Researchers develop antibody to save cancerous bones

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Bone Cancer Primary bone cancer called Osteosarcoma (OS) is a rare cancer most often affecting adolescents and children. While most bone cancers have their origin in other body tissues and spread to the bones through metastases, OS originates in the bone tissue. Common for all, is that they degrade the bones and are associated with high mortality.

At the Finsen Laboratory, Rigshospitalet and BRIC, University of Copenhagen a research group lead by Dr. Niels Behrendt and Dr. Lars Engelholm now shows that OS cells degrade the bone tissue through a completely different process than metastasised bone cancer. Through treatment with a specific antibody, the researchers blocked the process and reduced up to 80% of bone degradation in a cancer mouse model. Future treatment of OS patients with this type of antibody could reduce amputations among young patients and future studies will clarify if such a treatment strategy will also block lethal spreading of the OS cells to other organs.

Specialised cancer cells do their own dirty work

When cancer cells from eg breast or lung tumours invade the bones through metastasis, the bone tissue is degraded. Metastasized cancer cells then stimulate other cells in the bones to degrade the bone tissue, a mechanism also believed to take place in OS. However, examining OS tumours the research team behind the new results found that OS cancer cells express special enzymes and receptors, enabling them to degrade

bone tissue themselves.

'By treating mice with OS with the new antibody, we could block the micro processes OS cells use to degrade the bones and thereby effectively protect the bone tissue', explains Lars Engelholm.

Antibody treatment may reduce amputations

The research team has great hopes for the use of this new type of antibody in development of new treatment for OS patients.

- A large proportion of new targeted cancer therapies are based on antibodies. We developed this antibody for basic studies of the molecule uPARAP, but when we discovered shown that this molecule is upregulated in OS tumours, we became interested in the possible treatment effect, says Niels Behrendt.

Treatment of OS includes removal of the cancerous bone. To prevent complete amputation of arms or legs, pre-treatment with chemotherapy is used to shrink the tumour before operation. Limitation of bone degradation in this pre-treatment period is crucial and where the researchers see a clear potential for their finding. Surgeon Clement Trovik from Haukeland University hospital in Bergen, collaborator on the research project states:

'For cancer patients, especially children and young adults, amputation of an arm or a leg is a very serious consequence of illness and we have for years been searching for therapeutics to prevent cancer-induced bone degradation. These new results show promising results for such future treatments'. Treatment with the new antibody will - in addition to the traditional treatment enable us to save more bone tissue for reconstruction and thereby prevent amputations

uPARAP

Tumor cells in primary bone cancer degrade bone tissue by means of specialised enzymes and receptor proteins. A receptor is a molecule placed on the cell membrane which, in some cases, can direct material from the surroundings to be taken up by the cell and degraded, In the degradation of bone tissue, the receptor uPARAP plays a central role. It has long been known that uPARAP is active in bone growth and development in the healthy body. Cancer cells acquire their destructive ability through an abuse of the same mechanisms that are involved in the normal development of the same tissues and organs.

More information: Targeting a novel bone degradation pathway in primary bone cancer by inactivation of the collagen receptor uPARAP/Endo180, Engelholm et al. The *Journal of Pathology*, 2015, onlinelibrary.wiley.com/doi/10 … 2/path.4661/abstract

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