

PRESS RELEASE

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CeMM: Unknown Leukemia Protein Complex Identified

Scientists at the Research Center for Molecular Medicine of the Austrian Academy of Sciences (CeMM) for the first time mapped the precise molecular network of the oncogene Bcr-Abl. Bcr-Abl is a paradigmatic drug target in chronic myeloid leukemia.

Vienna, April 13, 2009

Scientists at CeMM discovered a protein complex associated with the product of the Bcr-Abl oncogene. The study, directed by the center's director Giulio Superti-Furga, appears as an advanced online publication in the journal *Proceedings of the National Academy of Sciences of the United States of America (PNAS)*. PhD student Marc Brehme, who together with postdoctoral fellow Oliver Hantschel is first author of the study, explains the findings: "For the first time, the precise molecular setup of the Bcr-Abl drug target has been systematically mapped in leukemic cells in an entirely unbiased way. The study revealed a large molecular machine composed of seven proteins that assemble around Bcr-Abl. Given the vast amount of available data on Bcr-Abl signal transduction in leukemia we were surprised to find that this defined set of seven partners very intimately associates with this cancer product in leukemic cells. Furthermore, we found a yet undescribed partner of Bcr-Abl, Sts-1, very prominently associated with Bcr-Abl. The protein Sts-1 is of significant future research interest as it could act as a potential negative regulator of the cancer-inducing protein Bcr-Abl. Finally, using state-of-the-art technology we were able to show that this machine is almost entirely destroyed by the action of specific leukemia drugs currently used as front-line therapeutic agents in the clinic. Yet part of the machine survives drug treatment in a modified form".

The scientific director of CeMM, Giulio Superti-Furga, adds: "This crucial observation leads us to an entirely novel way of looking at drug targets – which should be considered as protein complexes rather than just single proteins."

Bcr-Abl acquired paradigmatic status in drug discovery research as target of the successful drug imatinib, also known as Gleevec® (Novartis). Bcr-Abl is present in the majority of individuals suffering from chronic myeloid leukemia (CML) and imatinib can effectively treat the majority of patients suffering from this disease. However, as patients can develop resistances to the drug, scientists are still striving to further understand the molecular basis of the disease in order to develop therapeutic alternatives that can overcome resistance problems. The results presented in this study likely represent a major step forward in this direction.

"This study represents a rich resource for future efforts aimed to identify alternative, maybe complementary, drug targets in order to help CML patients who are resistant to current therapies", postulates Giulio Superti-Furga.

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The following downloads and photos are available at the CeMM website

<http://www.cemm.oeaw.ac.at/?cont=downloads>

Photos: CeMM Scientific Director Giulio Superti-Furga; Giulio Superti-Furga and First author Marc Brehme; CV Giulio Superti-Furga; CeMM Research Report 2007; CeMM Fact-Sheet; Publication; Cytoscape-File: The Bcr-Abl Protein-Protein Interaction Network;

Publication

Charting the Molecular Network of the Drug Target Bcr-Abl. Marc Brehme, Oliver Hantschel, Jacques Colinge, Ines Kaupe, Melanie Planyavsky, Thomas Köcher, Karl Mechtler, Keiryn L. Bennett and Giulio Superti-Furga. Proc Natl Acad Sci U S A, published online 13 April 2009, 11.00 pm (CET)

About CeMM

CeMM, the Research Center for Molecular Medicine of the Austrian Academy of Sciences, is an international, independent and interdisciplinary research institute in molecular medicine. "From the clinic to the clinic": Driven by medical needs, CeMM integrates basic research and clinical expertise to pursue innovative diagnostic and therapeutic approaches focused on cancer, inflammation and immune disorders. CeMM has six Principal Investigators recruited internationally and around 70 scientists. In 2010 CeMM will move into a new tailor-made building at the center of the Vienna General Hospital and in close proximity to research institutes of the Vienna Medical University providing space for 100 scientists. www.cemm.oeaw.ac.at

About the Austrian Academy of Sciences

The Austrian Academy of Sciences is the leading organisation promoting non-university open source basic research in Austria. The Academy gives new impetus by taking up new, forward-looking research areas. Scientific quality, innovation potential and sustainability are the main criteria for the Academy's research profile. Currently the Academy is promoting about 66 research institutions, including three limited liability companies, and counts about 1200 employees in research and administration.