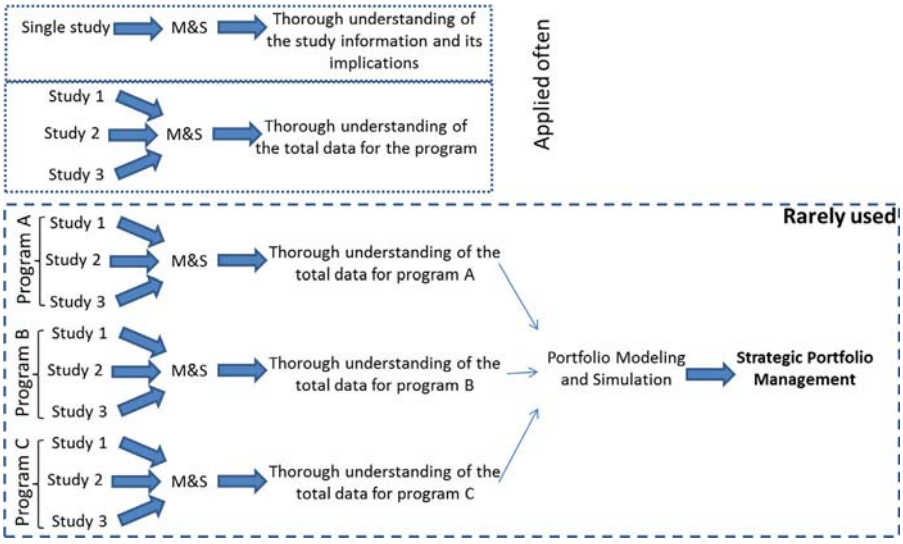


**Fig. 1**