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DMP1 Protein Inhibits Angiogenesis, Could Lead to New Treatments Against Cancer and Other Diseases

A team from the Metastasis Research Laboratory (GIGA-Cancer/Liège University Hospital) has just published, in the journal Blood, their work demonstrating that the DMP1 protein has previously unsuspected anti-angiogenic activities which could be used for the development of new treatments against cancer, but also against diseases in which angiogenesis (the formation of new blood vessels) plays a major role, such as psoriasis, rheumatoid arthritis or diabetic retinopathy.

This discovery has also led to the registering of a patent by the three research protagonists: Doctor Akeila Bellahcène, a Senior Research Associate at the National Fund for Scientific Research (NFSR) who is running the project, Sophie Pirotte, a TELEVIE (NFSR) researcher, and Professor Vincent Castronovo, the Laboratory's Director.

Dr Bellahcène has been interested in SIBLINGs proteins for several years. They are a family of glycoproteins initially discovered for their role in the formation of bones and teeth. It is now over fifteen years ago that the Liège laboratory was the first to show that two of these proteins, bone sialoprotein (BSP) and osteopontin (OPN), are produced by cancer cells and probably play a role in the progression of these cancers, notably through their involvement in the formation of bone metastases. These original observations, confirmed by other international teams, opened the way for numerous projects studying the role played by these two proteins in cancer. Up until recently, DMP1, known above all for its role in teeth mineralisation, had not attracted attention in terms of a role in the development and progression of cancer.

But Doctor Akeila Bellahcène's most recent research demonstrates that DMP1 also deserves very special attention. In effect the results published in the journal Blood show that DMP1 is capable of blocking angiogenesis. Yet angiogenesis is vital for the development of tumours beyond a few cubic millimetres, as well as for the formation of metastases.

The work shows that DMP1 prevents endothelial cells (the cells which form new blood vessels over the course of angiogenesis) to respond to VEGF, a molecular signal sent by cancer cells to activate the formation of new feeder blood vessels. The presence of DMP1 halts the different stages which lead to the formation of new capillaries: the endothelial cells are placed in a resting non proliferative state.

"In an *in vivo* model of angiogenesis linked to tumour development, we have shown that the tumours from cancer cells in which we had beforehand overexpressed DMP1 had a reduced growth combined with very modest vascularisation in comparison with the control tumours," points out Doctor Bellahcène.

"These results overall indicate that DMP1 could represent a new anti-angiogenesis molecule whose therapeutic implications would moreover go beyond their use in cancer pathology," states Professor Vincent Castronovo, who directs the Metastasis Research Laboratory at the ULg's GIGA-ResearchUnit. "In effect the processes of angiogenesis induced by VEGF also intervene in a significant manner in the development and progression of other pathologies such as rheumatoid arthritis, psoriasis and diabetic retinopathy."

Source: Blood, 2010; DOI: 10.1182/blood-2010-08-298810