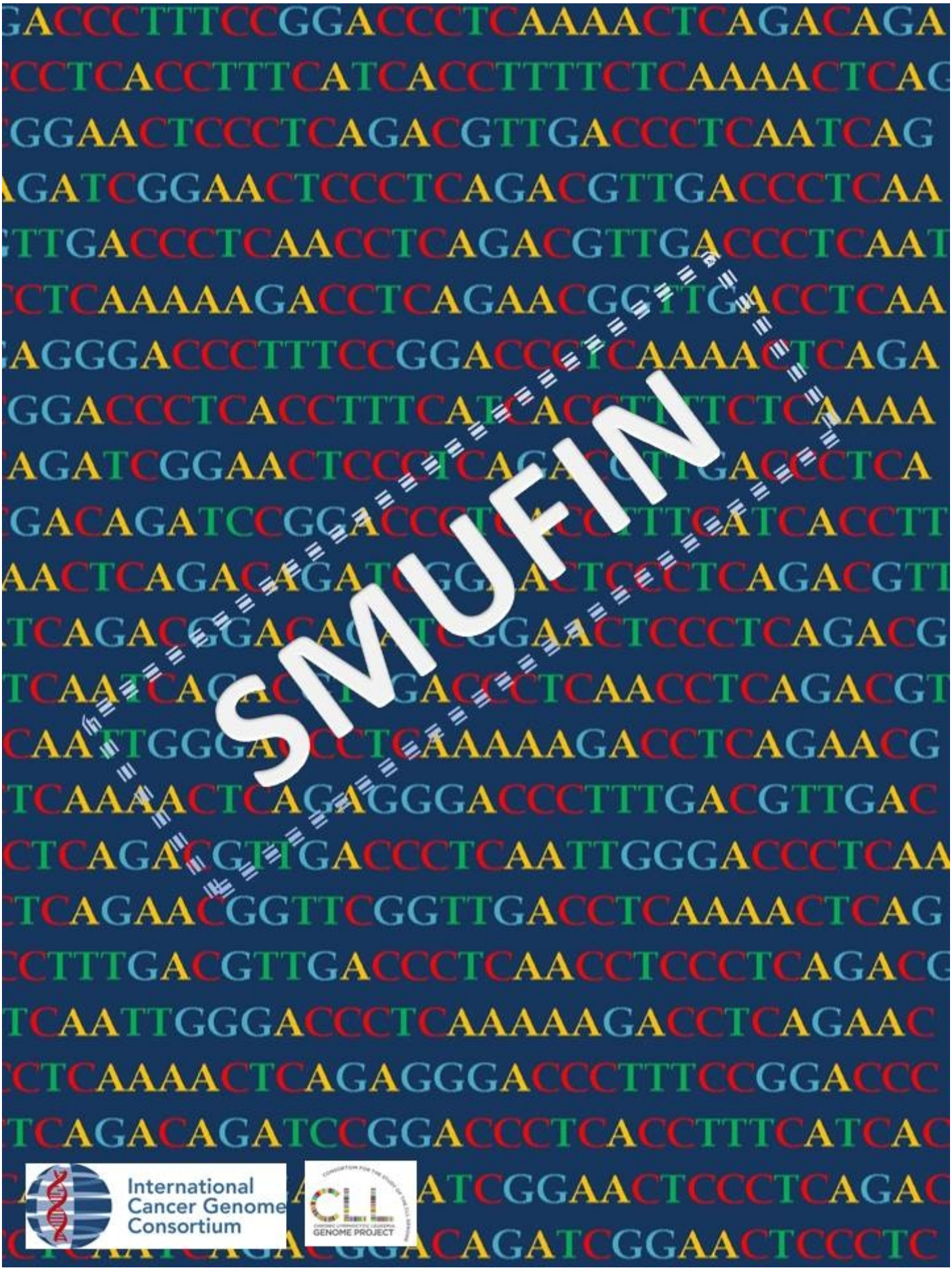
SMUFIN collaborated in genomic analysis of leukaemia

The BSC software has been used to analyze structural variants of complete genomes of patients with CLL in the study promoted by the International Cancer Genome Consortium


SMUFIN
International
Cancer Genome
Consortium
CLL
GENOME PROJECT

The study has identified recurring mutations in non-coding regions of the genome, which provides new clues about cancer development

SMUFIN, the software developed at Barcelona Supercomputing Center (BSC), has been used to locate and analyze the structural variants in the genomes of patients with chronic lymphocytic leukemia (CLL). One hundred and fifty pairs of whole genome chains have been analyzed with SMUFIN. The study has been done within the Spanish Consortium for the Study of Chronic Lymphocytic Leukemia Genome and has been led by Dr. Carlos López-Otín, from the Universidad de Oviedo, and Dr. Elías Campo, from Hospital Clínic de Barcelona and Universitat de Barcelona.

