Spotlight

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Malignant Melanoma and Neonatal UVB Exposure

Gaffal *et al*.
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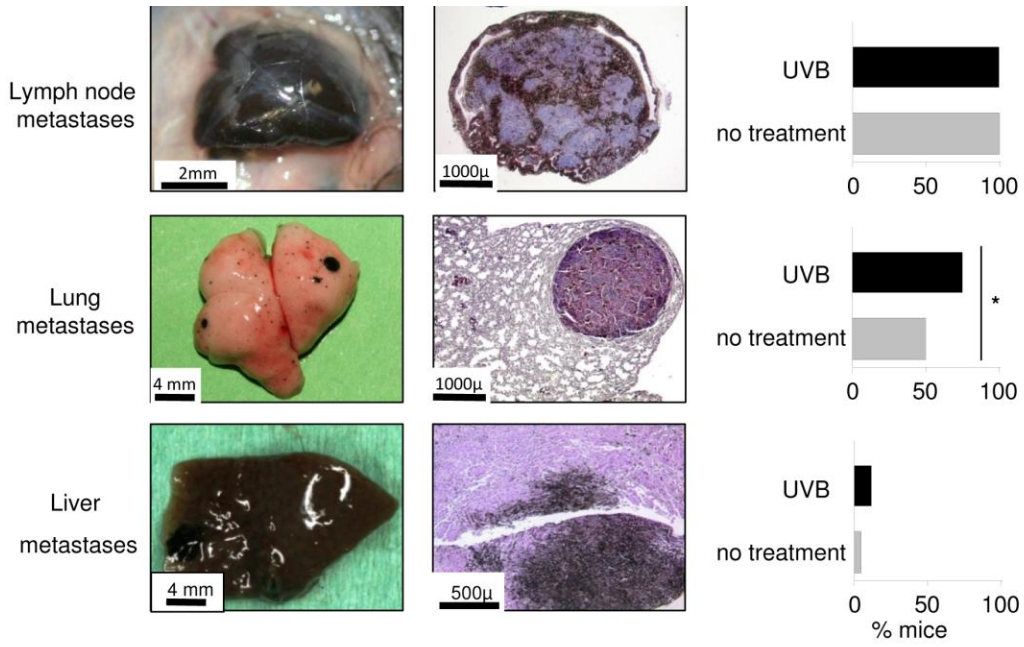
Although malignant melanoma, the most lethal form of skin cancer, is relatively rare, it is increasing in prevalence particularly among individuals with fair skin and blond or red hair living in regions where sunlight is intense. The major environmental risk factor for melanoma is UV radiation exposure, usually from the sun, with the highest risk associated with intermittent burning doses, especially during childhood. But the mechanism through which ultraviolet light leads to melanoma genesis is still largely unknown.

In their study, Gaffal *et al.* took advantage of a recently developed mouse model of melanoma—Hgf-CDK4^{R24C} mice on the pigmented C57BL/6 background, which are prone to developing nevi and melanomas—to start revealing the molecular connections between UV exposure and melanoma pathogenesis. When the authors irradiated a group of 15 newborn Hgf-CDK4^{R24C} mice, they found that UVB exposure equivalent to what would cause sunburn in human skin not only decreased the latency but also promoted melanoma progression without affecting the development of nevi when compared to a control group of untreated Hgf-CDK4^{R24C} mice.

Specifically, UVB irradiation enhanced tumor cell proliferation, invasive growth and angiogenesis, leading to an increase in the number of distant metastases. Naturally occurring human melanomas frequently show prominent immune infiltration; UVB-induced melanomas in the studied mouse model, however, only contained very few infiltrating immune cells and expressed very low levels of proinflammatory chemokines. These findings point to an UVB-induced molecular mechanism that can bypass the proliferative arrest of transformed melanocytes without alerting a cellular immune response.



Impact of neonatal UVB exposure on the development of melanoma metastases. (a) Representative macroscopic appearance of metastases in draining lymph nodes (top), lungs (middle) and liver (bottom) of UVB-treated Hgf-CDK4^{R24C} mice. (b) Corresponding H&E-stained sections at a magnification of 25x (top, middle) or 50x (bottom). (c) Percentage of UVB-treated (n=15) and untreated Hgf-CDK4^{R24C} mice (n=30) with metastases in draining lymph nodes (top), lungs (middle) and liver (bottom).