# Inactivation of the putative suppressor gene DOK1 by promoter hypermethylation in primary human cancers

Saulnier, Amandine

Vaissière, Thomas

Yue, Jiping

Siouda, Maha

Malfroy, Marine

Accardi, Rosita

Creveaux, Marion

Sebastian, Sinto

Shahzad, Naveed

Gheit, Tarik

Hussain, Ishraq

Torrente, Mariela

Maffini, Fausto Antonio

Calabrese, Luca

Chiesa, Fausto

Cuenin, C

The DOK1 gene is a putative tumour suppressor gene located on the human chromosome 2p13 which is frequently rearranged in leukaemia and other human tumours. We previously reported that the DOK1 gene can be mutated and its expression down-regulated in human malignancies. However, the mechanism underlying DOK1 silencing remains largely unknown. We show here that unscheduled silencing of DOK1 expression through aberrant hypermethylation is a frequent event in a variety of human malignancies. DOK1 was found to be silenced in nine head and neck cancer (HNC) cell lines studied and DOK1 CpG hypermethylation correlated with loss of gene expression in these cells. DOK1 expression could be restored via demethylating treatment using

5-aza-2?deoxycytidine. In addition, transduction of cancer cell lines with DOK1 impaired their proliferation, consistent with the critical role of epigenetic silencing of DOK1 in the development and maintenance of malignant cells. We further observed that DOK1 hyperme