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Press Release

The Achilles' heel of cancer cells

University and HZI researchers discover many tumor cells cannot survive without the presence of an enzyme known as 'Ark5'

Like all body cells, cancer cells are dependent upon a continual supply of nutrients to allow them to generate the energy needed to power their various metabolic processes. At the same time, however, they use up a large chunk of these nutrients for assembly of new cellular building blocks, cellular division, and proliferation. Because a cell's nutrient supply is finite, each cell contains, if you will, its own 'security guard' in charge of always making sure that plenty of resources are at hand to support the different activities the cell must perform. If the energy supply required to power everyday cellular activities becomes depleted, the security guard responds by limiting cellular growth.

Professor Martin Eilers and Dr. Daniel J. Murphy - both of the University of Würzburg's Biocenter - along with an international team of researchers recently set out to investigate what happens when a cancer cell's security guard is deliberately taken out of commission.

The results showed that "if a cancer cell no longer receives feedback about the fact that its energy balance is out of whack, it will waste all of its resources on cellular growth and division," explains Martin Eilers, Professor and Chair of Biochemistry and Molecular Biology at the University of Würzburg. In the process, the cell over-exerts itself to the point where no more energy is left for powering its everyday metabolic cellular activities. In fact, as the research showed, without heeding its security guard's 'warning call' the cancer cell quickly dies.

It was by pure chance that the researchers ended up stumbling upon this cellular security guard. In a series of experiments they switched off different enzymes in cancer cells called kinases and watched and analyzed the cells' response. In the case of the kinase enzyme 'Ark5' they scored a slam-dunk. "This particular kinase turned out to be the ideal target for potential new drug treatments," explains Daniel J. Murphy of the University of Würzburg's Department of Physiological Chemistry II. Their experiments showed that Ark5 is a genuine 'weak link' in cancer cells. Working closely with HZI Professor Lars Zender and his team, the researchers specifically inactivated the gene coding for Ark5 kinase in liver tumor cells of mice. "This allowed us to demonstrate that when Ark5 gene expression is being suppressed in tumor cells, the tumor shrinks and the mice end up living longer," explains Zender.

To the researchers' great surprise the experiments also showed that normal cells remain largely unaffected by targeted kinase inhibition. "We don't yet fully understand every last detail behind this observation," Murphy concedes. Potentially, there could be some long-term effects here as well. But, for the time being, "what matters most with respect to new drug design is that normal cells seem to respond differently to Ark5 inhibition than do cancer cells," says Murphy. Whether or not new therapeutic approaches will come out of this, only time will tell. So far, the method has proven effective both in the dish and in animal experiments - at least in the case of intestinal and liver cancer cells. To what extent other types of cancer cells may also be driven to their deaths using this approach remains to be seen.

With the pharmaceutical industry having already taken a keen interest in these findings, a collaboration between the University, HZI, and the pharmaceutical companies is now only a matter of time. However, the researchers are already warning against getting everyone's hopes up prematurely. Many more research studies are needed before it can be ascertained that these findings could in fact translate into new approaches to cancer therapy.

Original publication:

Deregulated MYC expression induces dependence upon AMPK-related kinase 5. Lidan Liu, Jannes Ulbrich, Judith Müller, Torsten Wüstefeld, Lukas Aeberhard, Theresia R. Kress, Nathiya Muthalagu, Lukas Rycak, Ramona Rudalska, Roland Moll, Stefan Kempa, Lars Zender, Martin Eilers & Daniel J. Murphy. doi:10.1038/nature10927

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