# 論 文 要 旨

## The transcription factor Snail expressed in cutaneous squamous cell carcinoma induces epithelial–mesenchymal transition and down-regulates COX-2

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Cutaneous spindle cell squamous cell carcinoma (SCC) is a rare, but highly malignant variant of SCC. The presence of spindle-shaped cells with a sarcomatous appearance, which are derived from squamous cells, suggests that these cells are produced as a result of epithelial–mesenchymal transition (EMT). EMT is a complex process in which epithelial cells lose their polarity and cell–cell contacts, while also acquiring increased motility and invasiveness. Snail regulates EMT by binding to proximal E-boxes in the promoter region of E-cadherin and repressing its transcription. When examining the expression of EMT markers and Snail in spindle cell SCCs, we found that cyclooxygenase-2 (COX-2) expression was down-regulated. Since it has been shown that COX-2 is constitutively overexpressed in a variety of malignancies, including colon, gastric, and lung carcinomas, the down-regulation of COX-2 expression was unexpected. The presence of E-box-like sequences in the promoter region of COX-2 prompted us to perform a more detailed analysis. We introduced a Snail expression vector into keratinocyte-derived cell lines (HaKaT, HSC5, and A431 cells), and isolated stable transfectants. We determined that COX-2 expression was down-regulated in cells expressing Snail. Consistent with these observations, reporter assays revealed that COX-2 promoter activity was repressed upon Snail overexpression. Thus Snail down-regulates COX-2 in these cells.