

HSP90: New point of view on melanoma of the eye

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Ocular melanoma is rarely detected before it has grown large enough to impair vision or to metastasize. This makes it a particularly challenging disease to fight, especially since chemotherapy is not very effective.

Now, the PhD research project led by Dr. Dana Faingold may open the door for very promising new treatment options for this pathology. Her first article was featured on the cover of the February 2008 issue of *Clinical Cancer Research*.

“The first step in developing a medication is to determine the precise target of action,” explained Dana Faingold. “In this study, we have shown that to effectively fight this malignant tumour in the vascular network of the eye, we had to target Heat Shock Protein 90 (HSP90).”

HSP90 is already a therapeutic target in many other types of cancer. In fact, this protein, which is called a “chaperone” because it guides the actions of other proteins, is at the centre of many metabolic pathways. By disrupting HSP90’s functioning, it is possible to affect multiple steps in cell metabolism, for example, signalling pathways, cell cycle regulation pathways, or growth hormone receptors. This blocks many vital cellular functions, so the cancer cells become unable to reproduce and the tumour regresses.

Clinical trials are currently being conducted to determine the effectiveness of an antibiotic called 17/AAG, an HSP90 inhibitor, against malignant tumours of the skin, breast and in patients with

multiple cancers. However, no one has yet studied this inhibitor's effect on ocular melanoma. "This is a pre-clinical study, which means we are examining in-vitro cell lines. Our results clearly prove not only that HSP90 is largely overexpressed in this type of tumour but also that the 17/AAG molecule is effective at reducing the growth of these tumoral cells," said Dana Faingold.

Several clinical trial stages will have to be completed before 17/AAG can be recognized as a possible treatment for melanoma of the eye. The first stage, which should begin shortly, aims at proving the effectiveness of the molecule in an animal model. This in vivo confirmation is necessary before testing for human treatment can begin.

Source: McGill University

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