

Healthcare industry BW

Cutting off the supply of nutrients and oxygen to tumours

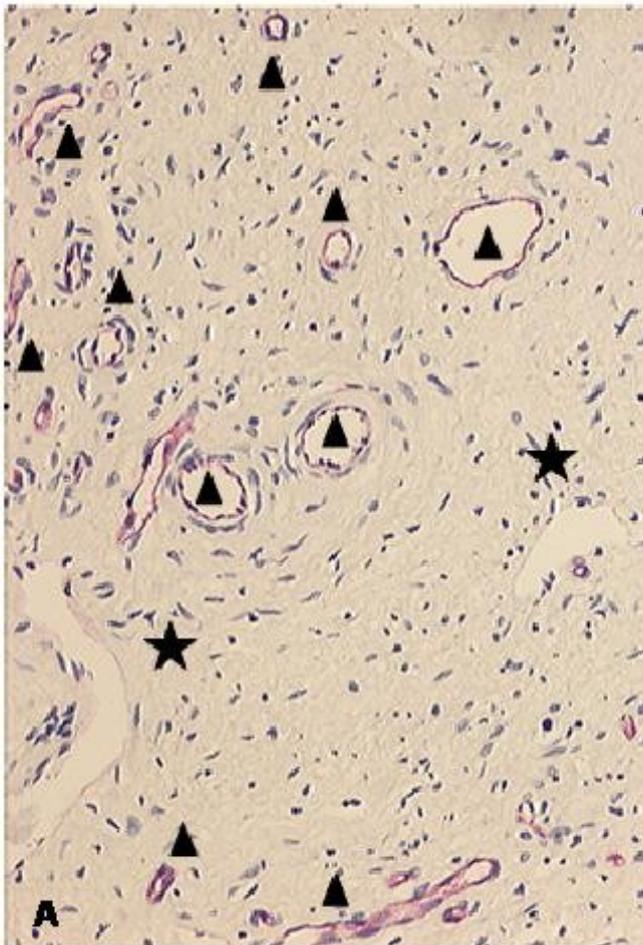
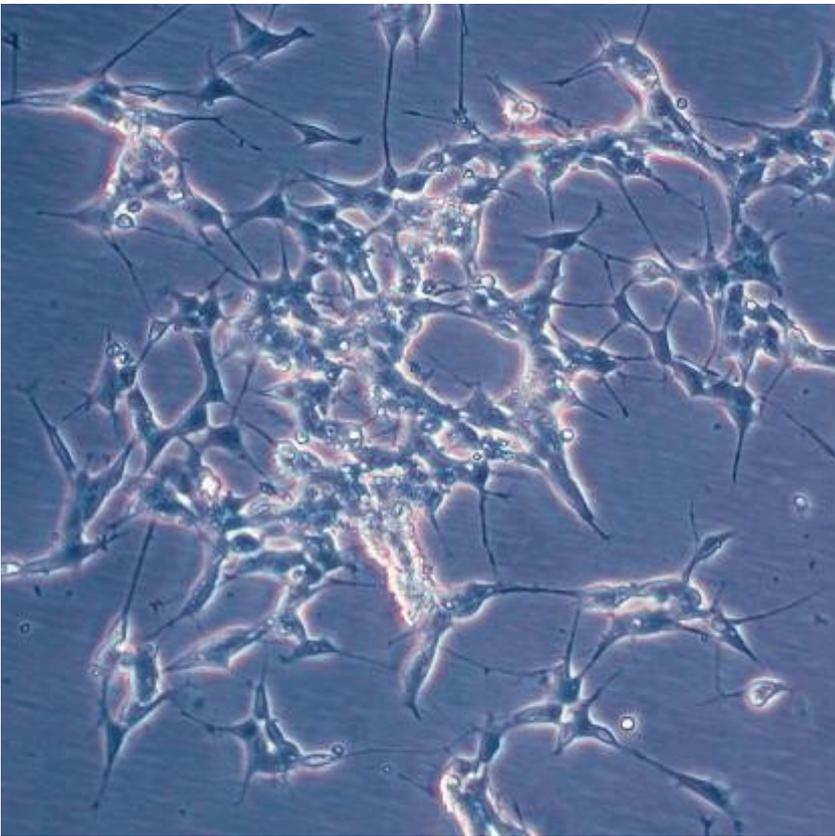
Cancer cells do not magically keep themselves alive; they rely on oxygen and nutrients just like all other cells. Is it possible to cut them off from the supply infrastructure and bring them to their knees? Dr. Jochen Rößler's research group from the Children's Hospital at the Freiburg Medical School is investigating how tumours establish contacts with blood and lymph vessels. The medical professionals are hoping to find new ways of treating tumours in children and adolescents.

