Genome of one of the most aggressive lymphomas sequenced

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Mantle cell lymphoma is a very aggressive and difficult to treat cancer originated in blood cells and lymph nodes. To identify the molecular alterations responsible for this tumor, and facilitate the development of new treatments, a team of scientists led by Dr. Xose S. Puente and Dr. Carlos López-Otín, at University of Oviedo, and Dr. Sílvia Beà and Dr. Elias Campo, at IDIBAPS, Hospital Clínic, University of Barcelona, have sequenced the genomes of over 30 of lymphomas. The result of this work, published today in *Proceedings of the National Academy of Sciences* (*PNAS*), presents the first comprehensive genomic analysis of this disease.

"The study provides insight into causes and evolution of this complex neoplasm and has identified targets for new treatments", says Dr. Silvia Beà, first author of the study.

The authors analyzed the genome of tumor cells at the onset of the disease and within several years after treatment, when the relapses occur. Thus, it has been possible to evaluate the genomic modifications associated with disease progression. These analyses have discovered the implication of several genes in the progression of these lymphomas and some mechanisms generating resistance to chemotherapy. They also defined a group of patients with very rapid progression of the disease with mutations in *NOTCH1* and *NOTCH2* genes. These mutations could become therapeutic targets because there are already drugs blocking the activity of these genes which may be useful in complicated cases of mantle cell lymphoma. Researchers also identified a group of patients

with a small number of mutations in the tumor whose disease progression was very slow. Thus, knowledge around the genome of these lymphomas might guide the selection of appropriate treatments for each patient.

This work was carried out with funding from the Association for International Cancer Research (United Kingdom), the Lymphoma Research Foundation (USA) and the Instituto de Salud Carlos III (Spain), and illustrates how new genome sequencing technologies are revolutionizing the study of different types of cancer. During the last three years the Spanish Consortium for the Study of the Genome of the Chronic Lymphatic Leukemia, where the researchers of the present study already collaborate, has sequenced the genome of hundreds of patients with the more common leukemia in our society, identifying new mechanisms of tumor progression and new therapeutic targets. These studies should allow the application of genomic studies in clinical practice to improve the diagnosis and treatment of cancer patients.

More information: Sílvia Beà, Rafael Valdés-Mas, Alba Navarro, Itziar Salaverria, David Martín-Garcia, Pedro Jares, Eva Giné, Magda Pinyol, Cristina Royo, Ferran Nadeu, Laura Conde, Manel Juan, Guillem Clot, Pedro Vizán, Luciano Di Croce, Diana A. Puente, Mónica López-Guerra, Alexandra Moros, Gael Roue, Marta Aymerich, Neus Villamor, Lluís Colomo, Antonio Martínez, Alexandra Valera, José I. Martín-Subero, Virginia Amador, Luis Hernández, Maria Rozman, Anna Enjuanes, Pilar Forcada, Ana Muntañola, Elena M. Hartmann, María J. Calasanz, Andreas Rosenwald, German Ott, Jesús M. Hernández-Rivas, Wolfram Klapper, Reiner Siebert, Adrian Wiestner, Wyndham H. Wilson, Dolors Colomer, Armando López-Guillermo, Carlos López-Otín, Xose S. Puenteb, and Elías Campoa. Landscape of somatic mutations and clonal evolution in mantle cell lymphoma. DOI: 10.1073/pnas.1314608110. *PNAS* October 21, 2013

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