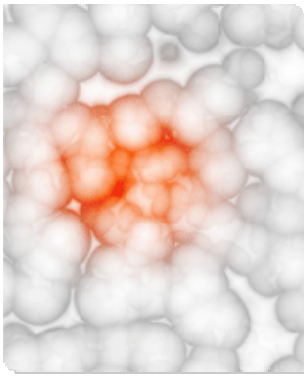
An innovative treatment for cancer by EU-supported SMEs and research institutes (Project ANGIOSTOP)

Treatment of cancer is one of the most important areas of research in the medical world. The small research-based pharmaceutical companies BioInvent and Thrombogenics have, together with their partners in the EU-funded project ANGIOSTOP, developed an innovative form of treatment that stops the growth of cancerous tumours through inhibition of angiogenesis, the process by which new blood vessels are formed in the body. In 2009, the companies have announced promising results and secured a EUR 50 million investment from global pharmaceutical giant Roche.



Background

Cancers constitute a heterogenous group of diseases, which complicates the development of drugs directed at tumour cells with the intention of killing them. A new and attractive strategy is to attack the blood supply to tumours indirectly by blocking the growth of new blood vessels. The formation of new blood vessels is a process called **angiogenesis.** These vessels supply growing tissue with nutrients and transport waste away from the tissue. Tumours over a certain size are dependent on the formation of new blood vessels in order to grow and survive.

A substance that inhibits the growth of new blood vessels could therefore reduce a variety of tumours' growth and increase the patient's chance of survival.

Several angiogenesis inhibitors have been developed lately and one **antibody**, Avastin, has already been approved for several cancer indications. Despite the success of this drug, is it clear that this inhibitor alone is not sufficient to halt tumour angiogenesis.

- Firstly, an increasing number of studies documents that such treatment leads to the induction of alternative signals that stimulate the formation of new blood vessels in the tumour and one such factor is **Placental Growth Factor** (PlGF).
- Furthermore, the currently available angiogenesis inhibitors have serious side effects thus mandating the development of additional angiogenesis inhibitors.

By gene targeting study in mice, it has been shown that loss of PlGF does not cause any vascular defect during development, reproduction or normal adult life, while it severely impairs angiogenesis during pathological conditions including ischemia, inflammation and cancer therefore indicating that the ANGIOSTOP anti-angiogenic strategy targeting PlGF could represent a safer and more effective approach.

Objectives

The primary goal of the ANGIOSTOP project was, therefore, an accelerated development of our anti-PlGF monoclonal antibody – a new and potentially efficacious and safer anti-angiogenic medicine that reduces the pathological blood vessel growth and can be used for the treatment of major progressive disorders such as cancer.

Within the ANGIOSTOP project a new therapy has been developed with the potential to treat a variety of cancers and interestingly patients resistant to present therapy. ANGIOSTOP has explored the therapeutic potential of antibodies against placental growth factor (PlGF), a growth factor secreted by tumours, which is specifically upregulated in diseases such as cancer. Anti-PlGF antibodies target the tumour's blood supply, i.e. the formation of new blood vessels or "angiogenesis", thereby starving it.

Distinct from present therapies also targeting angiogenesis, targeting PlGF has been found to prevent tumour infiltration of distinct inflammatory cells (macrophages). Such cells can promote tumour growth and convey tumour mechanisms that may lead to resistance to anti-angiogenic therapy.

Thus, anti-PlGF antibodies may be advantageous to present therapy and this additional mechanism is illustrated with anti-PlGF (depicted in blue) preventing PlGF (green) binding to its receptor VEGFR-1 (red) expressed on macrophages (orange).

Impact

The project has enabled the initiation of clinical development with the lead candidate anti-PlGF antibody as set out in the objectives. This, coupled with the advancement of our understanding of pathologic angiogenesis and development of new models and strategies, will be of more general utility for the development of new medicines aimed at increasing or reducing blood vessel formation.

A success story for the SMEs involved in the project

The SME coordinating the project BioInvent started together with Thrombogenics, another SME interested in developing antibodies for clinical use, by studying an antibody that specifically targets PlGF, previously identified by the Flanders Interuniversity Institute for Biotechnology (VIB) in Belgium.

The two SMEs joined forces and, combined with Flanders University and several clinical groups, created a detailed programme that outlined how they would develop the antibody for clinical use. After three years of research, the collaboration produced some considerable results: there was a significant effect from the antibody in tumour models in mice, the toxicology study revealed it to be safe for human use, and was able to produce enough antibody to enter into clinical studies.

The data compiled was so interesting and significant that the team was able to sell the results to Roche – the global pharmaceutical giant – for EUR 50 million, with the possibility of increasing this amount to EUR 450 million should the project reach certain development milestones.

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