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The quest of new cancer models and their properties in the NGS era

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It is today indisputable that great progresses have been made in our molecular understanding of cancer cells but an effective implementation of such knowledge into dramatic cancer-cures is still belated and yet desperately needed. This review gives a snapshot at where we stand today in this search for cancer understanding and definitive treatments, how far we have progressed and what are the major obstacles we will have to overcome both technologically and for disease modeling. In the first part, promising 3rd/4th Generation Sequencing Technologies will be summarized (particularly Ion Torrent and Oxford Nanopore technologies). Cancer modeling will be then reviewed from its origin in XIX Century Germany to today's NGS applications for cancer understanding and therapeutic interventions. Developments after Molecular Biology revolution (1953) are discussed as successions of three phases. The first, PH1, labeled "*Clonal Outgrowth*" (from 1960s to mid 1980s) was characterized by discoveries in cytogenetics (Nowell, Rowley) and viral oncology (Dulbecco, Bishop, Varmus), which demonstrated clonality. Treatments were consequently dominated by a "*cytotoxic eradication*" strategy with chemotherapeutic agents. In PH2, (from the mid 1980s to our days) the description of cancer as "Gene Networks" led to targeted-gene-therapies (TGTs). TGTs are the focus of Section 3: In view of their apparent failing (Ephemeral Therapies), alternative strategies will be discussed in review part II (particularly cancer immunotherapy (CIT). Additional Pitfalls impinge on the concepts of tumor heterogeneity (inter/intra; ITH). The described pitfalls set the basis for a new phase, PH3, which is called "NGS Era" and will be also discussed with ten emerging cancer models in the Review 2nd part..

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Searching of potential lung cancer biomarkers in bronchoalveolar lavage fluid using metabolomic approaches

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Lung cancer (LC) is one of the 10 most common causes of death in the World and the search for biomarkers in biological fluids, for early diagnosis of this disease is a very challenging task. Metabolomics of bronchoalveolar lavage fluid (BALF) provides information on cellular and biochemical epithelial surface of the lower respiratory tract yielding about 1 ml of pulmonary secretions. Metabolomic studies have not been previously performed with BALF samples from lung cancer patients for diagnosis purposes. In this study, two complementary metabolomic techniques based on direct infusion high resolution mass spectrometry (DI-ESI-QTOF-MS) and gas chromatography mass spectrometry (GC-MS) have been applied for the first time to establish statistically significant differences between LC and non-cancer controls (C), using partial least square discriminant analysis (PLS-DA) to identify potential biomarkers of lung cancer. A total of 43 altered metabolites were found in BALF from LC including urea, acetamide, palmitic acid, stearic acid, adenine and phosphocholine, which are overexpressed, while other 36 metabolites are underexpressed. Finally, biomarkers specificity and sensitivity was established according to the area under the curve of the receiver operator characteristic (ROC curves), which could be used to distinguish patients with lung cancer from control subjects. The pathway analysis indicated that glycerophospholipid metabolism was at the top altered pathway in this disease.

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