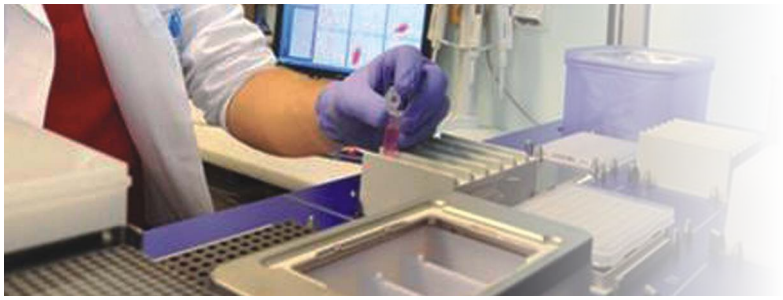
Next Generation Sequencing platform for targeted Personalized Therapy of Leukemia



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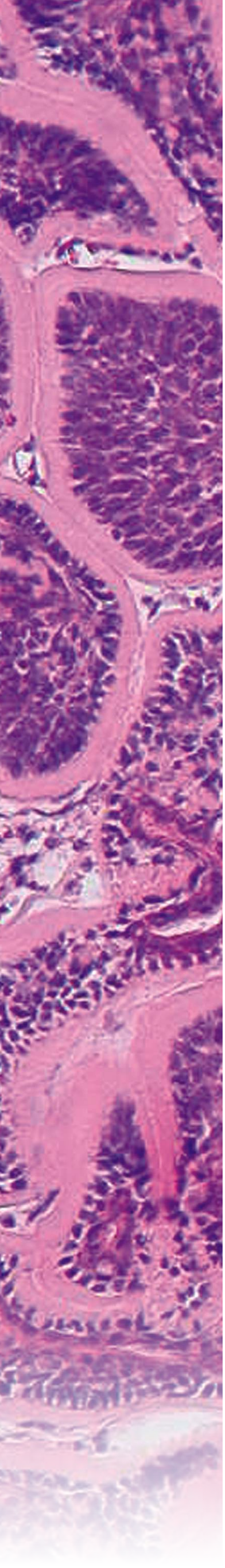
Numbers & facts:

Name of the project:
Next Generation Sequencing platform for targeted Personalized Therapy of Leukemia
Acronym: NGS-PTL
Program:
FP7-HEALTH-2012-INNOVATION-1, call: "Development of technologies with a view to patient group stratification for personalised medicine applications"
Organisation: Masaryk University
Participant of the project: prof. RNDr. Šárka Pospíšilová, Ph.D.
Beginning / end of the project: 2012-11-01 / 2015-10-31
Duration of the project: 36 months
Total costs: 7.634.819 EUR
EC contribution: 5.870.815 EUR
MU budget: 518.240 EUR (EU contribution: 396.720 EUR)
Type of contract: FP7 Grant Agreement
FP7 Reference: 306242
Consortium:
Alma Mater Studiorum Universita di Bologna (coordinator), Masaryk University, Universita Degli Studi di Torino, Personal Genomics SRL, Sinaptica IT SRL, Universitaet Ulm, KU Leuven, Fasteris SA, Fundacion de Investigacion del Cancer, MLL Munich Leukemia Laboratory

About the project:

Key words: next-generation sequencing, leukemia, personalized therapy

A considerable heterogeneity in development and progression can be observed in haematological diseases in different patients. High-throughput next generation sequencing (NGS) is new revolutionizing tool in genomics and transcriptomics providing very high resolution for a unified analysis of genetic variability within cohorts of leukemia patients. Main objective of the NGS-PTL project is developing European Haematological/NGS platform for improving outcomes for therapeutic interventions on acute and chronic leukaemias and developing strategies to personalize treatments to different stratified groups of leukemia patients, through deeper understanding of the influence of genetic alterations on leukaemias pathogenesis and treatment response. NGS-PTL aims at identification of novel prognostic biomarkers for leukemia, as well as molecular biomarkers and genome-wide profiles for the assessment of minimal residual disease. The originality of this project is to perform systematic deep whole exome/transcriptome studies on clinically characterized leukemia patients, by exploiting NGS technologies able to quickly produce data with a good cost-effectiveness and an unprecedented resolution.



