

EPIGENETICS

Disturbed imprinting in pre-eclampsia

Abnormal placental development and reduced fetal trophoblast invasion are thought to be involved in the pathogenesis of pre-eclampsia, but the molecular mechanisms are poorly understood. Now, an interdisciplinary team led by Zsuzsanna Izsvák, Ralf Dechend and Laurence Hurst report a causal role of disturbed placental expression of imprinted genes in this disease.

To identify genes that are aberrantly expressed in pre-eclampsia, the researchers analysed placental samples from women with and without the disease. They identified three distinct transcriptome patterns of pre-eclampsia and 150 imprinted or putatively imprinted genes that were dysregulated in at least one of these transcriptome clusters. One of the most significantly dysregulated of these genes was the maternally expressed transcription factor *DLX5*, which has previously been reported to inhibit trophoblast invasion.

DLX5 was strongly upregulated in ~70% of pre-eclampsia samples and its placental expression correlated with the levels of serum biomarkers of pre-eclampsia, including the PlGF:sFLT ratio.

In a trophoblast cell line, overexpression of *DLX5* resulted in reduced proliferation, increased metabolism and activation of the endoplasmic reticulum stress response. “These changes make sense in terms of the aetiology of pre-eclampsia,” says Dechend. The researchers also show that *DLX5* is part of a human-specific gene network that is associated with trophoblast differentiation.

“Our analysis provides what we think is the first solid evidence for an association between disturbed expression of imprinted genes and pre-eclampsia,” concludes Izsvák. “We don’t think that *DLX5* will have utility as a biomarker as its loss of imprinting is not observed in all cases of pre-eclampsia, but unpicking its mechanism may lead to the identification of other indicators that the disease is in its earliest stages, which could be used to identify mothers at high risk.”

Ellen F. Carney

ORIGINAL ARTICLE Zadora, J. et al. Disturbed placental imprinting in preeclampsia leads to altered expression of *DLX5*, a human-specific early trophoblast marker. *Circulation* <http://dx.doi.org/10.1161/CIRCULATIONAHA.117.028110> (2017)

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