The cells in the human body require oxygen and nutrients for growth and energy production; in addition, they have to excrete metabolic waste products. The substances are exchanged through a fine network of blood vessels that run through tissue. Cancer cells have a metabolism and require oxygen and nutrients in the same way as healthy cells. Diffusion processes alone are not sufficient to keep up with metabolic requirements once tumours have reached a diameter of two centimetres or more. Therefore, once they have reached this size, tumours induce blood vessels to connect with them to exchange substances. But how is this done? Can drugs block this process and thus cut off the supply of nutrients and oxygen to tumours? "Little is known about such processes in tumours in children and young adults, but we are hoping to change this by specifically concentrating on these aspects," said Dr. Jochen Rößler from the Department of Paediatric Haematology and Oncology at the Freiburg Childrens' Hospital.

Tumours manipulate their environment

Neuroblastoma is one of the cancers that Rößler's research in the Department of Angiogenesis is focusing on. This tumour is the second most common cancer in children occurring in solid tissue. In Germany, there are approximately 120 new cases every year. Neuroblastomas develop mainly in the peripheral nervous system, are often very aggressive and metastasise rapidly. Rößler and his team of researchers are investigating tissue samples from young cancer sufferers at the same time as using mice to see how the tumour cells use blood vessels. The researchers are also interested in how lymph vessels grow into the tumour. The lymph system is a kind of motorway through which the metastases spread into the lymph nodes and hence into the entire body. The researchers are specifically interested in growth factors such as the vascular endothelial growth factor (VEGF) because they mediate the recruitment of vessels.

Once a growing tumour has reached a specific size, the individual cancer cells then release VEGF molecules into the environment. The VEGF molecules interact with specific receptors on the surface of the endothelial cells of blood vessels. The endothelial cells form the sheath of arteries and capillaries. The receptors bind the VEGF molecules and translate this signal into the endothelial cells. This



Cut through tumour tissue: the dark spots are nuclei, the white areas are blood vessels (black triangle). The endothelial cells of the blood vessels are stained pink. The asterisks mark the position of lymph vessels.
© PD Dr. Jochen Rößler

causes the blood vessels to grow towards the tumour. Eventually, the vessels form a complex network in the tumour tissue. "At present, there are some drugs on the market that can specifically inhibit VEGF," said Rößler naming Avastin, an anti-VEGF monoclonal antibody, which has been used for a number of years to treat colon cancer. "But this drug has only been tested in adults; nobody knows whether and what kind of side effects it might have in children whose vascular system is still developing," said the Freiburg doctor.

Combining forces!

A milestone in child oncology is a European law that came into effect in 2007. According to this law, any company applying for market authorisation for a new drug must present a paediatric investigation of the drug. "All pharmaceutical companies now have to present data from trials conducted on children. And this means that knowledge of drug effects in children is growing." However, according to Rößler an even more important development is that a growing number of European research centres are joining forces to work together in the fight against tumours. For the last two years, Rößler himself worked as guest professor at the Institut Gustave Roussy (IGR) in the French city of Villejuif, where he was able to contribute to the planning of European-wide studies on the therapy of children suffering from cancer. "We hope to establish cooperations with many hospitals and research institutions across Europe, in order to ensure that centres in Europe do not just collect their own data without other centres having access to them," said Rößler. "We want to exchange data and discuss potential consequences."

Perhaps the possibilities to stop the growth of tumours in the future by cutting them off their supply infrastructure will increase. Rößler and his team are also investigating whether RNA interference is suitable for this task. Rößler envisages that small RNA molecules might be able to prevent cancer cells from producing VEGF by inhibiting the translation of the VEGF gene into the protein. This would interrupt the contact between tumour and blood and lymph vessels. "I started working on experimental child oncology about twelve years ago. At first, I mainly focused on finding out which genes and molecules played a role in supplying the tumour with blood," said Rößler. "It is good to see that we have been able to set up European networks and that our ideas are slowly being applied in clinical research. But it goes without saying that we have a lot of work ahead of us." In the end, Rößler and his team's main concern are the young patients who stand to benefit from the new developments.

Further information:

Dr. Jochen Rößler
Senior physician
Hospital IV: Paediatric Haematology and Oncology
Centre for Paediatrics and Youth Medicine
Freiburg Medical Centre
Mathildenstr. 1
79106 Freiburg
Tel.: +49 (0)761/270-4300
Fax: +49 (0)761/270-4518
E-mail: jochen.roessler(at)uniklinik-freiburg.de

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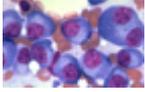
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Cancer therapy and cancer diagnostics