

Melanoma: Scientists find new link between pigment production and mitochondrial function

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A new research report published in the January 2015 issue of the *FASEB Journal* helps explain what goes wrong to when someone gets skin cancer and the relationship between changing skin pigment and the cancer itself. In particular, this research shows that there is a direct link between changes in mitochondrial function and melanin production in cancerous skin cells. This link may also serve as a viable drug target for the disease.

"This study reports a novel correlation between a protein involved in the bioenergy process within the human skin (i.e., Complex II) and skin pigmentation," said Mark Birch-Machin, Ph.D., a researcher involved in the work from the Department of Dermatological Sciences at the Institute of Cellular Medicine at The Medical School of Newcastle University in Newcastle Upon Tyne, United Kingdom. "This leads to interesting possibilities of Complex II playing a central role in coupling stress sensing and cellular adaptation via ROS signalling and as this study was performed in skin cancer cells may help in the development of anticancer drugs."

Scientists examined three types of melanoma skin cancer cell lines that displayed low, medium, and high pigment levels as standard and analyzed their levels of Reactive Oxygen Species (ROS) or oxidative stress and mitochondrial Complex II (a component of the mitochondrial energy generating protein chain) function in a resting state. They found



that the darker the cells, the higher the Complex II function. They also found that the rate of ROS generation by Complex II in darker cells was higher too. The researchers then triggered the light and medium cells to produce more melanin (a process called hyperpigmentation) by providing them with more L-tyrosine, a building block for melanin production. Both cell types gradually exhibited higher pigment levels, while simultaneously showing increased Complex II function. The amount of melanin present with gradual hyperpigmentation of medium pigment level cells was measured and compared to the amount of ROS produced the mitochondria. Study results demonstrated that immediately after treatment, the ROS level increased approximately 300%, but gradually reduced to a basal level with further hyperpigmentation.

"Melanoma may be preventable by using sunscreen," said Gerald Weissmann, M.D., Editor-in-Chief of the *FASEB Journal*, "but too many people still die of the disease. This research shows a direct relationship between pigment production (as when our skin tans) and the production of Reactive Oxygen Species by mitochondria (and/or the sun). It's not a very attractive relationship since it leads to cancer progression."

More information: Sarah Jayne Boulton and Mark A. Birch-Machin. Impact of hyperpigmentation on superoxide flux and melanoma cell metabolism at mitochondrial complex II. *FASEB J* January 2015 29:346-353; DOI: 10.1096/fj.14-261982

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