



CECAD, University of Cologne

Press release

New approach to targeted cancer therapy

Despite many advances in medicine, cancer remains the most common cause of death in Germany and the Western World. The further development of diagnostic tests and treatment is not only essential for individual patients, but also represents an enormous challenge to our public health care system. Scientists in Cologne led by Prof. Christian Reinhardt have identified a new approach to targeted cancer therapy.

Cologne, July 2, 2015 Through the molecular characterization of tumor cells, Prof. Christian Reinhardt and his team of scientists at the University of Cologne and CECAD have developed a new approach to treating cancer.

“These new findings offer a novel molecular approach to treating genetically-defined cancers more effectively in the future,” says Prof. Reinhardt, lead scientist of this new study, of the recent research success. An international team of scientists from Germany, Denmark and England was involved in the study, which has been published today in the high impact journal *Cell*.

In the Department of Internal Medicine I at the University of Cologne, Prof. Reinhardt leads a research group that is substantially sponsored by the German Research Foundation (DFG), the German Cancer Aid, and the Volkswagen Foundation.

With the aid of a new screening procedure, the research team has tested the efficacy of various compounds and, in particular, of novel compound combinations. Analytical results showed that tumor cells and cancers with a mutation in the *KRAS* gene depend on two distinct enzymes (Chk1 and MK2). The *KRAS* gene is one of the most commonly mutated genes appearing in human cancer cells. Mutated *KRAS* is found in almost all pancreatic cancers, and about one-third of lung and colorectal cancers. Detailed analyses showed that *KRAS* mutations lead to massively increased cell growth. But the very rapid proliferation of cancer cells causes problems: DNA duplication that has to take place prior to every cell division is much more difficult for cancer cells under conditions of accelerated growth. The latest data from the Cologne scientists show that *KRAS*-mutated cancer cells rely on MK2 and Chk1 enzyme function for error-free duplication of their DNA. This dependence on MK2 and Chk1

distinguishes *KRAS*-mutant cancer cells from healthy tissue, which is capable of duplicating DNA without these particular enzymatic functions. And the new therapeutic approach is based on this very difference between cancer cells and normal tissue. The research team has shown that tumor cells and cancers with *KRAS* mutations respond very well to combination therapy with Chk1 and MK2 inhibitors. Normal tissue, on the other hand, tolerates the combination therapy well and has very little in the way of adverse reactions.

Taking a closer look at these enzymes, Chk1 and MK2 are protein kinases. In the last 10 years, this particular enzyme group has increasingly come to the attention of the big pharmaceutical companies. Enzymes can potentially be inhibited and therefore provide options for developing new therapeutic agents. The combined pharmacological inhibition of Chk1 and MK2 is a therapeutic strategy that could be used specifically for treating *KRAS*-mutated cancers. “Chk1/MK2 inhibition works specifically in *KRAS*-mutant cancer cells. Normal tissue isn’t really affected, because healthy cells don’t contain *KRAS* genes that have undergone mutation,” explains Dr. Felix Dietlein, lead author of the publication, when describing the therapeutic concept.

Prof. Michael Hallek, Head of the Department of Internal Medicine I at the University of Cologne, finds the new therapeutic approach very promising. “MK2 is a protein kinase that has been investigated in depth for some time, as its function seems to have a role in the development of rheumatoid disease. The protein kinase Chk1 has also been closely scrutinized in recent years, and the first clinical trials of various Chk1 inhibitors are now underway. These fascinating findings may provide treating physicians with an effective new tool for treating *KRAS*-mutant cancers in the near future,” he confirms.

Even though they have been the subject of research and development as medicinal products for some time, none of the MK2 inhibitors has yet obtained regulatory approval. Work on this project was generously sponsored by the German Research Foundation (DFG), German Cancer Aid, and the Volkswagen Foundation.

For CECAD and the University Hospital Cologne, the development of this new therapeutic approach represents a significant and promising opportunity: additional treatment options for the fight against cancer in the near future – an important aspect of aging research at the Cluster of Excellence.

Contacts:

Prof. Christian Reinhardt
CECAD, University of Cologne
Department of Internal Medicine I
Cologne University Hospital
Phone +49 221 478-96701
christian.reinhardt@uk-koeln.de

Astrid Bergmeister MBA
Head of CECAD PR & Marketing
University of Cologne
Phone + 49 (0) 221-478 84043
astrid.bergmeister@uk-koeln.de