SKIN CANCER (OTHER THAN MELANOMA)

ARSENIC LEADS TO AUTOPHAGE OF KERATINOCYTES BY INCREASING AQUAPORIN 3 EXPRESSION: A NOVEL MECHANISM OF ARSENIC-INDUCED CARCINOGENESIS

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Introduction: Exposure to arsenic, a ubiquitous metalloid on Earth, results in human cancers. Skin cancer is the most common arsenical cancers and it usually heralds cancers of lungs and bladders. Pteris vittata, an arsenic hyper-accumulated plant, uses aquaporins as arsenic transporters.

Objective: This study aims to address how arsenic was transported into keratinocytes through aquaporins and how this process would induce autophage.

Materials and Methods: We measured the expression of aquaporin 3, the most common aquaporin in skin keratinocytes, in arsenical skin cancers and arsenic-treated keratinocytes. We also measured arsenic-induced autophage, an important tumor facilitator, in keratinocytes and examined if blocking aquaporin would interfere arsenic-induced autophage. Autophage was detected by beclin-1 expression.

Results: Expression of aquaporin 3 is increased in arsenical cancers and in arsenic-treated keratinocytes. Arsenic induced autophage in primary human keratinocytes. Notably, the arsenic-induced beclin-1 expression could be inhibited by pretreatment of keratinocytes with CuSO4, an aquaporin 3 inhibitor, or RNA interference against aquaporin 3.

Conclusions: The data indicate that aquaporin 3 is an important cell membrane channel to mediate arsenic uptake and it contributes to the arsenic-induced autophage.