Gene identified in some melanoma linked to increased resistance to treatment

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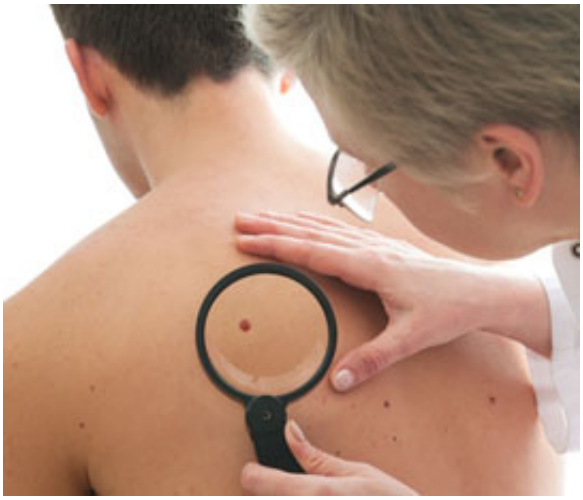

(Medical Xpress)—Scientists at Queen Mary, University of London have identified a gene present in some melanoma which appears to make the tumour cells more resistant to treatment, according to research published today in the *Journal of Experimental Medicine*.

The scientists discovered that the gene TP63 is unexpectedly expressed in some melanoma and correlates significantly with a worse prognosis. It is hoped this new understanding of what makes some melanoma cells so difficult to kill will help inform the development of new therapies.

Melanoma is a form of skin cancer which usually appears on the body as a new or changing mole. Almost 13,000 people in the UK are diagnosed with melanoma each year. While it is less common than other forms of skin cancer – around five per cent of skin cancers are melanoma – it results in around 75 per cent of skin cancer related deaths (more than 2000 deaths a year in the UK).

The number of cases of melanoma is rising faster than almost any other cancer and one of the main risk factors is ultraviolet light, which comes from the sun or sunbeds. While early-stage melanomas can often be removed by surgery, more advanced melanomas are much harder to treat.

Dr Daniele Bergamaschi, a senior lecturer in cutaneous research at Queen Mary said: "For most patients where the melanoma has spread beyond the skin, there are few effective treatments and overall survival rates for this disease have not changed much over the past 30 years.

"To develop better treatments we need to understand the basic biology underpinning why these cells are so resistant to being killed."

The researchers analysed 156 melanoma tissue samples from 129 individuals for expression of the protein p63 – the protein encoded by the gene TP63. They found that p63 was expressed in more than 50 per cent of the samples (58% of primary metastatic samples, 53% of recurrent samples and 66% of metastatic samples) and correlated significantly with death from melanoma.

Dr Bergamaschi said: "We did not expect to find the TP63 gene expressed in melanoma. It is not usually found in the melanocytes (skin pigment cells), which are the cells from which melanomas develop. However, it appears in some cases this gene is turned on as the tumour forms, and when it does it is linked to a worse prognosis."

The researchers suggest that the TP63 gene, and the subsequent production of the protein p63 in some melanoma, is inhibiting the apoptotic function of the protein p53. One of the main activities mediated by p53 is apoptosis – the process of programmed cell death and one of the main mechanisms by which cancer cells die.

Dr Bergamaschi said: "The apoptotic pathway is often not working in melanoma. However this is not explained by mutations in the TP53 gene, which encodes for the p53 protein, as evidence suggests this is mutated in less than 10 per cent of melanoma.

"This work suggests that in a significant number of cases it is actually the protein p63 which is inhibiting p53's apoptotic function, making some tumours more resistant to treatment. We therefore suggest that p63 should be considered when designing new treatments for melanoma which are focused on re-activating the apoptotic pathway in order to make the cancer cells easier to kill."

Provided by Queen Mary, University of London

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