NGS Sequencing Technology for Personalized therapy of Leukemia

Team of prof. RNDr. Šárka Pospíšilová, Ph.D. has prestigious and interesting opportunity to participate as a partner in a collaborative project „Next Generation Sequencing platform for targeted Personalized Therapy of Leukemia (NGS-PTL)" funded from 7th Framework Program INNOVATION. This Consortium conjugates complementary efforts from clinical medicine, industry research, development of NGS (next generation sequencing) technologies, molecular biology, genomics and transcriptomics, as well as biostatistics and bioinformatics. These expertise shared together will contribute to the identification and tweak of innovative tools aimed at finally including personalized medicine into routine clinical practise and to provide an incisive guidance to therapeutic interventions in leukemia patients. Participating in the consortium opens new possibilities to our researchers, deepening of our collaborations, broadening our expertise and coordinated exchange of data with other leukemia groups within Europe.

Goal of the project:

1. To develop a European Hematological/NGS network of physicians and scientists.
2. To discover novel insights into the mechanisms involved in leukemogenesis and to develop genetic models that accurately define novel leukemia subtypes based on the genomic profile of individual patients.
3. To develop biostatistic and bioinformatic tools for coupling scientific research data with clinical/molecular databases.
4. To develop "leukemia diagnostic panels" to drive personalized treatments and tailor therapies to different stratified groups of leukemia patients.

NGS-PTL consortium is coordinated by University of Bologna, represented by prof. Giovanni Martinelli. It consists of 10 partners from the Czech Republic, Italy, Germany, Belgium, Switzerland and Spain. The main objective of the consortium is to develop a European Haematological/NGS network of physicians and scientist. Using complementary and multidisciplinary approach they aim to resolve so far unexplored mechanisms involved in leukemogenesis and develop genetic models that accurately define novel leukemia subtypes based on the genomic profile of individual patients. To achieve this it is necessary to introduce new biostatistics and bioinformatics tools for coupling research data with clinical databases. As a final result the "leukemia diagnostic panel" is expected to be established to drive personalized treatments and therapies tailored for stratified groups of leukemia patients.

Haematological diseases account for approximately 9.5% of the new diagnosed cancers every year in european population. Most of the broadly adopted therapies are aggressive and result in increased short-term side effects that could be dangerous especially for elderly patients. Unfortunately, despite the huge advances in the clinical treatment of some subtypes of leukemia, several ones continue to have a poor prognosis and, in a proportion of long-term surviving patients, treatment results are unsatisfactory. Moreover, the exact leukemia etiology is still poorly understood and consequently also related prevention, diagnostic, prognostic and follow up methods remain mainly unidentified.

Haematological diseases as well as solid cancers have been proved to be fundamentally a condition of aberrant genetic programming, where changes in the genomic sequence of the specific cells alter their structure and function. Aberrant gene fusions produced by non-random chromosomal translocations or inappropriate expression of oncogenes are currently thought to be the main causes of most leukaemias. The present project focus on identifying low frequency alterations by exploiting high resolution massive parallel DNA/RNA sequencing techniques and at subsequent deciphering their biological significance by means of functional studies based on both *in vitro* and *in vivo* experimental models.

Amazing advances of the NGS technologies promise to play a substantial role in both preclinical research and diagnostics, leading to a quick and sustainable depiction of comprehensive catalogue of diagnostic and prognostic markers able to guide the targeting of therapeutic interventions.

Overall, the NGS approaches planned in our project will help physicians in (a) prediction of disease risk based on inherited or early somatic changes before neoplastic transformation for timely prevention; (b) early disease diagnostic; (c) disease classification, risk stratification, and prognostication; (d) selection of optimal treatment, especially molecular targeted therapy; and (e) prediction of treatment response.

We believe that tailored therapeutic treatments will undoubtedly favour a reduction of the economic burden for the healthcare system. Such treatments can be specifically directed only to the patients for whom they are safe and useful, thus avoiding potential harmful side-effects.

Prof. Pospíšilová leads Molecular Medicine program in CEITEC that has an excellent reputation in the field of haemato-oncological research. Her team has main focus on modern high-throughput genome analysis for characterization of cell behaviour on a molecular level, with emphasis on malignant transformation and mechanisms leading to disturbances of immune response. Group of prof. Pospíšilová intensively collaborates with Genomics Core Facility (head Dr. Boris Tichý) and Faculty Hospital of Brno (Internal Hemato-oncological Clinic, head Prof. Jiří Mayer). NGS-PTL project enables local scientists and physicians to broaden their expertise and exchange research data within European NGS platform. Such ambitious collaborative project promises that should at the end lead to depicting an exhaustive picture of the leukemia genome complexity.

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7th Framework Programmme of EU

7th Framework programme for research and technological development is the basic tool for financing research in Europe during the years 2007 – 2013. Budget for this program period is 50,5 milliard EUR (plus budget of Euratom is 2,7 million EUR).

7th FP has two main strategic aims:

- Inforcing the scientific and technological foundation of European industry
- Strengthening international competitiveness and supporting research that is in the line with strategic line of EU

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