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Scientists gain new insights into Taspase1 function

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Scientists at the University Medical Center of Johannes Gutenberg University Mainz in Germany identified a novel strategy to target the oncologically relevant protein-cleaving enzyme Taspase1. Taspase1 levels are not only elevated in cancer cells of patients with head and neck tumors and other solid malignancies but the enzyme is also critical for the development of leukemias. Central to this concept is the approach to inhibit the enzyme's activity by 'gluing together' individual Taspase1 molecules. The results of a study undertaken by Professor Dr. Roland Stauber of the ENT Department at the Mainz University Medical Center were recently published in *The FASEB Journal*.

Protein-cleaving enzymes, so-called proteases, are not only significantly involved in physiological processes in the healthy body, such as blood clotting, but also play critical roles in illnesses, such as cancer, Alzheimer's, and infectious diseases. Several protease inhibitors have already been developed and are being used against some of these 'disease-causing' enzymes with varying success in the clinics. However, one representative of this protein family in particular – the protease Taspase1 – is troubling researchers worldwide." We currently do not have any drug that can inhibit Taspase1. And we still do not understand in sufficient detail how this enzyme really works," says Stauber.

Almost ten years ago, the team found enhanced levels of Taspase1 in the cancer cells of patients with head and neck tumors. At that time, the function of the protease in tumor cells and its relevance for disease was still unknown. Recent findings support the oncological importance of

Taspase1 for solid malignancies and leukemias. Taspase1 appears to override control mechanisms in healthy cells by cleaving various other proteins, thereby significantly promoting cancer development. As a result of extensive research supported by funding provided by the Head and Neck Tumor Research Foundation [Stiftung Tumorforschung], the German Cancer Aid, the Thyssen Foundation, and Johannes Gutenberg University Mainz, the researchers have now gained new insights into the enzyme's molecular functions. "Previously, it was assumed that two Taspase1 enzymes had to come together in order to be active and cleave other cellular proteins," explains Stauber. "Our latest results not only demonstrate that one Taspase1 molecule is sufficient for this, but also that we can even block the tumor-promoting properties of the enzyme by 'gluing' two Taspase1 molecules together."

Hence, the Mainz-based researchers identified a completely novel approach to developing drugs that may be used to inhibit Taspase1. "We are now searching for chemical substances that could function as molecular Taspase1 'adhesives'," adds Stauber. As part of the so-called Chemical BioMedicine Initiative, the scientists are betting on nature's vast chemical repertoire. "Natural products from fungi and marine sponges are a highly privileged source for potential new drugs. Evolution already pre-checked the biological qualities of such chemical substances in living organisms. Thus, we have a good chance of finding the right chemical decoys," predicts Stauber. "The robotic platform at the Mainz Screening Center combined with our Taspase1 assays will play a leading role in this search for the 'needle in the haystack'."

Provided by Universitaet Mainz