COX-2 EXPRESSION IN MALIGNANT MELANOMA: LATEST EVIDENCE AND CLINICAL POTENTIAL.

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Inflammation has emerged as a major factor promoting cancer development. In the current literature there is an increasing interest for the role played by cyclooxygenase-1 (COX-1) and cyclooxygenase-1 (COX-2), the key rate-limiting enzymes involved in regulation of PGE2 synthesis. In particular, the COX-2 isoform has been shown to be constitutively expressed in various cancers, predominantly by stromal cells (Wang D and Dubois RN, 2010). In melanoma COX-2 expression has been detected in human specimens and murine models (Cahlin C. et al., 2000, Denkert C. et al., 2001). However, the possible correlation between COX-2 expression and disease progression in melanoma is still a matter of debate. Analysis of COX-2 expression in 45 lymph node melanoma metastases demonstrates a significant correlation between the percent of expression and progression free survival (PFS). A positive COX-2 expression ≥10% (COX-2high), as opposite to a positive expression ≤9% (COX-2low), translated into a striking significant reduction of PFS of about 3 years. The reduction in PFS correlated neither with BRAFV600E nor with NRASQ61 expression in the analyzed samples. This concept was reinforced by the finding that tumour development in COX-2-/- mice was almost blunted. Similarly, inhibition of COX-2 protein expression in human melanoma cell lines, by using siRNAs technology as well as selective inhibition of COX-2 activity by celecoxib, reduced cellular proliferation and invasiveness. In conclusion we show that COX-2high is a negative prognostic factor in metastatic melanoma. Our study also clarifies that the uncertainty about the role of COX-2 in metastatic malignant melanoma, found in the current relevant literature, is probably due to the fact that a threshold in COX-2 expression has to be reached in order to impact on cancer malignancy. Our findings suggest that COX-2 expression may become an useful diagnostic tool in defining melanoma malignancy as well as argue for a possible therapeutic use of NSAID as add on therapy in selected cases.

1. Wang and Dubois. (2010). Nature reviews Cancer. 10, 181-193.

2. Cahlin et al. (2000). Cancer research. 60, 1742-1749.

3. Denkert et al. (2001). Cancer research. 61, 303-308.