



Title	Circulating pigment epithelium-derived factor levels and the risk of hypertension in a community-based study
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Citation	The 16th Medical Resarch Conference (MRC), The University of Hong Kong, Hong Kong, China, 22 January 2011. In Hong Kong Medical Journal, 2011, v. 17, suppl. 1, p. 15, abstract no. 12
Issued Date	2011
URL	http://hdl.handle.net/10722/140444
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Absence of *NPM1* promoter hypermethylation in human myelodysplastic syndrome

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Introduction: *Npm1*^{+/-} heterozygous mice develop a haematological disorder with features resembling human myelodysplastic syndrome (MDS). Promoter hypermethylation of *NPM1* gene may lead to suppressed gene transcription and hence functional haploinsufficiency, which contributes to myelodysplasia. Furthermore, reversal of gene promoter hypermethylation by demethylating agents has been shown to be of therapeutic benefit. Therefore, we hypothesised that epigenetic alterations of *NPM1* might lead to *NPM1* haploinsufficiency, thereby contributing to the development of MDS.

Methods: A comprehensive methylation analysis of *NPM1* was evaluated in 31 MDS patients and eight normal individuals for promoter methylation and mRNA expression of *NPM1*. Methylation-specific polymerase chain reaction (MSP), combined bisulfite restriction analysis technique (COBRA) and bisulfite sequencing were used to examine the *NPM1* methylation status. Quantitative polymerase chain reaction was employed to assess the expression of *NPM1*.

Results: *NPM1* promoter methylation was rare, occurring in one of 31 cases as determined by MSP, but no significant methylation was found using COBRA and bisulfite sequencing. Furthermore, real-time quantitative RT-PCR showed that there was no significant difference in *NPM1* mRNA expression between MDS and normal blood samples. These results revealed that promoter methylation and functional haploinsufficiency of *NPM1* do not contribute to the development of human MDS.

Conclusion: Our findings suggested that *NPM1* methylation was infrequent in MDS and did not play a major role in its pathogenesis.

Circulating pigment epithelium-derived factor levels and the risk of hypertension in a community-based study

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Introduction: Pigment epithelium-derived factor (PEDF), a serine protease inhibitor, is secreted from the adipose tissue and circulates at high concentrations. A recent study found that PEDF played a causal role in obesity-induced insulin resistance and metabolic dysfunctions in mice. Previous cross-sectional studies had demonstrated a positive association of PEDF with increased systolic blood pressure, pulse pressure and lower small artery elasticity. The objective of this study was to determine whether high circulating PEDF levels predicted the development of hypertension in a 10-year prospective study.

Methods: Baseline plasma PEDF levels were measured by ELISA in 520 non-diabetic subjects recruited from the Hong Kong Cardiovascular Risk Factor Prevalence Study. Multiple logistic regression was used to analyse whether PEDF was an independent factor related to hypertension at baseline. The role of PEDF in predicting the development of hypertension over 10 years was analysed using Cox regression analysis.

Results: At baseline, sex-adjusted PEDF levels were significantly higher in subjects with hypertension ($P < 0.001$) and the association remained significant (odds ratio=1.203; 95% confidence interval [CI], 1.065-1.359; $P = 0.003$) after adjustment for covariates. Of the 386 subjects with normal blood pressure at baseline, 132 developed hypertension over 10 years. High baseline PEDF was predictive of hypertension, independent of the effects of age, sex, baseline obesity parameters and blood pressure (hazard ratio=1.135; 95% CI, 1.039-1.241; $P = 0.005$).

Conclusion: Our data suggest that plasma PEDF is significantly associated with both prevalent and incident hypertension, and may be involved in the pathogenesis of hypertension in humans.

Acknowledgement: This study was financially supported by the Health and Health Services Research Fund (06070951) to Annette WK Tso and Research Grant Council Collaborative Research Fund (HKU3/09C) to Karen SL Lam.