Arthritis drug could help beat melanoma skin cancer

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A breakthrough discovery by the University of East Anglia (UEA) and Children's Hospital Boston promises an effective new treatment for one of the deadliest forms of cancer.

Reporting in the March 24 edition (front cover story) of the journal *Nature*, the researchers found that leflunomide - a drug commonly used to treat rheumatoid arthritis – also inhibits the growth of malignant melanoma.

Melanoma is a cancer of the pigment cells in our skin. It is the most aggressive form of skin cancer and, unlike most other cancers, incidence of the disease is increasing. More than 10,000 patients in the UK are diagnosed with melanoma each year. If caught early, surgery can be used to safely remove the tumour but the chances of survival for patients whose tumour is already spreading are very low. Around 2000 people a year in the UK die from malignant melanoma because the cancer has returned after being removed surgically.

UEA scientists Dr Grant Wheeler and Dr Matt Tomlinson conducted a rigorous screen of thousands of compounds, looking for those that affect the development of pigment cells in tadpoles. They identified a number of compounds that affected pigment cell development and have now shown with their US collaborators at Children's Hospital Boston that leflunomide significantly restricts tumour growth in mouse models.

And when leflunomide is used in combination with PLX4720, a

promising new melanoma therapy currently undergoing clinical trials, the effect was even more powerful – leading to almost complete block of tumour growth.

The next stage is for clinical trials to be conducted into the use of leflunomide to fight melanoma. Because leflunomide is already licensed to treat arthritis, this process should be faster than usual and a new treatment for melanoma could be available within around five years.

"This is a really exciting discovery – making use of an existing drug specifically to target melanoma," said Dr Grant Wheeler, of UEA's School of Biological Sciences.

"Deaths from melanoma skin cancer are increasing and there is a desparate need for new, more effective treatments. We are very optimistic that this research will lead to novel treatments for melanoma tumours which, working alongside other therapies, will help to stop them progressing."

The novel work, which was partly funded by the Biotechnology and Biological Sciences Research Council (BBSRC), highlights the strength of carrying out large screens of compounds in developmental model systems such as the Xenopus tadpole used at UEA and the zebrafish used at Childrens Hospital Boston. The hope is that this approach will lead to the discovery of further compounds to treat different diseases in the future.

Lead author Dr Richard White of Children's Hospital Boston and Harvard Medical School, said: "Cancer is a disease not only of genetic mutations, but also one determined by the identity of the cell in which the tumor arises. By studying cancer development in zebrafish and frogs, we gain a unique insight into the very earliest changes that occur in those cells."

More information: 'Inhibitors of DHODH suppress neural crest development and melanoma growth via modulation of transcriptional elongation' by R White et al. is published in the March 24 edition of *Nature*.

Provided by University of East Anglia