The study, published today in the journal Nature, marks a milestone in the understanding of CLL, the most common leukemia in adults, as the genomes of normal and tumor cells for more than 500 patients have been sequenced providing novel mechanisms involved in the development of this tumor. This study shows that each tumor accumulates more than three thousand mutations in its genome, but only a handful of them are relevant for tumor growth. “We have been able to define 60 different genes whose mutations cause tumor initiation and development” comments Dr. López-Otín. The study also reveals the impact of several mutations in the clinical evolution of the patients. “This work provides a comprehensive catalogue of the most important genetic alterations involved in the development of this leukemia”, comments Dr. Elías Campo.

However, the most relevant finding of this study has been the identification of mutations in the dark side of the genome, regions which do not code for proteins, whose functional relevance is still hardly known and represent 98% of our genome. One in every five tumors originates due to mutations in the so called dark regions and knowing this information is essential. Among these alterations stand out the structural variants in the genome, underexplored so far and that have been able to be characterized by comparing whole genomes chains. "Our software has again demonstrated its suitability to detect major structural changes, out of reach of most programs," said Dr. David Torrents, leader of SMUFIN project and ICREA researcher at BSC.

Cancer originates due to the progressive accumulation of mutations in the genome of normal cells. This is why seven years ago the International Cancer Genome Consortium (ICGC) was established. The main aim of this consortium was to sequence the genome of tumor cells from at least 500 patients, and do it for each of the 50 most frequent types of cancer in the world. The Spanish-led consortium in charge of the chronic lymphocytic leukemia study has been the first team to accomplish this ambitious objective. More than 60 researchers from different centers have collaborated to mine the three billion bases of each tumor genome in search of alterations responsible for the development of this disease.

Chronic lymphocytic leukemia is the most frequent leukemia in Western countries, with more than 12,000 new cases diagnosed in Europe every year. Knowing the genetic alterations present in a tumor is a fundamental step to understand cancer development and improve current treatments.

The Spanish Consortium for the Study of Chronic Lymphocytic Leukemia Genome belongs to the International Cancer Genome Consortium, led by Tom Hudson from the Ontario Cancer Institute in Toronto. The results generated by this Consortium are providing the grounds for the upcoming use of Precision Medicine initiatives worldwide. Thus, the increasing use of tumor genomic analysis will allow a better classification of patients, as well as better treatment decisions based on the type of genetic alterations present in the tumor. In fact, novel generations of drugs for chronic lymphocytic leukemia are approved for patients with specific genomic alterations, and this situation will become more common as the mutations which determine the response to specific drugs are identified. The study published today confirms the utility of genome sequencing to uncover the genetic causes of cancer and to identify novel mechanisms implicated in its development, as well as to define new therapeutic approaches for its treatment.

More than 15 institutions collaborated on the Chronic Lymphocytic Leukemia Genome Project, including:

Hospital Clínic de Barcelona, Instituto de Oncología Universidad de Oviedo, Institut d'Investigacions Biomèdiques August Pi i Sunyer, Universitat de Barcelona, Barcelona Supercomputing Center, Universidad de Deusto, Centro Nacional de Análisis Genómico, Hospital Universitario de Salamanca, Hospital Universitario Central de Asturias, Hospital Clínico de Valencia, Institut Català d'Oncologia, Centro de Investigación del Cáncer de Salamanca, Columbia University, Radboud University, Center for Research and Technology of Thesaloniki, Centre de Regulació Genòmica de Barcelona and Centro Nacional de Investigaciones Oncológicas. The research was funded by the Spanish Ministerio de Economía y Competitividad through Instituto de Salud Carlos III.

Puente XS, Bea S, Valdes-Mas R et al. Non-coding recurrent mutations in chronic lymphocytic leukaemia. Nature, July, 2015.

More info about SMUFIN: http://cg.bsc.es/smufin/

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